Study information

Title	A study assessing the use of GOlimumab in current clinical PRACTICE and its impact on patients with chronic inflammatory rheumatic disease.
Protocol number	MK8259 - 020
Version identifier of the clinical study report (CSR)	Version 1
Date of final version of the clinical study report	
EU Post Authorization Study (PAS) register number	NA
Active substance	Golimumab
Medicinal product	SIMPONI
Product reference	MK8259
Procedure number	NA
Marketing Authorization Holder (MAH)	MSD France 34, avenue Léonard de Vinci 92418 Courbevoie Cedex France
Joint PASS	No
Research question and objectives	This study was designed to comply with a request made by the French Health authorities (HAS) in February 2012, in view of a re-evaluation of Simponi® scheduled in 2018. The authorities requested for additional long-term data in patients with chronic inflammatory rheumatic diseases (CIRDs) in the form of a post-registration study. The primary objective is to assess the persistence of golimumab therapy 24 months after initial prescription in adult patients with CIRDs, in routine clinical practice in France.
Country of study	France

Marketing Authorization Holder(s)	MSD France 34, avenue Léonard de Vinci 92418 Courbevoie Cedex France
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3 ABSTRACT (STAND-ALONE DOCUMENT)

Study rationale

The aim of this study was to provide the French Health Authorities (L'Haute Authorité de Santé – HAS) with long-term post-marketing data, concerning the treatment of patients with chronic inflammatory rheumatic disease with golimumab, in French clinical practice.

Study design

This was an observational, multicenter, prospective, national (France) study with a 2-year follow-up. Adult patients with chronic inflammatory rheumatic (CIR) diseases, namely rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) were consecutively included upon initial golimumab prescription. They were then followed up for two years as per routine clinical practice.

Study objectives

Primary objective: To assess the persistence of golimumab treatment, 24 months after initial prescription in adult patients with CIR disease, in routine clinical practice in France. The primary endpoint was the overall proportion of patients persisting on golimumab therapy 24 months from initial prescription.

Secondary objectives

Secondary objectives include evaluating the following: 1) patient characteristics, 2) the therapeutic strategy of golimumab, its modalities of use (injection dates, injection device and person(s) administering the treatment) and its modalities of prescription (dose, frequency, co-prescriptions, respect of contraindications and reasons for discontinuation), 3) golimumab persistence at 1 year, 4) its safety profile, 5) its impact on disease activity evolution, 6) its impact on patient-reported outcomes (PROs) such as functional disability, health status and quality of life and, 7) healthcare resource utilization.

Main results

Between 15/01/2015 and 29/03/2016, 770 patients were enrolled in the study. Of these, 754 patients were included in the final analysis.

Main baseline demographics and clinical characteristics

The mean age was 46.1 years and the majority were females (60.6%). Most patients were of normal weight (BMI 18.5 – 24.9, 43.5%), 32.7% were overweight (BMI 25.0 – 29.9) and 19.9% were obese (BMI ≥ 30). Most patients (58.7%) were full-time or part-time employees, 14.6% were retired and 10.3% were declared as unable to work.

Most patients (85.3%) presented with at least 1 comorbidity in addition to the chronic rheumatic illness. Over a third of the study cohort (37.4%) were severely ill, presenting at least 3 co-morbidities, and about a half had undergone a surgical procedure in the past (51.2%).

Patients with 3 types of chronic rheumatic illnesses were included: 478 (63.5%) patients with ankylosing spondylitis (AS), 170 (22.4%) with rheumatoid arthritis (RA) and 106 (14.1%) suffering from psoriatic arthritis (PsA). The mean duration since diagnosis was 7.59 years in the overall population.

Disease activity at baseline

- For rheumatoid arthritis (RA) patients, the mean duration since RA diagnosis was 8.63 years (calculated from 165 patients with available data). Rheumatoid factors and anti-cyclic citrullinated peptide (CCP) antibodies were present in the majority of patients: 72.2% and 67.7%, respectively. Mean serum CRP levels were 11.6 mg/l, and the mean DAS28-CRP score was 4.34. For whom data was available, most patients presented with a moderate to high disease activity score at baseline: 63.8% moderate (3.2 < DAS28-CRP ≤ 5.1) and 21.9% high (DAS28-CRP > 5.1). The remaining 14.4% of patients had low disease activity (DAS28-CRP ≤ 3.2). In addition to elevated DAS-CRP scores, other factors indicating considerable disease severity in RA patients at baseline were that about 1 in 2 patients (55.6%) presented with bone erosion and 12.4% with extra-articular manifestations.

- For psoriatic arthritis (PsA) patients, the mean duration since diagnosis was 6.06 years (calculated from 99 patients with available data). Almost all patients did not present with rheumatoid factors at baseline (92.0%). The mean CRP level was 8.52 mg/l and the mean DAS28-CRP score was 3.89. For whom data was available, most patients had a moderate-to-high disease activity at baseline: 66.0% moderate and 11.3% high, and 22.7% had low disease activity. The majority presented with cutaneous psoriasis at baseline (83.0%). Disease severity appeared to be comparatively lower in this sub-population at inclusion (compared to RA): 23.6% of PsA patients presented with bone erosion, 29.2% with joint space narrowing. And 5.94% with extra-articular manifestations.
- In Ankylosing spondylitis (AS) patients, the mean duration since diagnosis was 7.55 years. The majority (66.5%) were positive for the HLA-B27 antigen at baseline. The mean CRP level was 11.4 mg/l. Mean ASDAS-CRP score was 3.16. Disease activity was high in almost all AS patients for whom data was available at baseline (91.9%), and moderate in only 7.83% of cases. Thus, baseline disease severity was observed to be the highest in this sub-population. Extra-articular manifestations were reported in 27% (n=129) of AS patients – a higher proportion than in the RA and PsA groups – of which 85 (65.9%) manifested acute anterior uveitis and 33 (25.6%) had inflammatory bowel disease (IBD).
For AS patients, available data could not allow for the distinction between the non-radiographic and radiographic stage of axial AS.

Prior treatments

A total of 282 patients (37.5%) had received at least one biotherapy prior to golimumab initiation, of which 135 (47.9%), 84 (29.8%) and 63 patients (22.3%) had received one, two and three or more lines of biotherapy, respectively. As per disease group, 34.9%, 34.0% and 39.1% of RA, PsA and AS patients were biotherapy pretreated. Analgesics were commonly prescribed in the study cohort (85.3%), and in each disease group it was prescribed to 71.2% of RA, 86.8% of PsA and 90.0% of AS patients (p < .001). Disease-modifying anti-rheumatic drugs (DMARDs) were previously used by 53.4% of the study patients; a large majority of RA and PsA patients were previously treated with DMARDs (91.8% and 79.2%, respectively), whereas only a third of AS patients had ever received DMARDs (34.1%, p < .001). Prior corticosteroid use was moderate in the total cohort (29.7%), but highly variable among the sub-groups: 63.5% of RA, 34.9% of PsA and 16.5% of AS patients (p < .001). Prior surgery was carried out in 27.9% of study patients, with almost twice the proportion of RA and PsA patients (38.8% and 39.6%) having a history of surgical intervention, compared to AS patients (21.3%, p < .001).

Golimumab prescription and concomitant treatments

In most cases, initial golimumab prescription in the cohort (n = 754) was in line with the instructions for use (IFU) and standard recommendations, in terms of dosage (50 mg per dose) and frequency (one injection a month). Only 13 patients (1.72%) were prescribed a dose of 100 mg and 5 patients (0.66%) were prescribed injections 1.25 times a month at baseline.

Golimumab was prescribed in combination with other treatments for most patients at inclusion; 84.1% for the total cohort and 97.6%, 85.8% and 78.9% for RA, PsA and AS patients, respectively. in those who received concomitant treatment(s) (n=633), DMARDs were co-prescribed to 45.0% of study patients and to 86.7%, 65.9% and 21.8% of patients with RA, PsA and AS, correspondingly. Co-prescriptions for analgesics were made to 84.2% of the study cohort who received co-treatments, and to 62.4%, 85.7% and 93.4% of RA, PsA and AS patients, respectively. Corticosteroids were co-prescribed to 22.9% of the study cohort, to 54.5% of RA, 29.7% of PsA and only 7.43% of AS patients.

Persistence of golimumab treatment at 2-years

At the time of the database lock in August 2018, 754 CRFs were received at inclusion and 391 CRFs were received after 2 years of follow-up. At 2-years, 340 patients discontinued the treatment, 362 patients persisted on golimumab therapy and 52 patients were lost to follow-up. In total, the golimumab persistence status (Yes or No) was known for 702 patients at 2-years.

In the base case, golimumab persistence 2 years after its initial prescription was assessed for patients with available data on persistence using descriptive statistics. A sensitivity analysis was performed using two assumptions for patients lost to follow-up (n = 52), i.e; the “best case” and the “worst case”.

- Best case: all patients lost to follow-up at 2 years and with missing data are still continuing golimumab therapy at year 2
- Worst case: all patients lost to follow-up at 2 years and with missing data have definitively discontinued golimumab.

The base case results indicate that golimumab persistence at 2 years was 51.6% (362/702) in the overall population with increased sensitivity ranges of 48.0% (362/754) for the worst-case and 54.9% (414/754) for the best-case scenario.

4 LIST OF ABBREVIATIONS

ACR	American College of Rheumatology
ADA	Adalimumab
AE	Adverse Event
AS	Ankylosing Spondylitis
ASAS	Assessments in Ankylosing Spondylitis International Society
ASDAS	Ankylosing Spondylitis Disease Activity Score
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BT-n	Biotherapy naïve
BT-p	Biotherapy pretreated
CCP antibodies	Anti-Cyclic Citrullinated Peptide Antibodies
CIRD	Chronic Inflammatory Rheumatic Disease.
CRF	Case Report Form
CRO	Contract Research Organization
CRP	C-Reactive Protein
CRPV	Centre Regional de Pharmacovigilance
CT	Computerized Tomography
DAS28	Disease Activity Index Score 28
DIP	Distal Interphalangeal
DMARD	Disease-Modifying Anti-Rheumatic Drug
EQ-5D	European Quality of Life-5 Dimensions
ESR	Erythrocyte Sedimentation Rate
ETA	Etanercept
GLM	Golimumab
HAS	“Haute Autorité de Santé” – French Healthcare Authorities
HAQ	Health Assessment Questionnaire
I1, I2, I3…	Day of the 1st, 2nd, 3rd… golimumab injection
IBD	Inflammatory Bowel Disease
IFU	Instructions for Use
IFX	Infliximab
IgG1κ	Human Immunoglobulin G1κ
IL-6	Interleukin-6
LDA	Low disease activity
ln	Natural Logarithm
MCP	MetaCarpo-Phalangeal (joint)
MRI	Magnetic Resonance Imaging
MTX	Methotrexate
NRS	Numerical Rating Scale
NSAEs	Non-Serious Adverse Events
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
GA	Global Assessment

PASI	Psoriasis Area Severity Index
PGIC	Patient Global Impression of Change
PIP	Proximal Inter-Phalangeal (joint)
PsA	Psoriatic Arthritis
QoL	Quality of Life
RA	Rheumatoid Arthritis
RAPID3	Routine Assessment Of Patient Index Data 3
RF	Rheumatoid Factor
SC	Subcutaneous
SJC28	28-Joint Count for Swelling
SmPC	Summary of Product Characteristics
SQRT	Square Root
TJC28	28-Joint Count for Tenderness
TNFα	Tumor Necrosis Factor Alpha
VAS	Visual Analogue Scale
WPAI	Work Productivity and Activity Impairment

5 SCIENTIFIC COMMITTEE

Name, degree(s)	Title	Affiliation	Date	Signature
PPD				

6 SPONSOR REPRÉSENTATIVES

Name	Role at MSD	Date	Signature
PPD			

7 OTHER RESPONSIBLE PARTIES

Responsible party name and affiliation	Role in the study
ClinSearch	Contract Research Organization (CRO)
ClinSearch	Statistical analysis

8 MILESTONES

Milestone	Planned date	Actual date	Comments
Approval from the regulatory authorities (Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé, CCTIRS)	February-August 2014	June 12, 2014	Cf. Appendix
Approval from Commission nationale de l'Informatique et des Libertés (CNIL)	February-August 2014	December 18, 2014	Cf. Appendix
Start of data collection	September 2014- September 2015	January 16 2015	
End of data collection	January 2018	July 2018	
Interim report I	September 2016	January 19 2017	
Final report of study results	May 2018	July 08 2019	

9 RATIONAL AND BACKGROUND

9.1 Background

9.1.1 Chronic Inflammatory Rheumatic Diseases

Rheumatoid arthritis (RA)

RA is an autoimmune disease that causes chronic inflammation of the joints resulting in joint destruction and functional disability. It is known to affect approximately 1% of the population [1, 2], and mainly women in their 40s or 50s. The French Health authorities estimated the number of adult patients with severe, progressive RA in France to be around 200,000 in 2011. It is responsible for a marked decrease in quality of life (QoL), with important psychological consequences. The existing European regulatory guidelines state that the aims of anti-rheumatic therapy should be to relieve pain, to decrease inflammatory synovitis, to improve or sustain physical function and to prevent structural damage of the joints [3]. The utility of targeted biological agents, such as inhibitors and antagonists of tumor necrosis factor alpha (TNFα) and interleukin-6 (IL-6) receptors, have been established during the previous decade [4]. However, a medical need for improved therapeutic options still persists, given that even these therapies may undergo failure in many RA patients [5]. In terms of Public Health, the burden of RA is significant [2, 6]. Economic consequences are considerable and include consumption of care and medical goods as well as loss of working days [7].

Psoriatic arthritis (PsA)

PsA is a chronic, inflammatory arthritis associated with psoriasis. The prevalence of psoriasis in the general Caucasian population is approximately 2% [8]; approximately 6% to 42% of psoriasis patients develop PsA [9]. Based on a PsA prevalence of 0.19% in 2001, the French Health authorities estimated that the number of adult patients with PsA in 2012 was 97,000 in France [10]. Affecting men and women equally, PsA typically manifests between the ages of 30 and 50 years. PsA leads to joint destruction and disability, but can also cause inflammation in tissues other than the joints and the skin, such as in the eyes, heart, lungs and kidneys. It can be distinguished from RA by factors such as the manifestation of psoriasis, sero-negativity for rheumatoid factor (RF) (observed in >80% of patients), joint damage involving asymmetry, distal interphalangeal disease, and spinal disease. PsA and RA are, nevertheless, closely related diseases with similar approved therapies [11]. The burden of PsA is comparatively moderate. Improvements in the early diagnosis of PsA, in the management of PsA patients and their QoL is an important public health need and has been claimed as a priority in France.

Ankylosing spondylitis (AS)

AS is a chronic inflammatory disease of unknown etiology that involves the sacroiliac joints, axial skeleton, entheses, and peripheral joints. Its estimated prevalence is between 0.1% and 1.1% of the population, and it chiefly affects men before their 40s. Chronic AS leads to new bone formation and ankylosis of joints, resulting in disability. The disease may also present with non-skeletal manifestations, including uveitis, carditis, pulmonary fibrosis, and cardiac conduction abnormalities. AS is classed as a type of spondyloarthropathy and is associated with the presence of the HLA-B27 allele [12]. Although patients may experience a variety of musculoskeletal symptoms, the most common symptom is lower-back pain. Treatment of AS involves a combination of physical therapy and medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), systemic or intra-articular corticosteroids, sulfasalzine and methotrexate (MTX). More recently, anti-TNFα therapies have demonstrated efficacy against active AS disease, and were incorporated into the therapeutic strategy for moderate to severe AS patients, who have had inadequate response to conventional therapy [13]. The burden of AS is moderate. Economic consequences are, nonetheless, considerable [14] and include consumption of care and medical goods

as well as loss of working days. Similar to PsA, improvements in earlier diagnosis and management of AS patients, and their QoL, is a Public Health need of a high priority in France [15, 16].

9.1.2 Golimumab (Simponi®)

Golimumab, the active substance of Simponi®, is a novel human anti-TNFα monoclonal antibody indicated for the treatment of RA, PsA and AS [17]. It is a human immunoglobulin G1κ (IgG1κ) monoclonal antibody, that binds with high affinity and specificity to both, soluble and transmembrane forms of TNFα, thereby neutralizing its biological activity. Golimumab is produced via recombinant DNA technology, in a murine hybridoma cell line.

Efficacy

The efficacy of golimumab in the treatment of RA, PsA and AS was demonstrated in five multicenter, randomized, double-blind, placebo-controlled studies. The primary endpoints were based on the percentages of patients achieving 20% or 50% reductions in the number and severity of symptoms (ACR20/50 response and ASAS20 response) after 14 or 24 weeks of golimumab treatment. The following results refer to primary endpoints that were achieved at the approved dose of 50 mg once a month.

Efficacy in the treatment of RA

For RA, golimumab was compared with placebo in three studies involving a total of 1,542 patients with moderate to severe RA, including patients who had not received or responded adequately to other treatments.

• In the GO-FORWARD study [18], which included RA patients who were non-responders to MTX, patients were randomized in a 2:3 ratio to receive golimumab 50 mg injections and oral MTX (n = 89) or placebo injections plus oral MTX (n = 133). At 14 weeks, 55% of RA patients in the golimumab arm achieved an ACR20 response compared to 33% in the placebo arm (p = 0.001). Furthermore, at 24 weeks, those who received golimumab experienced significantly greater improvements in performing daily tasks (Health Assessment Questionnaire, HAQ).

• The GO-AFTER study [19] included patients previously treated with anti-TNF therapy. At 14 weeks, 35% of patients who received golimumab alone (54 of 153) achieved an ACR20 response, versus 18% of patients who received placebo (28 of 155; p<0.001).

• The GO-BEFORE study [20] was performed in MTX-naïve patients. At 24 weeks, 40% (64 of 159) of patients treated with golimumab and MTX achieved an ACR50 response, compared to 29% (47 of 160) of patients on placebo and MTX (p=0.053). Data from X-rays assessed before and after one year of treatment showed less joint damage in patients receiving golimumab than in those receiving placebos.

Efficacy in the treatment of PsA

Golimumab was compared against placebo over 24 weeks in the GO-REVEAL [21] study, which involved 405 PsA patients who did not respond adequately to NSAIDs or disease-modifying anti-rheumatic drugs (DMARDs). After 14 weeks of treatment, 51% of patients receiving golimumab (74 of 146) achieved an ACR20 response compared to 9% of patients taking placebo (10 of 113; $p < .001$). Mean change in the SF-36 PCS score at 14 weeks from baseline was also significantly improved for patients treated with golimumab (6.53 ± 8.88) than with placebo (0.63 ± 7.68, p < .001).

Furthermore, at week 24, golimumab-treated participants had significant improvements in HAQ scores compared to those on placebo (mean change from baseline of 0.33 ± 0.55 versus -0.01 ± 0.49, respectively; p < .001). Among those in whom ≥ 3% of the body surface area was affected by psoriasis

at baseline, 40% in the golimumab arm had ≥ 75% improvement of the Psoriasis Area Severity Index (PASI), versus 3% of placebo-treated patients (p < .001).

Efficacy in the treatment of AS

In the GO-RAISE study [22], golimumab efficacy was compared with placebo over 104 weeks in a study involving 356 patients who did not respond adequately to NSAIDs or DMARDs.

After 14 weeks, 59% of golimumab-treated patients (82 of 138) achieved an ASAS20 response (the primary efficacy endpoint) compared to 22% in the placebo arm (17 of 78); p<0.001.

Safety

The most common side effects with golimumab are upper respiratory tract infections, such as those of the nose, throat, or larynx. The most serious side effects include serious infections (including sepsis, pneumonia, tuberculosis and fungal or yeast infections), demyelinating disorders, lymphoma, hepatitis B reactivation, congestive heart failure, lupus-like syndrome, and hematological reactions.

Like most other anti-TNFα therapies, golimumab must not be used in patients with tuberculosis, severe infections, or moderate or severe heart failure. Due to an increased risk of infection, patients taking golimumab must be monitored closely for infections, including tuberculosis.

Approved therapeutic indications

The initial golimumab (Simponi®) marketing authorization was granted for the EU in 2009. Currently, the approved therapeutic indications in the EU (including France) are as follows:

1) Golimumab, in combination with MTX, is indicated for:

- the treatment of moderate to severe active RA in adults who have demonstrated inadequate response to DMARDs, including MTX.
- the treatment of severe, active and progressive RA in adults not previously treated with MTX.

Golimumab, in combination with MTX, has been shown to improve physical function and to reduce the progression rate of joint damage, as measured by X-ray.

2) Golimumab, alone or in combination with MTX, is indicated for the treatment of active and progressive PsA in adult patients, who have had an inadequate response to DMARDs. Golimumab has been shown to improve physical function and to reduce the progression rate of peripheral joint damage in patients with polyarticular symmetrical subtypes of the disease (as measured by X-ray). Golimumab is not reimbursed in this indication when it is prescribed alone.

3) Golimumab is indicated for the treatment of severe, active AS in adults who have responded inadequately to conventional therapy.

For the three indications, golimumab is to be administered once a month, at the same date, as a 50 mg subcutaneous (SC) injection. These are described in the Summary of Product Characteristics (SmPC) for the drug product

9.2 Rationale

The GO-PRACTICE study was designed to comply with a request made by the French Health Authorities (HAS) in February 2012, in view of a reevaluation of Simponi®, scheduled for 2018. The authorities requested for additional long-term data, particularly in French patients with chronic inflammatory rheumatic diseases, in the form of a post-registration study with the following objectives:

- To describe the prescription patterns of golimumab (dosage quantities and regimens, co-prescription with MTX and other treatments), the modalities of golimumab administration and the characteristics of treated patients (such as socio-demographic data, history and severity of the disease, disability and invalidity, other medical history and co-morbidities)
- To evaluate the impact of treatment on the concerned population's health in terms of morbidity and mortality (in particular, progression of disease and disability, patients' QoL, development of treatment resistance, long-term adverse events, etc.)
- To describe the therapeutic strategy of golimumab (unresponsiveness to previous treatments including MTX and/or other anti-TNFα therapies, with reasons for discontinuation and/or a switch to other biotherapies, etc.)
- To assess healthcare resource utilization.

Therefore, the present non-interventional, prospective, national (France) study has been designed. The aim of this study was to describe the use of golimumab in routine clinical practice and its impact on treated patients. Consecutive adult patients with chronic inflammatory rheumatic diseases (CIRDs) were included at the time of initial golimumab prescription, and followed up for two years as per routine practice.

An independent study-specific Scientific Committee was set up, which included five rheumatologists, including a methodologist. The present study protocol was designed, reviewed and approved by the Scientific Committee.

This is the first time that the persistence of golimumab is studied in a real-life setting. As in all chronic disorders, long-term treatment persistence is a crucial issue in the management of CIRDs. Increasing the understanding of reasons underpinning golimumab discontinuation, including switches to other treatments, could improve the treatment management of patients in routine practice.

Following the submission of the GO-PRACTICE study protocol to the HAS, the latter recommended an auxiliary study to endorse the validity of the collected data in Go-Practice, particularly regarding information on the management of CIRDs and the extent of golimumab persistence at 24 months. To perform this auxiliary study, HAS suggested the use of the SNIIR-AM database. Accordingly, MSD France implemented the RIC-SNIIR-AM study and analyses were performed by the PELyon.

10 RESEARCH QUESTIONS AND OBJECTIVES

10.1 Primary Objective

The primary objective of this study was to assess the persistence of golimumab treatment in adult patients with chronic inflammatory rheumatic disease 24 months after initial prescription, in French clinical practice.

The primary endpoint was the overall proportion of patients continuing golimumab treatment 24 months after initial prescription.

10.2 Secondary Objectives

The secondary objectives were as follows:

(1) To describe the therapeutic strategy of golimumab, including prior treatments, prescription patterns of golimumab in routine clinical practice (with regards to dose, regimen and co-prescriptions), respect of contraindications and reasons for golimumab withdrawal.

(2) To describe the treated patients (socio-demographics, history and seriousness of the disease, handicap and invalidity, medical history and comorbidities)

(3) To assess golimumab persistence at 1 year

(4) To assess the safety profile of golimumab in terms of adverse events (AE).

(5) To describe the use of golimumab, including the dates and frequency of injections, the injection device, and who administered the treatment.

(6) To assess the consumption of healthcare resources in terms of direct costs such as hospitalization, physician visits, lab tests, imaging, and indirect costs such as sick leaves and productivity loss.

(7) To assess the evolution of disease activity and pain over time. Disease activity was assessed using a disease-specific questionnaire, and pain was evaluated via the visual analogue scale (VAS) for pain.

(8) To assess the evolution of functional disability using the Health Assessment Questionnaire (HAQ).

(9) To assess the evolution of patient reported health status using the EQ-5D questionnaire, and patient-reported quality of life using the SF-12 questionnaire.

11 AMENDMENTS AND UPDATES

There were no protocol amendments or updates.

12 RESEARCH METHODS

12.1 Study design

This is a non-interventional, multicenter, prospective, national (France) study with a 2-year follow-up. Consecutive adult patients with chronic inflammatory rheumatic diseases (CIRDs) were included at the time of initial golimumab prescription and followed up for two years as per routine clinical practice.

The primary endpoint was the proportion of patients continuing golimumab treatment 2 years after initial prescription. As mentioned above in section 9.2, persistence to treatment is a crucial issue in the management of CIRDs. This endpoint was chosen as it was suitable for all the approved indications of golimumab.

The study was planned to be conducted over 2 years, the duration of which was decided by the Scientific Committee to fulfill the request made by the HAS (section 9.2).

This report describes the final results from the analysis of CIRD patients enrolled in the GO-PRACTICE study, at the end of the 2-year follow-up period.

An interim analysis was carried out on patients for whom data at 1-year of follow-up was available at 2nd September 2016 (n = 255), which is detailed in the GO-PRACTICE Interim Analysis Report dated 19 January 2017.

12.2 Settings

Initial prescriptions and yearly renewals of anti-TNFα medications in France are to be carried out in a hospital setting. The physicians who participated in this study were, thus, hospital rheumatologists and/or rheumatologists in private clinics.

A representative sample of 145 rheumatologists was randomly constructed from a list of 1422 rheumatologists practicing in public and private hospitals (data from CEGEDIM, Boulogne-Billancourt, France; 01-Mar-2013). To assess the representativeness of rheumatologists in this study, a registry was created to collect demographics, geographic information, and the practice setting (public/private/both) for each of them.

As for any non-interventional study, no study-specific visits were requested by the protocol, no additional tests or medical procedures were performed as a part of this study, and any non-available data has been reported as missing.

Physician reported outcomes

Yearly follow-ups were performed in the hospital as per the routine practice in France. Rheumatologists collected data at the time of initial golimumab prescription, just before treatment initiation (baseline), and then at year 1 and year 2 visits for prescription renewal. Rheumatologists also collected data during additional unprogrammed visits (in the hospital or in his/her private practice), and in case of definitive golimumab discontinuation.

During each follow-up visit, rheumatologists completed a brief questionnaire, capturing information such as date and reason of the visit, prescription data (of golimumab and concomitant treatments), C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR) data, disease activity score and the occurrence of any serious adverse events (SAEs) since the previous visit.

Patient-reported outcomes (PROs)

Follow-up data were also recorded by the patients themselves, in a patient diary.

Patients were required to record data just prior to golimumab initiation (baseline), then approximately monthly at the time of injection, throughout the 2-year follow-up period (injections I1 to I25). The patient diary consisted of questionnaires related to treatment administration modalities, disease activity, pain evaluation, HAQ, health status, QoL, and healthcare resource utilization. In case of an intermediate or unplanned visit in a private practice, the patient was required to request the consulting rheumatologist to complete a brief, dedicated questionnaire. In case of treatment discontinuation, the patient was referred to his/her hospital rheumatologist, as per routine medical practice and he/she also had to complete the same questionnaires as for the monthly PROs.

12.3 Study Population

Adult patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) were recruited successively upon initial golimumab prescription, as per routine clinical practice. The patients were treated as per each center's standard practice. The decision to treat was at the physician's discretion, and had to be made prior to the patient's inclusion in the study.

The study centers maintained a registry of all patients who were screened, but not included in the study, to assess the representativeness of patients at the end of the study. All patients who met the selection criteria and had received a golimumab prescription were also listed in this registry. Socio-demographics, indication and the reason for non-inclusion were collected.

750 patients were planned to be included in this study by 150 rheumatologists distributed throughout France. The planned duration of patient recruitment was 1 year. Together with the 2-year follow-up period, the duration of the study was planned to be a total of 3 years.

12.3.1 Inclusion Criteria

1. Patients aged 18 years or older.
2. Patients having given their verbal consent to participate in the study, after having received verbal and written information about the study.
3. Patients diagnosed with a chronic rheumatic inflammatory disease.
4. Patient with an initial hospital prescription for golimumab but who did not yet initiate golimumab treatment.
5. Patients capable of understanding and completing the PRO questionnaires.

12.3.2 Exclusion Criteria

1. Patients who were previously treated with golimumab and/or stopped golimumab before inclusion
2. Patients who had participated in previous studies of golimumab.
3. Patients who had already started golimumab treatment prior to the inclusion visit and/or who were receiving golimumab at the time of the inclusion visit.
4. Conditions or situations that, in the opinion of the investigator, limited the patient's ability to fully participate in the study or to fulfill study requirements,

12.4 Variables

12.4.1 Socio-Demographic Data

After having informed the patient about the study, obtaining his/her verbal consent to participate, and upon fulfillment of the selection criteria, the following baseline data for the patient were recorded by the rheumatologist upon inclusion: 1) Date of birth, 2) Gender, 3) Weight and height, 4) Occupational status.

12.4.2 History and Baseline Characteristics of the Studied Disease

The following data were recorded by the rheumatologist at baseline.

1. Diagnosis and date of diagnosis
2. Date of the first signs and symptoms of the CIRD
3. CRP and/or ESR values: date and value of the most recent test(s)
4. Disease-specific characteristics:
   a) **For RA:**
      i. Rheumatoid factors
      ii. Anti-cyclic citrullinated peptide (CCP) antibodies
      iii. Extra-articular manifestations
      iv. Radiological data
      v. DAS28 questionnaire and the physician's global assessment (GA) of disease activity
   b) For PsA:
      i. Rheumatoid factors
      ii. Dermatological, articular and extra-articular manifestations
      iii. Radiological data
      iv. DAS28 questionnaire and the physician's GA of disease activity
   c) For AS:
      i. HLA-B27 genotyping
      ii. Articular and extra-articular manifestations
      iii. Radiological data
      iv. The ASDAS questionnaire.

The **Disease Activity Index Score 28 (DAS28)** is a validated instrument [23, 24] and is used routinely in rheumatology. It is an index combining the number of tender and swollen joints (among 28 joints), CRP or ESR, and the patient's GA of disease activity. The DAS28 ranges from 0 to 10, indicating the severity of the existing disease's activity. A DAS28 ≤3.2 implies low disease activity, 3.2< DAS28 ≤ 5.1 moderate disease activity, and DAS28 > 5.1 high disease activity. A DAS28 below 2.6 implies remission [34]. A reduction in DAS28 by ≥1.2 points is considered to be a significant improvement [33].

The DAS28 is a continuous parameter, which can be defined as follows:

$$DAS28(CRP) = 0.56 \times \sqrt{TJC28} + 0.28 \times \sqrt{SJC28} + 0.36 \times \ln(CRP + 1) + 0.014 \times PGA + 0.96$$

OR

$$DAS28(ESR) = 0.56 \times \sqrt{TJC28} + 0.28 \times \sqrt{SJC28} + 0.70 \times \ln(ESR) + 0.014 \times PGA,$$

Where, **TJC28** is the tender joint count out of 28 joints, **SJC28** is the swollen joint count out of 28 joints; **ln** is the natural logarithm and **PGA** is the patient global assessment of disease activity on a 100-mm

visual analogic scale (VAS) ranging from 0 to 100, where 0 = non-active disease and 100 = extremely active disease [25].

The set of 28 joint counts is based on the shoulder, elbow, wrist, the 5 metacarpophalangeal (MCP) joints, the 5 proximal interphalangeal (PIP) joints of the upper right and left extremities, as well as the knee joints of the lower right and left extremities.

The **Ankylosing spondylitis Disease Activity Score (ASDAS)** [26] measures disease activity using an algorithm that includes an assessment of back pain, morning stiffness duration, joint pain/swelling, patient global disease activity assessment, and CRP. Back pain, morning stiffness duration, and peripheral pain and swelling are recorded via questions 2, 3 and 6. The global score ranges from 0 to 10. ASDAS < 1.3 indicates inactive disease, between 1.3 and 2.1 it implies moderate disease activity, between 2.1 and 3.5 it indicates high disease activity and ASDAS >3.5 implies very high disease activity [27]. A change ≥1.1 units is considered as a "clinically important improvement" and a change ≥2.0 units is considered a "major improvement" [27].

12.4.3 Previous Treatments for the Studied Disease

The following data were recorded by the rheumatologist at baseline.

- Treatment class(es) (biotherapies, DMARDs, systemic/local corticosteroids, NSAIDs) and treatment name(s)
- For each treatment: start date, stop date (and reason for discontinuation) or ongoing at inclusion.

12.4.4 Healthcare resource utilization related to the Studied Disease

The following data were recorded by the rheumatologist at baseline and by the patient at each injection day, and upon golimumab discontinuation (if applicable). The recall period was 3 months at baseline and one month during follow-up.

- Hospitalizations (≥24h and <24h): number, duration and reason for hospitalization
- Physician office visits: number of visits and physician specialty
- Laboratory tests: number of times blood samples were collected
- Imaging: number of X-ray/MRI/CT-scan examinations
- Physical therapy: number of sessions
- Sick leaves: number of days
- Loss of work productivity loss, using the WPAI questionnaire

The **Work Productivity and Activity Impairment (WPAI)** questionnaire is a validated questionnaire [28]. A French version is provided by the developer (http://www.reillyassociates.net/Index.html). The WPAI yields four types of scores: absence from work (work time lost due to illness), impairment at work (reduced on-the-job effectiveness), work productivity loss (overall work impairment, including total absence from work and impairment at work), and daily activity impairment. The sum of impairment related to a specific disease and impairment due to other health problems is equal to impairment due to all health problems. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

12.4.5 Medical History Other than the Studied Disease and Comorbidities

The following data were recorded by the rheumatologist at baseline.

- Diagnosis and whether the disorder is currently active

12.4.6 Prescription of Golimumab and other Treatments

The following data were recorded by the rheumatologist at each visit.

- Golimumab: dose and regimen
- In case of golimumab dosage modification since the previous prescription: reason for modification
- In case of permanent golimumab discontinuation: reasons for discontinuation, including non-response, secondary resistance and intolerance
- Concomitant treatments: prescription or dosage modifications of MTX, other DMARDs, corticosteroids (systemic/local), and/or NSAIDs:

12.4.7 Golimumab administration

The following data were recorded by the patient during each monthly administration of golimumab, from I1 to I25 (injection 1 to 25).

- Actual injection date and dose
- If applicable, reason for deviating from the planned injection date
- Injecting device: pen, syringe
- Person who administered the injection
- Administration satisfaction, measured using a 5-point Likert scale ranging from "Not satisfied at all" to "Extremely satisfied"

12.4.8 Health status

Recorded by the patient at baseline, every 3 injections, and upon golimumab discontinuation.

The **European Quality of Life-5 Dimensions (EQ-5D)** measurement tool is validated [29] and widely used in economic studies and assessments by health services. The EQ-5D-5L questionnaire was chosen for this study as it is more precise than the -3L version. A French version is provided by the EuroQol Group (http://www.euroqol.org/). The questionnaire comprises of 5 questions assessing 5 dimensions of well-being: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. The EQ-5D score ranges from 0 (death) to 1 (perfect health). Since some health statuses, such as those characterized by incapacity and severe pain, are considered to be worse than death, these are attributed negative values.

In the interest of keeping the patient diary of as reasonable a size as possible, the Scientific Committee estimated that recording this data every 3 months would be sufficient.

12.4.9 Functional Disability

Recorded by the patient at baseline, every 3 injections, and at golimumab discontinuation.

The **Health Assessment Questionnaire (HAQ)** disability index is used in routine medical practice in rheumatology. It is a 20-question instrument which assesses the degree of difficulty the subject had in accomplishing tasks in 8 functional areas over the previous week: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and daily chores) [30]. A validated French version is also available [31]. Responses in each functional area are scored from 0 (no difficulty) to 3 (inability to perform that

task). The highest score recorded for any question in a category is the score for that category, unless aids, devices, or help from another person was required. Dependence on aids, devices or help from others implies a minimum category score of 2 (i.e. maximum category scores of 0 or 1 are increased to 2). If a question is left blank, the category is scored based on responses to the other question or questions. The HAQ score is calculated as the sum of the category scores divided by the number of categories scored, giving a possible range of scores from 0 to 3. The disability index cannot be calculated if the subject has scores for fewer than 6 categories.

In the interest of keeping the patient diary of as reasonable a size as possible, the Scientific Committee estimated that recording this data every 3 months would be sufficient.

12.4.10 Pain Related to the Studied Disease

Recorded by the patient on injection days and at golimumab discontinuation.

• Severity of pain in the morning (on the day of injection), using a **visual analog scale (VAS)**.

The VAS ranges from 0 (best score) to 10 (worse score). It is widely used in routine practice in rheumatology.

12.4.11 Patient Global Impression of Change (PGIC)

This was completed by the patient on each injection day (except I1 at baseline) and at golimumab discontinuation.

The PGIC scale [32] estimates the degree of change, since treatment initiation, in activity limitations, symptoms, emotions, and overall QoL related to a painful condition. It uses a 7-point numerical scale ranging from 1 (no change) to 7 (a great deal better).

12.4.12 Progression of the Studied Disease

- **By the physician**

The following were recorded by the rheumatologist at each yearly follow-up visit (at a hospital or private clinic) and upon golimumab discontinuation.

• CRP and/or ESR: date and value of the most recent test

• Disease activity

- For RA: the DAS28 questionnaire and physician GA of disease activity
- For PsA: the DAS28 questionnaire and physician GA of disease activity
- For AS: the ASDAS questionnaire.

The physician GA of disease activity is a 100-mm VAS ranging from 0 (inactive disease) to 100 (extremely active disease).

In addition, the following data were recorded by the rheumatologist at the year 1 and year 2 hospital visits and at golimumab discontinuation.

• Specific characteristics of the disease

- For RA: new articular and extra-articular manifestations since the previous visit
- For PsA: new localizations and extra-articular manifestations since the previous visit
- For AS: new localizations and extra-articular manifestations since the previous visit

- **By the patient**

The following data were recorded by the patient at baseline, every 3 injections and at golimumab discontinuation.

• For RA and PsA: the **Routine Assessment of Patient Index Data 3 (RAPID3)** questionnaire

This a validated, self-evaluation instrument [35] comprising a score assessing functional capacity and two VAS (ranging from 0 to 10) that assess pain and patient global estimate of status.

• For AS: the **Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)** questionnaire

This is a validated instrument [36], which is also available in French [37], and is used routinely in rheumatology. It consists of 6 questions pertaining to the 5 major symptoms of AS: 1 question each for fatigue, spinal pain, joint pain/swelling and areas of localized tenderness, and 2 questions relating to morning stiffness. To give each symptom equal weighting, the mean of the two scores on morning stiffness is taken. The resulting 0 to 50 score is divided by 5 to give a final BASDAI score from 0 to 10.

In the interest of keeping the patient diary of as reasonable a size as possible, the Scientific Committee estimated that recording this data every 3 months would be sufficient.

12.4.13 Quality of life (QoL)

The QoL, as assessed via the SF-12 questionnaire, was reported by the patient at inclusion, at 1 and 2 years, and upon golimumab discontinuation.

The SF-12 is a shortened version of the SF-36 questionnaire. It assesses the patient's perception of health including energy levels, physical pain, physical and social functioning and performing daily tasks. It evaluates two dimensions of overall well-being, yielding a mental component summary (MCS) score and a physical component summary (PCS). Both scores were constructed in a way that the average of the general population would be 50. The MCS and PCS may range from 5.89058 to 71.96825, and from 9.94738 to 70.02246, respectively.

In the interest of keeping the patient diary of as reasonable a size as possible, the Scientific Committee estimated that SF-12 data collection every 12 months would be sufficient.

12.4.14 Safety Data

Safety data are presented for the global population (n=754) and include all the adverse events (AEs) that occurred since the start of the study.

AEs were reported by the physicians using a safety declaration form, as described in Section 7 of the study protocol. On the other hand, AEs were also reported spontaneously by the patients. As there was no standard safety reporting for patients, causality and seriousness were not provided by the patients. When mentioned, it was ruled by the company.

All the adverse events, reported by the physicians and the patients, were coded to MedDRA terms. Two separate safety analyses were performed: 1) AEs reported by the physicians and 2) AEs reported by the patients.

The total number of AEs and Serious AEs (SAEs) were presented for each analysis set, with the number of patients having at least one AE/SAE. The action taken with golimumab (temporary or permanent discontinuation, dosage change), the relationship with golimumab and the outcomes were analyzed and described using standard statistics. The SAEs were described by preferred terms (PT) and system organ class (SOC). For AEs/SAEs reported by the physicians, time to onset and intensity were also described. These data were not provided by the patients.

12.5 Data sources and measurement

At inclusion (baseline hospital visits for initial prescription according to routine practice)

- Rheumatologists recorded the following baseline data for each patient in a paper case report form (CRF): socio-demographic data, history and baseline characteristics of the studied disease, previous and concomitant treatments for the studied disease, healthcare resource utilization (for the previous 3 months), medical history other than the studied disease, prescription of golimumab and concomitant treatments (if any), CRP and/or ESR values, and disease activity (the DAS28 and physician GA of disease activity for RA and PsA patients; ASDAS for AS patients).
- Patients completed self-evaluation questionnaires on health status (EQ-5D), quality of life (SF-12), functional disability (HAQ), pain (VAS for pain), disease activity (RAPID3 or BASDAI) and WPAI.

PROs during the follow-up period

- At each monthly injection patients had to record the following:
  - injection date and dose (with scheduled date and reason for deviating from this date, if applicable), the injection device used (syringe or pen), who performed the injection, and their satisfaction with the injection.
  - VAS for pain (recall period of 1 week)
  - PGIC (since treatment initiation)
  - Utilization of healthcare resources (1 month recall period) and WPAI (1 week recall period).
- Every 3 injections (i.e. I4, I7, I10, I13, I16, I19, I22 and I25), the patients recorded the following: EQ-5D, HAQ, and RAPID3 or BASDAI questionnaires.
- The CRO reminded patients by phone to return the completed questionnaires, when these were not received within 7 days of the planned injection dates (calculation based on the first injection date). This call aimed to remind patients to complete their questionnaires; it helped in limiting missing data.
- Every 12 months (i.e. I13 and I25), the patients recorded the SF-12 questionnaire

At yearly follow-ups (recorded by the investigating physician):

- CRP and ESR values
- Appearance of new extra-articular manifestations, and if yes, to specify them (for PsA and AS patients, the occurrence of new attacks since the last visit was also recorded).
- Disease activity (DAS28 and physician's GA of disease activity for RA and PsA patients; ASDAS for AS patients)
- Golimumab continuation or discontinuation with reasons
- Renewal of golimumab prescription and concomitant treatments
- Any AEs since inclusion

At intermediate follow-ups (in a private clinic or private/public hospital)

In case of an intermediate visit, after informing the physician of his/her participation in an observational study, the patient had to ask the physician to complete a questionnaire and send it directly to the CRO. The following was recorded: date and reason of the visit, prescription data (golimumab and concomitant treatments), CRP and/or ESR, disease activity and SAEs since the last visit.

In case of golimumab discontinuation, treatment modification or study exit

- Rheumatologists recorded the visit date, reason for treatment discontinuation (or modification or leaving the study), data regarding the prescription (switch to other treatments), CRP and/or ESR, disease activity, and SAEs and attributed AEs since the last visit if any.
- Patients completed self-questionnaires on health status (EQ-5D), functional disability (HAQ), pain (VAS for pain), global impression of change (PGIC), disease activity (RAPID3 or BASDAI), and consumption of health care and health services (including WPAI).

12.6 Study Flow chart

Table 1: Data collected by the rheumatologists throughout the study (CRF)

Visit title	**Baseline visit** (initial hospital prescription)	**Intermediate follow-up visit(s)**	**1-year follow-up visit**	**Intermediate follow-up visit(s)**	**2-year follow-up visit** (end of study)	**Golimumab discontinuation**
Setting	Hospital	Hospital or private practice	Hospital	Hospital or private practice	Hospital	
Patient information and oral consent	X					
Inclusion and exclusion criteria	X					
Socio-demographic data	X					
History and characteristics of the CIRD	X		X		X	X
Previous and concomitant treatments for the CIRD	X					
Consumption of healthcare and health services	X					
Other medical history	X					
Prescription of golimumab and other treatments	X	X	X	X	X	X
Reason for golimumab discontinuation		X	X	X	X	X
CRP and/or ESR	X	X	X	X	X	X
Disease activity: -For RA: DAS28 and physician GA -For PsA: DAS28 and physician GA -For AS: ASDAS	X	X	X	X	X	X
Serious adverse events (regardless of causality) Related adverse events (regardless of seriousness)		X	X	X	X	X

Abbreviations: **AS**: Ankylosing spondylitis, **ASDAS**: Ankylosing spondylitis Disease Activity Score, **CIRD**: Chronic Inflammatory Rheumatic Disease, **CRF**: Case report form, **CRP**: C-reactive protein, **DAS28**: Disease Activity Score 28, **ESR**: Erythrocyte Sedimentation Rate, **GA**: Global Assessment, **PsA**: Psoriatic Arthritis; **RA**: Rheumatoid Arthritis.

Table 2: Data collected by the patients throughout the study (patient diary)

I1, I2, I3… is the day of the 1st, 2nd or 3rd… golimumab injection. The baseline visit is the hospital visit during which the initial hospital prescription of golimumab was made. The baseline visit and the first golimumab injection (I1) occurred most often on the same day, or otherwise, they were separated by a few days only.

Visit title	**Baseline visit [(a)] (initial hospital prescription)**	**I1**	**I2**	**I3**	**I4**	**I5**	**I6**	**I7**	**I8**	**I9**	**I10**	**I11**	**I12**	**I13 ≈1 yr**	**I14 - I25 (≈2 yrs) Similar to I1-I13**	**Golimumab discontinuation**
Consumption of healthcare and health services, including WPAI			X	X	X	X	X	X	X	X	X	X	X	X	Every month	X
Administration of golimumab[(b)]		X	X	X	X	X	X	X	X	X	X	X	X	X	Every month	
Health status: EQ-5D	X				X			X			X			X	I16, I19, I22, I25	X
Functional disability: HAQ	X				X			X			X			X	I16, I19, I22, I25	X
Pain severity: VAS for pain	X		X	X	X	X	X	X	X	X	X	X	X	X	Every month	X
PGIC			X	X	X	X	X	X	X	X	X	X	X	X	Every month	X
Progression of disease: -For RA and PsA: RAPID3 -For AS: BASDAI	X				X			X			X			X	I16, I19, I22, I25	X
Quality of life : SF-12	X													X	I25	X

[(a)] Questionnaire data was recorded at baseline visit, in the presence of the physician, but was completed in the I1 diary.

[(b)] Injection date/dose and reason of date deviation was collected for all injections from I1 to I25.

Abbreviations: **BASDAI**: Bath Ankylosing Disease Activity Index; **EQ-**5D: EuroQoL 5 Dimensions; **HAQ**: Health Assessment Questionnaire; **PGIC**: Patient Global Impression of Change, **RAPID3**: Routine Assessment of Patient Index Data 3, **SF-12**: Short form (12) Health Survey, **VAS**: Visual Analogue Scale, **WPAI**: Work Productivity and Activity Impairment.

12.7 Bias

All potential biases and study limitations were taken into account when interpreting the results.

12.7.1 Methods to Minimize Bias

Selection biases were limited by the inclusion of consecutive patients, and the analysis of the reasons for exclusion.

Biases related to patients lost to follow-up and missing data for PROs were limited by monthly telephone reminders, made from the second treatment injection until the end of the study. Moreover, monitoring visits were planned in approximately 30% of investigational sites to handle missing data.

As telephone reminders were scheduled to be performed 7 days after the planned injection date (if necessary) and concerned only the return of PRO questionnaires, it was unlikely to impact compliance to treatment.

For data collected by the investigating rheumatologist, biases due to missing data were limited by requesting the investigator to complete missing information and to verify inconsistent data. In the case of excessive missing data, methods for simple or multiple imputations were planned.

12.7.2 Limitations

Due to the nature of non-interventional studies and the length of follow-up, it was acknowledged that the number of patients lost to follow-up may be higher and that the collected data would be less controlled, compared to randomized and controlled clinical trials.

Due to constraints related to hospital prescriptions, much of the data were collected by the patients themselves. It was acknowledged that the volume and frequency of PRO questionnaires may discourage some patients from participating in the study or that they may discontinue later on. Also, due to the absence of data monitoring (an intrinsic aspect of non-interventional research and PROs), and the possibility of unplanned clinic visits, a certain amount of missing data was expected.

12.8 Study size

Sample size calculation was based on the estimated proportion of patients who would continue golimumab treatment 24 months after initial prescription.

The sample size was estimated at 576 patients, assuming that 40% of patients would continue golimumab treatment after 24 months, with an accuracy of 4% and a confidence interval of 95%.

Based on the clinical experience of rheumatologists, the Scientific Committee estimated that approximately 70% of patients would attend the follow-up visit at year 2. Therefore, considering a 30% lost to follow-up rate at year 2, 750 patients were estimated to be enrolled in the study.

This calculation was performed on the total study population.

Based on the prevalence of the 3 indications, it was estimated that the enrollment target per indication would be 40% of patients with RA (300), 40% of patients with AS (300) and 20% of patients with PsA (150). However, to respect the real-life use of golimumab, the Scientific Committee decided that all patients meeting the inclusion criteria should be included consecutively, regardless of the real-life prevalence of each CIRD.

12.8.1 Data transformation

No data transformations were carried out.

12.9 Statistical methods

A statistical analysis plan was prepared separately and is available in the Appendix. The main analyses will be described in the following sections.

Data review was performed on June 5th, 2018. The date of database lock was August 9th, 2018.

An interim analysis report was prepared on January 19th 2017, based on the number of patients who completed follow-up at the 1-year timepoint (i.e. those who were enrolled before 30 June 2015). Two separate analyses were performed:

- Description at baseline of all enrolled patients meeting the selection criteria
- Description at baseline and at year 1 of patients who completed the 1-year follow-up.

12.9.1 Main summary measures

- Primary objective

The primary objective is to determine the overall proportion of patients who persisted on golimumab treatment 24 months after the initial prescription.

The percentage of treatment persistence was assessed with common descriptive statistics, and reported for the entire population, by disease and by prior biotherapy.

For patients lacking any follow-up data, best-case and worst-case sensitivity analyses were applied. The best-case hypothesis assumes that patients lost to follow-up are still treated with golimumab, and the worst-case hypothesis assumes that patients lost to follow-up have discontinued golimumab.

- Secondary objective

The prescription patterns of golimumab in routine clinical practice, the use of golimumab and the reasons for treatment discontinuation were analyzed using common descriptive statistics. Patient characteristics and healthcare resource utilization were also presented using descriptive statistics.

The change over time of disease activity, pain, functional disability, health status and quality of life were analyzed using a Mixed Model Repeated Measure and paired t-tests to compare scores at baseline with scores at 2 years.

The results are presented for each indication and also by prior biotherapy history (naïve vs biotherapy-pretreated). A global analysis of these secondary objectives is also provided.

12.9.2 Main statistical methods

The statistical analyses were performed using version 9.2 of the SAS® software. All enrolled patients having received a golimumab prescription and having met inclusion criteria were included in the analysis. Common descriptive statistics were performed for all parameters. For ordinal and categorical variables, frequencies were calculated. For numeric variables, mean, standard deviation, median and range were calculated. Graphs were presented when judged as necessary. Groups were compared using Student t-test, Wilcoxom test, an ANOVA method or Kruskal-Wallis test for numeric variables and Chi^2 or exact test of Fischer for categorical variables.

12.9.3 Missing values

Multiple imputation techniques were planned in the SAP, in case of high rates of missing data. Missing data were frequent for several patient reported outcomes over time (such as the DAS28, ASDAS, PGA, EQ5D, SF-12 and pain VAS). If the baseline value was missing, the value was considered as missing and no replacement was made.

12.10 Amendments to the statistical analysis

There were no amendments to the statistical analysis.

12.11 Quality control

Quality control visits were carried out in 10% of active participating centers. The centers were randomly selected.

12.12 Protection of human subjects

Being a non-interventional, this study is beyond the scope of Article L.1121-1 and the French Code of Public Health (CSP), relating to biomedical research being performed on human subjects. According to French laws and regulations, an Ethics Committee's approval is not requested for carrying out observational studies (other regulatory approvals are mandatory) and a written informed consent to participate is not required either.

However, hospital rheumatologists had to fully inform patients about the study, verbally and in writing, and to obtain the patients' verbal consent to participate prior to inclusion in the study. A copy of the information sheet was given to each patient before participation in the study.

13 RESULTS PART I - DESCRIPTION OF THE ENTIRE COHORT AT BASELINE

13.1 Participating centers

A total of 1327 rheumatologists were contacted, of which 145 accepted to participate in this study. Of these, 134 were active and enrolled at least one patient.

Participating centers were geographically well distributed in France. Almost half the participating rheumatologists were male (n=69, 51.5%), and most were aged between 40 and 59 years (n=91, 67.9%), whereas a quarter were under 39 years old (n=34, 25.4%). A minority were over 60 years old n=8, 6.00%).

Most rheumatologists were practicing exclusively in the hospital (n=96, 71.6%), whereas the remaining had a mixed public-private healthcare establishment activity (n=38, 28.4%).

13.2 Patient registry

Table 3 : Comparison of eligible patients who were "included" and "non-included" in the study, as reported in available patient registries

	Non-included patients (n=84)	Included patients (n=483)	Total (n=567)	p
Gender				0.058
n	84	476	561	
Male	43 (51.2)	191 (40.1)	234 (41.8)	
Female	41 (48.8)	285 (59.9)	326 (58.2)	
Age				0.746
n	83	468	551	
Mean (SD)	46.5 (14.1)	47.1 (13.4)	47.0 (13.5)	
Median	47.0	48.0	48.0	
Range	18.0 - 75.0	19.0 - 83.0	18.0 - 83.0	
Disease				0.110
n	83	475	559	
Rheumatoid arthritis (RA)	21 (25.3)	117 (24.6)	138 (24.7)	
Psoriatic arthritis (PsA)	11 (13.3)	67 (14.1)	78 (14.0)	
Ankylosing spondylitis (AS)	46 (55.4)	283 (59.6)	329 (59.0)	
Other disease	3 (3.61)	7 (1.47)	10 (1.79)	
RA + AS	1 (1.20)	0 (0)	1 (0.18)	
PsA + AS	1 (1.20)	1 (0.21)	2 (0.36)	
Reasons for non-inclusion				
Patient refusal	26 (31.0)	-	-	-
Patient unable to participate	20 (23.8)	-	-	-
Forgetting to propose the study	16 (19.0)	-	-	-
Other reasons	22 (26.2%)	-	-	-

At the time of the database lock (on August 9th, 2018) 79 of 134 patient registries were received and analyzed. All patients meeting the selection criteria and having received a golimumab prescription were listed in the patient registry by the participant centers, regardless of their inclusion status. The representativeness of included patients was verified by comparing their characteristics against eligible

patients not included in the study. A total of 570 patients were reported in the patient registry. Of these, 483 patients were reported to be included in the study and 84 patients were not included (Table 3); the information was missing for 3 patients. The main reasons for non-inclusion were patient refusal to participate (n=26, 31.0%), patient being assessed as unable to participate by the investigator (n=20, 23.8%) and the investigator forgetting to propose the study (n=16,19.0%).

Socio-demographic characteristics and the distribution of patients as per rheumatic disease were similar in included and non-included patients, suggesting the representativeness of the study patients. However, results should be interpreted bearing in mind that a considerable proportion of registry data was missing, as 55 patient registers were not received.

13.3 Summary of visits and patients' diaries received

On the database lock date, the following CRFs were received and recorded in the database: Enrollment: n=770; Study inclusion: n=754 (see Table 4).

- 1-year follow-up: 557 CRFs received
- 2-year follow-up: 391 CRFs received
- Treatment withdrawal or modification: n=303 CRFs
- Date of the first inclusion: 15/01/2015
- Date of the final inclusion: 29/03/2016

Similarly, the following patient diaries were received and recorded in the database:

- Baseline/Injection N°1: n= 710
- Injection N°2: n = 666
- Injection N°3: n = 643
- Injection N°4: n = 600
- Injection N°5: n = 545
- Injection N°6: n = 508
- Injection N°7: n = 479
- Injection N°8: n = 446
- Injection N°9: n = 425
- Injection N°10: n = 409
- Injection N°11: n = 396
- Injection N°12: n = 372
- Injection N°13: n = 355
- Injection N°14: n = 348
- Injection N°15: n = 339
- Injection N°16: n = 327
- Injection N°17: n = 320
- Injection N°18: n = 302
- Injection N°19: n = 290
- Injection N°20: n = 274
- Injection N°21: n = 260
- Injection N°22: n = 255
- Injection N°23: n = 240
- Injection N°24: n = 233
- Injection N°25: n = 199

13.4 Study population

Between 15/01/2015 and 29/03/2016, 770 patients were enrolled in the study. Patient enrollment trends over the study period is presented for the global population in Figure 1 and also by disease in Figure 2. Of these, 754 patients were included in the final analysis (Table 4). The reasons for non-inclusion are reported in Table 4. Although the birth date was missing for one patient [PPD], this patient was included in the analysis as his/her socio-professional category was [PPD], implying that he/she was over 18 at baseline.

Figure 1: Actual vs. projected patient enrollment over the study period for the global population

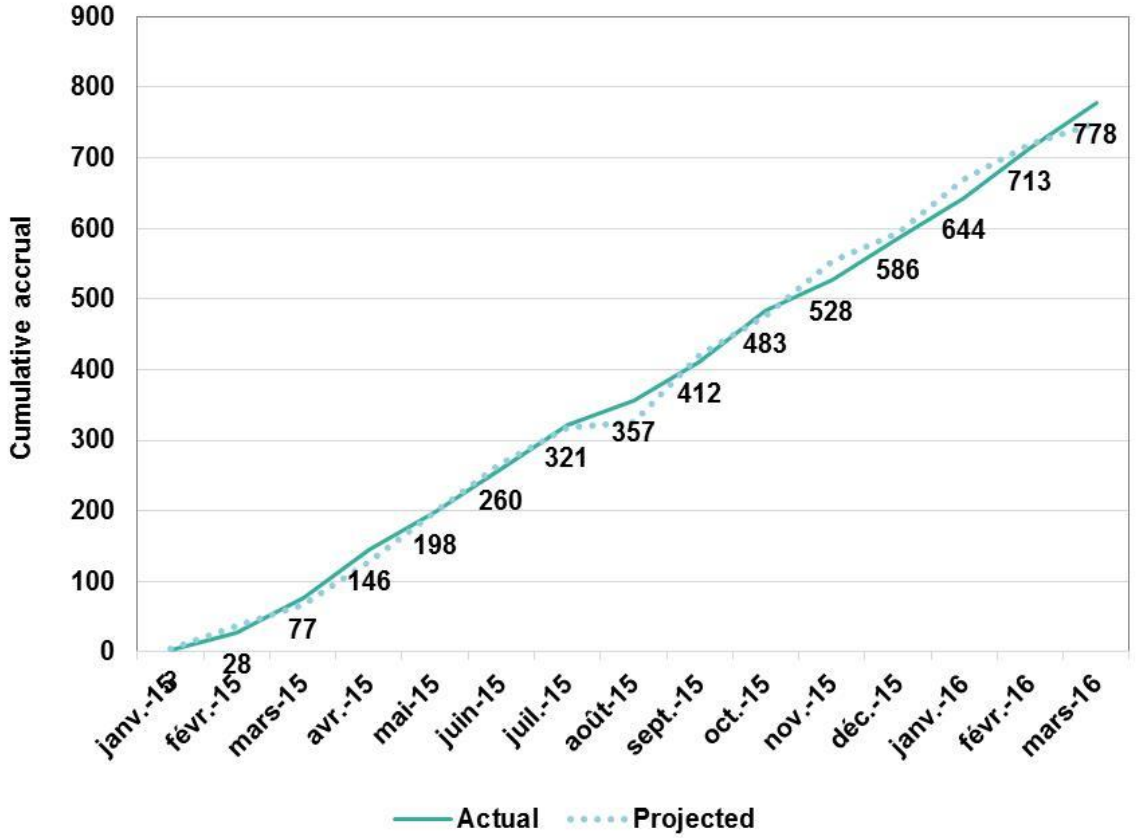


Figure 2: Actual vs. projected patient enrollment over the study period by disease

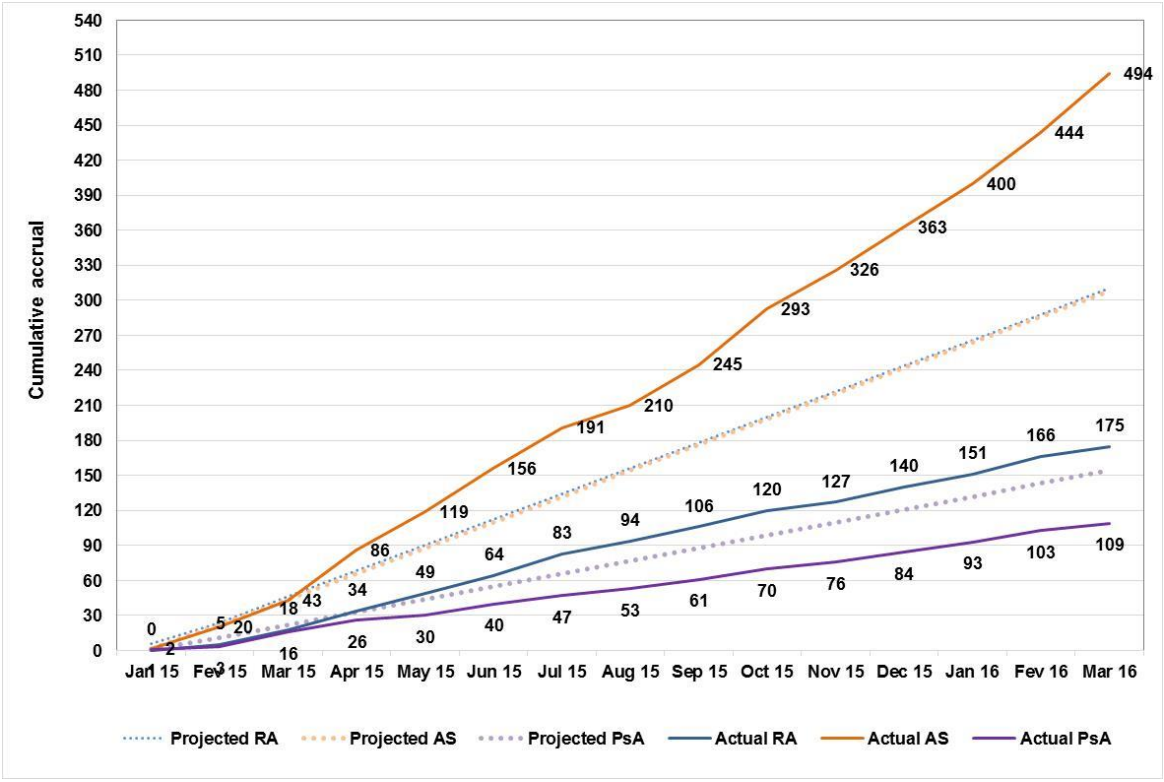


Table 4: The analysis population

	n (%)
Patients included in the analysis	
n	770
No	16 (2.08)
Yes	754 (97.9)
Reason for non-inclusion	
n	16
Patient did not take the treatment [a]	12 (75.0)
Change of the rheumatic disease during the study PPD	1 (6.25)
Diagnosed with fibromyalgia PPD	1 (6.25)
Lack of clinical evaluation at inclusion PPD	1 (6.25)
Invalid date of birth PPD	1 (6.25)

[a] PPD

13.5 Baseline descriptive data

Patients with the following CIRDs were recruited consecutively: 170 (22.5%) patients with rheumatoid arthritis (RA), 106 (14.1%) with psoriatic arthritis (PsA) and 478 (63.4%) with ankylosing spondylitis (AS). The distribution of CIRDs in the cohort was different than the actual prevalence of each of the three CIRDs (see section 12.8), thereby reflecting the real-life use of golimumab.

It should be mentioned that the number of patients in each disease group at baseline presented in this report is slightly different to those recounted in the interim report: 167 RA patients, 101 PsA patients and 486 AS patients. There were 8 patients (diagnosed with AS) who underwent a pathology modification between the interim and final analyses. For 1 patient, the modification occurred following a change in diagnosis of the rheumatic disease. In the other cases, the divergent pathologies were due to data recording errors in the CRF, which were resolved during data cleaning.

13.5.1 Sociodemographic characteristics at baseline

Baseline sociodemographic characteristics are reported for the total study population and by disease in Table 5. Mean patient age in the total cohort was 46.1 years and the majority were female (60.6%).

Patients with RA were significantly older (mean age 54.3 years) than those with PsA and AS (mean ages 48.1 and 42.8, respectively; $p < .001$). Also, there were significant differences in the gender ratio within each disease group, with 74.1% of RA patients being female, followed by 66.0% females in the PsA group and 54.6% females in the AS group ($p < .001$).

BMI data was available for 744 patients, among whom 43.5% had a normal BMI, about a third were overweight (32.7%), 1 in 5 were obese (19.9%) and 3.90% were underweight. Most patients were full-time or part-time employees (58.7%), 14.6% were retired and 10.3% were reported as unable to work.

Table 5: Sociodemographic characteristics at baseline for the total cohort and by disease

	Rheumatoid arthritis (RA) (n=170)	Psoriatic arthritis (PsA) (n=106)	Ankylosing spondylitis (AS) (n=478)	Total (n=754)	*p*
Age					**< .001**
n	169	106	478	753	
Mean (SD)	54.3 (12.3)	48.1 (12.9)	42.8 (12.1)	46.1 (13.1)	
Median	55.0	48.5	41.0	45.0	
Range	22.0 - 86.0	22.0 - 77.0	19.0 - 79.0	19.0 - 86.0	
Gender, n (%)					**< .001**
n	170	106	478	754	
Male	44 (25.9)	36 (34.0)	217 (45.4)	297 (39.4)	
Female	126 (74.1)	70 (66.0)	261 (54.6)	457 (60.6)	
BMI, n (%)					NC
n	168	105	471	744	
< 18.5 kg/m^2	9 (5.36)	1 (0.95)	19 (4.03)	29 (3.90)	
18.5 - 24.9 kg/m^2	71 (42.3)	32 (30.5)	221 (46.9)	324 (43.5)	
25 - 29.9 kg/m^2	62 (36.9)	34 (32.4)	147 (31.2)	243 (32.7)	
>30 Kg/m^2	26 (15.5)	38 (36.2)	84 (17.8)	148 (19.9)	
Socio-professional categories (SPC), n (%)					NC
n	170	106	478	754	
Part-time employment	18 (10.6)	19 (17.9)	75 (15.7)	112 (14.9)	
Full-time employment	59 (34.7)	38 (35.8)	233 (48.7)	330 (43.8)	
Student	1 (0.59)	0 (0)	6 (1.26)	7 (0.93)	
Retired	49 (28.8)	21 (19.8)	40 (8.37)	110 (14.6)	
Unemployed	16 (9.41)	9 (8.49)	49 (10.3)	74 (9.81)	
Stay-at-home husband/wife	5 (2.94)	3 (2.83)	12 (2.51)	20 (2.65)	
Disability/Unable to work	14 (8.24)	15 (14.2)	49 (10.3)	78 (10.3)	
2 SPCs provided	8 (4.71)	1 (0.94)	14 (2.93)	23 (3.05)	

NC = Not calculated

13.5.2 Sociodemographic characteristics at baseline by biotherapy history

As planned, descriptive analyses were also performed comparing “biotherapy-naïve” patients (BT-n) with those previously treated with biotherapy (BT-p), for each pathology. Among patients with RA (n=170), 110 patients (64.7%) were BT-n, 59 (34.7%) were BT-p and biotherapy history was missing for 1 patient (0.59%). In the PsA group (n=106), 70 patients (66.0%) were BT-n and 36 (34.0%) were BT-p; and among AS patients (n=478), 291 patients (60.9%) were BT-n and 187 (39.1%) were BT-p.

As seen in Table 6, no significant differences in sociodemographic attributes were noted between BT-n and BT-p patients with RA and PsA, except that in the RA cohort, the proportion of females in the BT-p group was significantly greater than in the BT-n group (86.4% vs. 67.3%, *p*= .007).

For patients with AS, the average age of patients in the BT-p group was significantly higher than for BT-n patients (46.8 vs. 40.2 years, respectively; *p* < .001), and there was a higher proportion of females in the BT-p than the in the BT-n group (62.0% vs. 49.8%, *p*= .009).

BMI and SPC distribution between BT-n and BT-p patients in RA, PsA and AS groups were similar. The above data are elaborated in Table 6.

Table 6: Baseline sociodemographic characteristics for RA, PsA and AS patients by biotherapy history

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169 [a])	*p*
Age				.611
n	110	58	168	
Mean (SD)	54.4 (12.0)	53.8 (12.9)	54.2 (12.3)	
Median	56.0	54.0	55.0	
Range	24.0 - 81.0	22.0 - 86.0	22.0 - 86.0	
Gender				**.007**
n	110	59	169	
Male	36 (32.7)	8 (13.6)	44 (26.0)	
Female	74 (67.3)	51 (86.4)	125 (74.0)	
BMI				.071
n	108	59	167	
< 18.5 kg/m^2	6 (5.56)	3 (5.08)	9 (5.39)	
18.5 - 24.9 kg/m^2	52 (48.1)	19 (32.2)	71 (42.5)	
25 - 29.9 kg/m^2	39 (36.1)	23 (39.0)	62 (37.1)	
>30 Kg/m^2	11 (10.2)	14 (23.7)	25 (15.0)	
SPC				NC
n	110	59	169	
Part-time employment	12 (10.9)	6 (10.2)	18 (10.7)	
Full-time employment	40 (36.4)	19 (32.2)	59 (34.9)	
Student	1 (0.91)	0 (0)	1 (0.59)	
Retired	30 (27.3)	18 (30.5)	48 (28.4)	
Unemployed	10 (9.09)	6 (10.2)	16 (9.47)	
Stay-at-home husband/wife	4 (3.64)	1 (1.69)	5 (2.96)	
Disability/Unable to work	8 (7.27)	6 (10.2)	14 (8.28)	
2 SPCs provided	5 (4.55)	3 (5.08)	8 (4.73)	

[a] *Prior biotherapy history was missing for 1 RA patient out of 170*

Psoriatic arthritis (PsA)	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)	*p*
Age				.069
n	70	36	106	
Mean (SD)	46.6 (12.3)	51.1 (13.9)	48.1 (12.9)	
Median	46.0	53.5	48.5	
Range	23.0 - 77.0	22.0 - 73.0	22.0 - 77.0	
Gender				.738
n	70	36	106	
Male	23 (32.9)	13 (36.1)	36 (34.0)	
Female	47 (67.1)	23 (63.9)	70 (66.0)	
BMI				.483
n	69	36	105	
< 18.5 kg/m^2	1 (1.45)	0 (0)	1 (0.95)	

18.5 - 24.9 kg/m^2	22 (31.9)	10 (27.8)	32 (30.5)	
25 - 29.9 kg/m^2	19 (27.5)	15 (41.7)	34 (32.4)	
>30 Kg/m^2	27 (39.1)	11 (30.6)	38 (36.2)	
SPC				NC
n	70	36	106	
Part-time employment	13 (18.6)	6 (16.7)	19 (17.9)	
Full-time employment	29 (41.4)	9 (25.0)	38 (35.8)	
Student	0 (0)	0 (0)	0 (0)	
Retired	11 (15.7)	10 (27.8)	21 (19.8)	
Unemployed	6 (8.57)	3 (8.33)	9 (8.49)	
Stay-at-home husband/wife	3 (4.29)	0 (0)	3 (2.83)	
Disability/Unable to work	8 (11.4)	7 (19.4)	15 (14.2)	
2 SPCs provided	0 (0)	1 (2.78)	1 (0.94)	
Ankylosing spondylitis (AS)	**AS BT-n (n=291)**	**AS BT-p (n=187)**	**Total AS (n=478)**	***p***
Age				**< .001**
n	291	187	478	
Mean (SD)	40.2 (11.2)	46.8 (12.3)	42.8 (12.1)	
Median	39.0	46.0	41.0	
Range	19.0 - 75.0	22.0 - 79.0	19.0 - 79.0	
Gender				**.009**
n	291	187	478	
Male	146 (50.2)	71 (38.0)	217 (45.4)	
Female	145 (49.8)	116 (62.0)	261 (54.6)	
BMI				.360
n	284	187	471	
< 18.5 kg/m^2	10 (3.52)	9 (4.81)	19 (4.03)	
18.5 - 24.9 kg/m^2	134 (47.2)	87 (46.5)	221 (46.9)	
25 - 29.9 kg/m^2	95 (33.5)	52 (27.8)	147 (31.2)	
>30 Kg/m^2	45 (15.8)	39 (20.9)	84 (17.8)	
SPC				NC
n	291	187	478	
Part-time employment	42 (14.4)	33 (17.6)	75 (15.7)	
Full-time employment	158 (54.3)	75 (40.1)	233 (48.7)	
Student	6 (2.06)	0 (0)	6 (1.26)	
Retired	13 (4.47)	27 (14.4)	40 (8.37)	
Unemployed	35 (12.0)	14 (7.49)	49 (10.3)	
Stay-at-home husband/wife	8 (2.75)	4 (2.14)	12 (2.51)	
Disability/Unable to work	22 (7.56)	27 (14.4)	49 (10.3)	
2 SPCs provided	7 (2.41)	7 (3.74)	14 (2.93)	

NC = not calculated

13.5.3 Medical history and comorbidities for the total cohort

Table 7 : Baseline medical history and co-morbidities for the total population and by disease

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	*p*
Number of co-morbidities					**< .001**
n	170	106	478	754	
0	21 (12.4)	3 (2.83)	87 (18.2)	111 (14.7)	
1	42 (24.7)	20 (18.9)	116 (24.3)	178 (23.6)	
2	48 (28.2)	28 (26.4)	107 (22.4)	183 (24.3)	
3	31 (18.2)	33 (31.1)	80 (16.7)	144 (19.1)	
4 or more	28 (16.5)	22 (20.8)	88 (18.4)	138 (18.3)	
At least one comorbidity	149 (87.6)	103 (97.2)	391 (81.8)	643 (85.3)	**< .001**
Tobacco consumption	n = 150 71 (47.3)	n = 95 28 (29.5)	n = 406 210 (51.7)	n = 651 309 (47.5)	**< .001**
Psoriasis	n = 146 11 (7.53)	n = 102 94 (92.2)	n = 402 94 (23.4)	n = 650 199 (30.6)	**< .001**
Hypertension	n = 151 45 (29.8)	n = 96 23 (24.0)	n = 399 65 (16.3)	n = 646 133 (20.6)	**.001**
Uveitis	n = 147 1 (0.68)	n = 93 3 (3.23)	n = 398 92 (23.1)	n = 638 96 (15.0)	**< .001**
Depressive disorder	n = 147 15 (10.2)	n = 96 10 (10.4)	n = 399 52 (13.0)	n = 642 77 (12.0)	.583
Thyroid disease	n = 149 27 (18.1)	n = 96 10 (10.4)	n = 396 29 (7.32)	n = 641 66 (10.3)	**.001**
Gastrointestinal disease	n =148 16 (10.8)	n = 95 5 (5.26)	n = 395 35 (8.86)	n = 638 56 (8.78)	.327
Asthma	n = 147 6 (4.08)	n = 96 7 (7.29)	n = 400 36 (9.00)	n = 643 49 (7.62)	.156
Type I or II diabetes	n = 147 13 (8.84)	n = 96 10 (10.4)	n = 397 22 (5.54)	n = 640 45 (7.03)	.152
Inflammatory bowel disease (IBD)	n = 147 2 (1.36)	n = 94 5 (5.32)	n = 393 40 (10.2)	n = 634 47 (7.41)	**.002**
Lung disease	n = 146 19 (13.0)	n = 94 5 (5.32)	n = 396 14 (3.54)	n = 636 38 (5.97)	**< .001**
Prior surgery	n = 151 88 (58.3)	n = 96 55 (57.3)	n = 403 190 (47.1)	n = 650 333 (51.2)	**.029**
Other physical illness	n = 146 11 (7.53)	n = 95 5 (5.26)	n = 395 22 (5.57)	n = 636 38 (5.97)	.659

Patient medical history, including comorbidities and health-risk factors with more than a 5% prevalence in the cohort, are summarized in Table 7. Most patients in the total cohort (85.3%) had at least one comorbidity, and about a half had already undergone a surgical procedure (51.2%). We found that 37.4% of the study patients were severely ill (282 of 754 patients), presenting 3 co-morbidities or more in addition to the CIRD. In particular, 51.9% of patients diagnosed with PsA, had ≥ 3 co-morbidities (versus 34.7% of RA and 35.1% of AS patients, respectively; $p < .001$).

In patients for whom the data was available, tobacco consumption was reported in 47.5% of the cohort, with significantly fewer PsA patients who were smokers (29.5%) than RA (47.3%) or SA patients (51.7%; $p < .001$). Psoriasis was among the most prevalent comorbidities in the total cohort (in 30.6% of patients), and the bulk of affected patients were found in the PsA cohort (92.2%), compared to 23.4% of AS patients and 7.53% of RA patients ($p < .001$).

Hypertension was found in about 1 of 5 patients (20.6%). Its prevalence was significantly lower in AS patients (16.3%) than in PsA (24.0%) and RA patients (29.8%, $p = .001$), an observation that follows the same trend as the mean age of patients in each disease group (RA highest mean age, AS lowest mean age). Thyroid disease was prevalent in a higher proportion of RA participants (18.1%) than PsA (10.4%) or AS patients (7.32%, p = .001). Lung disease was more common in the RA group (13.0%) than in PsA and AS groups (5.32% and 3.54%, respectively; $p < .001$). A lower number of AS patients had previously undergone surgery (47.1%) compared to RA (58.3%) and PsA (57.3%) participants ($p = .029$).

Uveitis and inflammatory bowel disease (IBD) are two common extra articular manifestations associated with AS. As such, uveitis was found predominantly in AS patients (23.1%), and occurred in only 1 RA patient (0.68%) and 3 PsA patients (3.23%, $p <.001$). IBD was significantly more prevalent in AS patients (10.2%) than in RA (1.36%) or PsA patients (5.32%; $p = .002$).

The prevalence of depressive disorders, gastrointestinal disease, asthma, diabetes and other physical illnesses in the total cohort was 12.0%, 8.78%, 7.62%, 7.03% and 5.97%, respectively, with no significant differences in prevalence among rheumatic disease groups.

13.5.4 Medical history and comorbidities for BT-n and BT-p patients by pathology

RA: Table 8 below shows the medical history of biotherapy-naïve (BT-n) and biotherapy pre-treated (BT-p) RA patients. Only co-morbidities with a ≥ 5% prevalence in the cohort are listed. No significant differences in comorbidity prevalence were found between BT-n and BT-p patients, except for tobacco consumption; a significantly higher proportion of BT-n patients were tobacco consumers than BT-p patients (54.6% vs. 34.6%, respectively, $p = .020$).

Most RA patients had 2 comorbidities (28.4%) and over 4 out of 5 had at least one comorbidity (87.6%). The three most common comorbidities or risk factors were tobacco consumption (47.7%), hypertension (29.3%) and thyroid disease (17.6%). Prior surgery was reported in 58.0% of patients.

PsA: Table 9 shows the medical history of BT-n and BT-p patients with PsA; co-morbidities with ≥ 5% prevalence are reported. No significant differences in comorbidity prevalence were found, except that IBD was more common in BT-p (12.9%) than in BT-n patients (1.59%, $p = .039$).

Most PsA patients had 3 comorbidities (31.1%). The three most common comorbidities or risk factors were psoriasis (92.2%), tobacco consumption (29.5%) and hypertension (24.0%), the first being the most evident phenotype of the PsA disease. Prior surgery was reported in 57.3% of patients.

AS: Table 10 shows the medical history of BT-n and BT-p patients with AS. Several comorbidities were significantly more prevalent in BT-p rather than BT-n patients, with 86.6% vs. 78.7% suffering from at least one co-morbidity ($p = .028$). These included IBD, psoriasis, uveitis, asthma, lung disease, liver disease, thyroid disease, gastro-intestinal disease, depressive disorders and other physical illnesses; the prevalence for each is provided in Table 10. BT-p patients also underwent significantly more surgical procedures than BT-n patients (57.7% vs. 40.0%, $p< .001$).

Generally, the three most frequent comorbidities in the AS cohort were tobacco consumption (51.7%), psoriasis (23.4%) and uveitis (23.1%), the latter two being prominent extra-articular manifestations of the AS disease.

Table 8: Medical history and co-morbidities at baseline for BT-n and BT-p rheumatoid arthritis (RA) patients

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169 [a])	*p*
Number of co-morbidities	n = 110	n = 59	n = 169	.605
0	14 (12.7)	7 (11.9)	21 (12.4)	
1	29 (26.4)	13 (22.0)	42 (24.9)	
2	34 (30.9)	14 (23.7)	48 (28.4)	
3	17 (15.5)	13 (22.0)	30 (17.8)	
4 or more	16 (14.5)	12 (20.3)	28 (16.6)	
At least one comorbidity	96 (87.3)	52 (88.1)	148 (87.6)	.871
Tobacco consumption	n = 97	n = 52	n = 149	**.020**
	53 (54.6)	18 (34.6)	71 (47.7)	
Psoriasis	n = 96	n = 49	n = 145	.509
	6 (6.25)	5 (10.2)	11 (7.59)	
Hypertension	n = 98	n = 52	n = 150	.158
	25 (25.5)	19 (36.5)	44 (29.3)	
Type I or II diabetes	n = 96	n = 50	n = 146	.062
	5 (5.21)	8 (16.0)	13 (8.90)	
Asthma	n = 96	n = 50	n = 146	.181
	2 (2.08)	4 (8.00)	6 (4.11)	
Lung disease	n = 95	n = 50	n = 145	.816
	12 (12.6)	7 (14.0)	19 (13.1)	
Liver disease	n = 95	n = 50	n = 145	.496
	5 (5.26)	4 (8.00)	9 (6.21)	
Thyroid disease	n = 96	n = 52	n = 148	.080
	13 (13.5)	13 (25.0)	26 (17.6)	
Gastrointestinal disease	n = 96	n = 51	n = 147	.759
	11 (11.5)	5 (9.80)	16 (10.9)	
Malignant disease	n = 96	n = 51	n = 147	.449
	4 (4.17)	4 (7.84)	8 (5.44)	
Depressive disorder	n = 96	n = 50	n = 146	.100
	7 (7.29)	8 (16.0)	15 (10.3)	
Prior surgery	n = 99	n = 51	n = 150	.620
	56 (56.6)	31 (60.8)	87 (58.0)	
Other physical illness	n = 95	n = 50	n = 145	.513
	6 (6.32)	5 (10.0)	11 (7.59)	

[a] Data in this table is presented for a total of n=169 RA patients (compared to n=170 in Table 7), as biotherapy history was missing for 1 patient at inclusion, meaning that 1 patient could not be classed as either BT-n or BT-p.

Table 9: Medical history and co-morbidities at baseline for BT-n and BT-p patients with psoriatic arthritis (PsA)

Psoriatic arthritis (RA)	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)	*p*
Number of co-morbidities	n = 70	n = 36	n = 106	.160
0	3 (4.29)	0 (0)	3 (2.83)	
1	12 (17.1)	8 (22.2)	20 (18.9)	
2	23 (32.9)	5 (13.9)	28 (26.4)	
3	19 (27.1)	14 (38.9)	33 (31.1)	
4 or more	13 (18.6)	9 (25.0)	22 (20.8)	
At least one comorbidity	67 (95.7)	36 (100.0)	103 (97.2)	.549
Tobacco consumption	n = 64	n = 31	n = 95	.169
	16 (25.0)	12 (38.7)	28 (29.5)	
IBD	n = 63	n = 31	n = 94	**.039**
	1 (1.59)	4 (12.9)	5 (5.32)	
Psoriasis	n = 68	n = 34	n = 102	.436
	64 (94.1)	30 (88.2)	94 (92.2)	
Hypertension	n = 64	n = 32	n = 96	.866
	15 (23.4)	8 (25.0)	23 (24.0)	
Type I or II diabetes	n = 64	n = 32	n = 96	.293
	5 (7.81)	5 (15.6)	10 (10.4)	
Asthma	n = 64	n = 32	n = 96	1.000
	5 (7.81)	2 (6.25)	7 (7.29)	
Lung disease	n = 63	n = 31	n = 94	1.000
	3 (4.76)	2 (6.45)	5 (5.32)	
Thyroid disease	n = 64	n = 32	n = 96	.293
	5 (7.81)	5 (15.6)	10 (10.4)	
Gastrointestinal disease	n = 64	n = 31	n = 95	.326
	2 (3.13)	3 (9.68)	5 (5.26)	
Depressive disorder	n = 65	n = 31	n = 96	1.000
	7 (10.8)	3 (9.68)	10 (10.4)	
Prior surgery	n = 65	n = 31	n = 96	.737
	38 (58.5)	17 (54.8)	55 (57.3)	
Other physical illness	n = 65	n = 30	n = 95	.176
	5 (7.69)	0 (0)	5 (5.26)	

Table 10: Medical history and co-morbidities at baseline for BT-n and BT-p patients with ankylosing spondylitis (AS)

Ankylosing spondylitis (AS)	AS BT-n (n=291)	AS BT-p (n=187)	Total AS (n=478)	*p*
Number of co-morbidities	n = 291	n = 187	n = 478	**< .001**
0	62 (21.3)	25 (13.4)	87 (18.2)	
1	79 (27.1)	37 (19.8)	116 (24.3)	
2	78 (26.8)	29 (15.5)	107 (22.4)	
3	40 (13.7)	40 (21.4)	80 (16.7)	
4 or more	32 (11.0)	56 (29.9)	88 (18.4)	
At least one comorbidity	229 (78.7)	162 (86.6)	391 (81.8)	**.028**
Tobacco consumption	n = 244	n = 162	n = 406	.075
	135 (55.3)	75 (46.3)	210 (51.7)	
IBD	n = 234	n = 159	n = 393	**.001**
	14 (5.98)	26 (16.4)	40 (10.2)	
Psoriasis	n = 239	n = 163	n = 402	**.004**
	44 (18.4)	50 (30.7)	94 (23.4)	
Uveitis	n = 235	n = 163	n = 398	**.024**
	45 (19.1)	47 (28.8)	92 (23.1)	
Hypertension	n = 237	n = 162	n = 399	.122
	33 (13.9)	32 (19.8)	65 (16.3)	
Type I or II diabetes	n = 237	n = 160	n = 397	.065
	9 (3.80)	13 (8.13)	22 (5.54)	
Asthma	n = 238	n = 162	n = 400	**.022**
	15 (6.30)	21 (13.0)	36 (9.00)	
Lung disease	n = 235	n = 161	n = 396	**.003**
	3 (1.28)	11 (6.83)	14 (3.54)	
Liver disease	n = 237	n = 160	n = 397	**.009**
	5 (2.11)	12 (7.50)	17 (4.28)	
Thyroid disease	n = 235	n = 161	n = 396	**.041**
	12 (5.11)	17 (10.6)	29 (7.32)	
Gastrointestinal disease	n = 235	n = 160	n = 395	**.036**
	15 (6.38)	20 (12.5)	35 (8.86)	
Depressive disorder	n = 236	n = 163	n = 399	**.003**
	21 (8.90)	31 (19.0)	52 (13.0)	
Prior surgery	n = 240	n = 163	n = 403	**< .001**
	96 (40.0)	94 (57.7)	190 (47.1)	
Other physical illness	n = 234	n = 161	n = 395	**.007**
	7 (2.99)	15 (9.32)	22 (5.57)	

13.5.5 Chronic inflammatory rheumatic disease (CIRD) characteristics at baseline

As mentioned in section 13.5, 170 patients with RA, 106 patients with PsA, and 478 with AS were recruited consecutively in the study, corresponding to 22.5%, 14.1% and 63.4% of the 754 participants, respectively. The duration since diagnosis was missing for 36 patients. Mean duration since diagnosis was not significantly different among disease groups, and was on average 7.6 years for the cohort (Table 11).

Since the biotherapy treatment history was missing for 1 patient with RA, the pertaining data is presented for 753 patients. As shown in Table 11, most patients at baseline had never received biotherapy treatment (BT-n, 62.5%).

Table 11: Chronic rheumatic inflammatory disease classification and duration

	Rheumatoid arthritis (n=170)	Psoriatic arthritis (n=106)	Ankylosing spondylitis (n=478)	Total (n=754)
Prior biotherapy				
n	169	106	478	753
Biotherapy-naive patients (BT-n)	110 (65.1)	70 (66.0)	291 (60.9)	471 (62.5)
Biotherapy-pretreated (BT-p)	59 (34.9)	36 (34.0)	187 (39.1)	282 (37.5)
Duration since diagnosis				
n	165	99	454	718
Mean (SD)	8.63 (9.86)	6.06 (7.01)	7.55 (9.24)	7.59 (9.13)
Median	4.99	2.90	4.18	4.09
Range	0.23 - 63.3	0.068 - 34.2	0.025 - 51.8	0.025 - 63.3

13.5.5.1 Rheumatoid arthritis (RA)

The baseline clinical characteristics of patients with RA are summarized in Table 12. On average, BT-p patients had a longer disease duration at inclusion than BT-n patients (13.7 vs. 5.87 years, $p < .001$). Rheumatoid factors and anti-cyclic citrullinated peptide (CCP) antibodies were present in the majority of patients (72.2% and 67.7%, respectively). Moreover, CCP antibodies were present in a significantly higher proportion of BT-n than BT-p participants (75.9% vs. 52.5%, $p = .002$). The mean erythrocyte sedimentation rate (ESR) was 20.2 mm/h and mean CRP was 11.6 mg/l, and for BT-n and BT-p RA patients these means were comparable.

Disease activity at baseline was assessed with the DAS28 questionnaire and in combination with the CRP and ESR results for each patient. DAS28-ESR was available for 151 RA patients, and the average score for the RA cohort was 4.54. DAS28-CRP was available for 160 patients and the mean score was 4.34. Average DAS28 scores were similar between BT-n and BT-p RA patients.

Radiological results (n=169): Imaging results detected bone erosion and joint space loss in 55.6% and 40.2% of RA patients, respectively. Bone demineralization and complete fusion of joints were noted in 36.1% and 2.96% of patients. Overall, bone and joint lesions were reported in 138 RA patients (81.7%), of which 35 (20.7%) had 2 lesions and 27 (16.0%) had 3 or more lesions (Table 12).

Extra-articular manifestations (n=169) were observed in only 21 RA patients (12.4%), of which 7 suffered from pleuro-pulmonary complications (Table 12).

Table 12 : Baseline clinical characteristics of patients with RA by prior biotherapy

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169)	*p*
Duration since diagnosis (years)				**< .001**
n	107	58	165	
Mean (SD)	5.87 (7.41)	13.7 (11.7)	8.63 (9.86)	
Median	2.81	10.3	4.99	
Range	0.23 - 39.8	2.01 - 63.3	0.23 - 63.3	
	n=110	n=59	n=169	.196
Presence of rheumatoid factors	83 (75.5)	39 (66.1)	122 (72.2)	
	n=108	n=59	n=167	
Presence of CCP antibodies	82 (75.9)	31 (52.5)	113 (67.7)	**.002**
ESR (mm/h)				.221
n	101	56	157	
Mean (SD)	19.8 (16.9)	21.0 (15.2)	20.2 (16.3)	
Median	15.0	18.0	16.0	
Range	1.00 - 71.0	2.00 - 73.0	1.00 - 73.0	
CRP (mg/l)				.605
n	108	58	166	
Mean (SD)	11.8 (16.5)	11.2 (17.1)	11.6 (16.7)	
Median	6.05	5.03	5.95	
Range	0 - 95.0	0 - 114	0 - 114	
DAS 28 (ESR)				.301
n	98	53	151	
Mean (SD)	4.46 (1.35)	4.68 (1.05)	4.54 (1.25)	
Median	4.55	4.68	4.61	
Range	0.68 - 7.16	1.88 - 6.82	0.68 - 7.16	
DAS 28 (CRP)				.669
n	105	55	160	
Mean (SD)	4.33 (1.14)	4.38 (1.06)	4.34 (1.11)	
Median	4.33	4.33	4.33	
Range	1.72 - 7.18	1.41 - 6.74	1.41 - 7.18	
	Radiological characteristics			
Type of lesion	n=110	n=59	n=169	
Bone demineralization	37 (33.6)	24 (40.7)	61 (36.1)	.364
Bone erosion	61 (55.5)	33 (55.9)	94 (55.6)	.952
Loss of joint space	41 (37.3)	27 (45.8)	68 (40.2)	.283
Ossification/complete fusion	1 (0.91)	4 (6.78)	5 (2.96)	.051
Patients with lesions, Yes	89 (80.9)	49 (83.1)	138 (81.7)	
Number of lesions per patient				
n	89	49	138	.339
1	53 (48.2)	23 (39.0)	76 (45.0)	
2	21 (19.1)	14 (23.7)	35 (20.7)	

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169)	*p*
3 or more	15 (13.6)	12 (20.3)	27 (16.0)	
Extra-articular manifestations				
No. of extra-articular manifestations	n=110	n=59	n=169	.756
0	97 (88.2)	51 (86.4)	148 (87.6)	
1	12 (10.9)	8 (13.6)	20 (11.8)	
3 and more	1 (0.91)	0 (0)	1 (0.59)	
Type of extra-articular manifestation				
n	13	8	21	
Pleuro-pulmonary complications	4 (30.8)	3 (37.5)	7 (33.3)	
Cardiac complications	1 (7.69)	1 (12.5)	2 (9.52)	
Vascular complications	1 (7.69)	0 (0)	1 (4.76)	
Hepatic complications	1 (7.69)	0 (0)	1 (4.76)	
Hematological manifestations	1 (7.69)	0 (0)	1 (4.76)	
Felty's syndrome	1 (7.69)	0 (0)	1 (4.76)	
Others	10 (76.9)	4 (50.0)	14 (66.7)	

13.5.5.2 Psoriatic arthritis (PsA)

The baseline clinical characteristics of patients with PsA are summarized in Table 13. The mean duration of PsA illness was significantly longer in BT-p than in BT-n patients (7.93 vs. 5.04 years, *p* =.009). Rheumatoid factors were present in only 8 patients, all of whom were BT-n. The mean ESR was 19.9 mm/h and mean CRP was 8.52 mg/l, and for BT-n and BT-p PsA patients these means were similar.

DAS28-ESR was available for 91 PsA patients, and the mean score was 3.98. DAS28-CRP was available for 97 patients and the mean score was 3.89. Average DAS28 scores of BT-n and BT-p PsA patients were similar.

Skin manifestations (n=106): cutaneous psoriasis was evident for most PsA patients (n=88, 83.0%), with it being significantly more prevalent in BT-n than BT-p patients (88.6% vs. 72.2%, *p* = .034). Among the 88 patients with skin manifestations, scaly or erythematous plaques were observed in the majority (n=81, 92.0%), affected nails in 16 patients (18.2%) and oral or genital lesions in only 8 patients (9.09%).

Radiological results (n=106): Imaging results detected bone erosion and joint space loss in 23.6% and 29.2% of patients, respectively. Bone demineralization and complete fusion of joints were noted in 10.4% and 6.60% of patients. Bone and joint lesions were present in 50 (47.2%) of PsA patients, of whom 11 (22.0%) had two lesions and 6 (12.0%) had three or more lesions; Interestingly, a significantly higher proportion of BT-p patients with PsA presented with 3 or more lesions (n=5, 33.3%), compared to BT-n patients (n=1, 2.86%, *p*= .009).

Clinical forms of PsA (n=106): the clinical forms observed were similar between BT-n and BT-p groups. Peripheral forms were reported in the majority of patients (90.6%); more specifically 49 (46.2%) had enthesitis and 87 (82.1%) had an affected peripheral joint. Among the latter, peripheral joint afflictions included active synovitis in 52 patients (59.8%) followed by affected distal interphalangeal joints in 39 (44.8%), dactylitis in 26 (29.9%) and affected hip joints in 6 patients (6.90%). Axial forms of PsA were found in 56 (52.8%) patients; 41 (38.7%) had sacroiliac joint involvement and 32 (30.2%) had axial skeleton involvement. Both axial and peripheral forms of the disease were found in 47 PsA patients (44.3%). Extra-articular manifestations (n=101) were observed in only 6 (5.94%) PsA patients.

Table 13 : Baseline clinical characteristics of patients with PsA by prior biotherapy

Psoriatic arthritis (PsA)	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)	*p*
Duration since diagnosis (years)				**.009**
n	64	35	99	
Mean (SD)	5.04 (6.37)	7.93 (7.80)	6.06 (7.01)	
Median	2.35	3.83	2.90	
Range	0.19 - 27.7	0.068 - 34.2	0.068 - 34.2	
	n=67	n=33	n=100	.065
Presence of rheumatoid factors	8 (11.9)	0 (0)	8 (8.00)	
ESR (mm/h)				.705
n	68	29	97	
Mean (SD)	19.2 (20.6)	21.5 (24.5)	19.9 (21.8)	
Median	12.5	9.00	12.0	
Range	2.00 - 103	2.00 - 100	2.00 - 103	
CRP (mg/l)				.455
n	70	32	102	
Mean (SD)	9.54 (12.8)	6.30 (5.99)	8.52 (11.2)	
Median	5.00	4.60	5.00	
Range	0.20 - 77.0	0.14 - 21.9	0.14 - 77.0	
DAS 28 (ESR)				.290
n	65	26	91	
Mean (SD)	3.89 (1.16)	4.19 (1.34)	3.98 (1.22)	
Median	4.01	4.47	4.05	
Range	0.53 - 6.43	1.22 - 6.23	0.53 - 6.43	
DAS 28 (CRP)				.113
n	67	30	97	
Mean (SD)	3.79 (0.92)	4.12 (1.15)	3.89 (1.00)	
Median	3.93	4.25	4.01	
Range	1.11 - 5.71	1.11 - 5.80	1.11 - 5.80	
	Skin manifestations			
	n = 70	n = 36	n = 106	
Personal or family history of psoriasis	44 (62.9)	29 (80.6)	73 (68.9)	.062
Presence of skin psoriasis	62 (88.6)	26 (72.2)	88 (83.0)	**.034**
Type of psoriasis	n = 62	n = 26	n = 88	
Scaly or erythematous plaques	58 (93.5)	23 (88.5)	81 (92.0)	.417
Erythematous oral or genital lesions	6 (9.68)	2 (7.69)	8 (9.09)	1.000
Nails	12 (19.4)	4 (15.4)	16 (18.2)	.769
	Radiological characteristics			
Type of lesion	n = 70	n = 36	n = 106	
Bone demineralization	7 (10.0)	4 (11.1)	11 (10.4)	1.000
Bone erosion	17 (24.3)	8 (22.2)	25 (23.6)	.813
Loss of joint space	18 (25.7)	13 (36.1)	31 (29.2)	.265
Ossification/complete fusion	3 (4.29)	4 (11.1)	7 (6.60)	.225
Patients with lesions, Yes	35 (50.0)	15 (41.7)	50 (47.2)	
Number of lesions per patient				**.009**

Psoriatic arthritis (PsA)	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)	*p*
n	35	15	50	
1	26 (74.3)	7 (46.7)	33 (66.0)	
2	8 (22.9)	3 (20.0)	11 (22.0)	
3 or more	1 (2.86)	5 (33.3)	6 (12.0)	
Clinical forms of PsA	**n=70**	**n=36**	**n=106**	
1) Axial forms	39 (55.7)	17 (47.2)	56 (52.8)	.407
- Sacroiliac joints	33 (47.1)	8 (22.2)	41 (38.7)	**.013**
- Axial skeleton	22 (31.4)	10 (27.8)	32 (30.2)	.698
2) Axial and Peripheral forms	31 (44.3)	16 (44.4)	47 (44.3)	.988
3) Peripheral forms	62 (88.6)	34 (94.4)	96 (90.6)	.489
Enthesis	31 (44.3)	18 (50.0)	49 (46.2)	.576
Insertions of quadricipital and patellar tendons	*6 (19.4)*	*7 (38.9)*	*13 (26.5)*	*0.184*
Insertions of calcaneal tendon and superficial plantar facia	*24 (77.4)*	*15 (83.3)*	*39 (79.6)*	*0.726*
Chest	*10 (32.3)*	*5 (27.8)*	*15 (30.6)*	*0.743*
Affected peripheral joint	57 (81.4)	30 (83.3)	87 (82.1)	.809
Hips	*3 (5.26)*	*3 (10.0)*	*6 (6.90)*	*.411*
Distal interphalangeal joints	*21 (36.8)*	*18 (60.0)*	*39 (44.8)*	***.039***
Dactylitis	*20 (35.1)*	*6 (20.0)*	*26 (29.9)*	*.144*
Active synovitis	*37 (64.9)*	*15 (50.0)*	*52 (59.8)*	*.178*
Type of Peripheral involvement				.409
n	58	31	89	.209
Unilateral	14 (24.1)	4 (12.9)	18 (20.2)	
Bilateral	44 (75.9)	27 (87.1)	71 (79.8)	
Extra-articular manifestations				
Number of extra-articular manifestations	n = 68	n = 33	n = 101	.132
0	66 (97.1)	29 (87.9)	95 (94.1)	
1	2 (2.94) [a]	3 (9.09) [b]	5 (4.95)	
2	0 (0)	1 (3.03) [b]	1 (0.99)	
Type of extra-articular manifestation				
n	n = 2	n = 4	n = 6	
Acute anterior uveitis	0 (0)	1 (25.0)	1 (16.7)	
Cardiac complications	0 (0)	3 (75.0)	3 (50.0)	
Others	2 (100)	1 (25.0)	3 (50.0)	

13.5.5.3 Ankylosing spondylitis (AS)

Baseline clinical characteristics of AS patients are given in Table 14. Similar to the RA and PsA cohorts, mean rheumatic disease duration in AS patients was longer in BT-p than in BT-n participants (10.7 vs. 5.52 years, $p<.001$); 317 patients (66.5%) were HLA-B27 positive and mean ESR was 16.4 mm/h. The mean CRP for BT-n patients was higher than for BT-p patients (12.5 mg/L vs. 9.66 mg/L, $p<.001$). The mean ASDAS ESR (available for 409 AS patients) was slightly greater for BT-p patients relative to BT-

n patients (3.03 vs. 2.87, *p*= .025). The mean ASDAS CRP (available for 447 patients) was 3.16, with no significant differences between BT-n and BT-p groups.

Radiological results (n=478): bone demineralization, joint space loss and complete fusion of joints were found in 9.62%, 23.4% and 15.9% of patients, respectively. Bone erosion (31.6%) was found in a significantly greater proportion of BT-n than BT-p patients (36.4% vs. 24.1%, *p* = .005).

Clinical forms of AS (n=478): axial forms were observed in almost all AS patients (95.6%); 304 had axial skeleton involvement (63.6%) and 414 had sacroiliac joint involvement (86.6%), the latter being more prevalent in BT-n than in BT-p patients (91.4% vs. 79.1%, *p* < .001).

Peripheral forms of AS occurred in a significantly higher proportion of BT-p than BT-n patients (69.0% vs. 48.8%, *p* < .001); enthesitis was found in a greater percentage of BT-p than BT-n patients (47.6% vs. 32.6%, *p* = .001) and peripheral joint complications occurred in 44.4% of BT-p patients compared to 34.0% of BT-n patients (*p*= .023). Details of the types of peripheral joint afflictions are elaborated in Table 14. Both axial and peripheral forms of the disease were also found together in a higher proportion of BT-p versus BT-n participants (63.6% vs. 45.7%, *p* < .001).

Extra-articular manifestations (n=478) were observed in 129 (27.0%) AS patients, of whom 85 (65.9%) had acute anterior uveitis and 33 (25.6%) had IBD.

Table 14 : Baseline clinical characteristics of patients with AS by prior biotherapy

Ankylosing spondylitis (AS)	AS BT-n (n=291)	AS BT-p (n=187)	Total AS (n=478)	*p*
Duration since diagnostic (years)				
n	276	178	454	
Mean (SD)	5.52 (7.87)	10.7 (10.3)	7.55 (9.24)	**< .001**
Median	1.68	6.90	4.18	
Range	0.025 - 45.1	0.21 - 51.8	0.025 - 51.8	
Presence of HLA-B27 antibodies	n=291	n=186	n=477	
Yes, n (%)	199 (68.4)	118 (63.4)	317 (66.5)	.494
ESR (mm/h)				
n	259	165	424	
Mean (SD)	16.4 (18.1)	16.3 (17.9)	16.4 (18.0)	.876
Median	10.0	10.0	10.0	
Range	1.00 - 112	1.00 - 89.0	1.00 - 112	
CRP (mg/l)				
n	285	178	463	
Mean (SD)	12.5 (18.2)	9.66 (17.3)	11.4 (17.9)	**< .001**
Median	6.00	3.25	5.00	
Range	0.10 - 137	0.0 - 146	0.0 - 146	
ASDAS (ESR)				
n	249	160	409	
Mean (SD)	2.87 (0.79)	3.03 (0.73)	2.93 (0.77)	**.025**
Median	2.83	3.01	2.91	
Range	0.96 - 5.16	1.05 - 5.25	0.96 - 5.25	
ASDAS (CRP)				
n	274	173	447	
Mean (SD)	3.18 (0.79)	3.12 (0.78)	3.16 (0.79)	.337
Median	3.16	3.08	3.14	
Range	1.35 - 5.39	1.17 - 5.76	1.17 - 5.76	
Radiological characteristics				

Ankylosing spondylitis (AS)	**AS BT-n (n=291)**	**AS BT-p (n=187)**	**Total AS (n=478)**	***p***
Type of radiological manifestation	n = 291	n = 187	n = 478	
Bone demineralization	24 (8.25)	22 (11.8)	46 (9.62)	.203
Bone erosion	106 (36.4)	45 (24.1)	151 (31.6)	**.005**
Loss of joint space	66 (22.7)	46 (24.6)	112 (23.4)	.629
Ossification/complete fusion	42 (14.4)	34 (18.2)	76 (15.9)	.274
Patients with lesions, Yes	166 (57.0)	107 (57.2)	273 (57.1)	
Number of lesions per patient				.795
n	166	107	273	
1	102 (61.4)	70 (65.4)	172 (63.0)	
2	58 (34.9)	34 (31.8)	92 (33.7)	
3 or more	6 (3.61)	3 (2.80)	9 (3.30)	
Clinical forms for AS	n = 291	n = 187	n = 478	
1) Axial forms	282 (96.9)	175 (93.6)	457 (95.6)	.084
- Sacroiliac joints	266 (91.4)	148 (79.1)	414 (86.6)	**< .001**
- Axial skeleton	182 (62.5)	122 (65.2)	304 (63.6)	.550
2) Axial and peripheral forms	133 (45.7)	119 (63.6)	252 (52.7)	**< .001**
3) Peripheral forms	142 (48.8)	129 (69.0)	271 (56.7)	**< .001**
- Enthesitis	95 (32.6)	89 (47.6)	184 (38.5)	**0.001**
Insertions of quadricipital and patellar tendons	*15 (15.8)*	*21 (23.6)*	*36 (19.6)*	*.182*
Insertions of calcaneal tendon and superficial plantar facia	*58 (61.1)*	*57 (64.0)*	*115 (62.5)*	*.675*
Chest	*45 (47.4)*	*52 (58.4)*	*97 (52.7)*	*.133*
- Affected peripheral joint	99 (34.0)	83 (44.4)	182 (38.1)	**.023**
Hips	*28 (28.3)*	*23 (27.7)*	*51 (28.0)*	*.932*
Distal interphalangeal joints	*23 (23.2)*	*25 (30.1)*	*48 (26.4)*	*.294*
Dactylitis	*19 (19.2)*	*22 (26.5)*	*41 (22.5)*	*.239*
Active synovitis	*29 (29.3)*	*30 (36.1)*	*59 (32.4)*	*.325*
Type of Peripheral involvement				**.009**
n	102	92	194	
Unilateral	28 (27.5)	26 (28.3)	54 (27.8)	
Bilateral	74 (72.5)	66 (71.7)	140 (72.2)	
Extra-articular manifestations				
Number of extra-articular manifestations	n = 291	n = 187	n = 478	**< .001**
0	230 (79.0)	119 (63.6)	349 (73.0)	
1	57 (19.6)	58 (31.0)	115 (24.1)	
2	4 (1.37)	10 (5.35)	14 (2.93)	
Type of extra-articular manifestation				
n	61	68	129	
Acute anterior uveitis	40 (65.6)	45 (66.2)	85 (65.9)	.943
Cardiac complications	0 (0)	1 (1.47)	1 (0.78)	1.000
Inflammatory bowel disease	11 (18.0)	22 (32.4)	33 (25.6)	.063
Other	14 (23.0)	10 (14.7)	24 (18.6)	.230

13.5.6 Prior treatments related to the chronic rheumatic inflammatory disease

13.5.6.1 Biotherapies

As mentioned above, 282 patients (37.5%) had received at least one biotherapy prior to study initiation. Of these, the majority had received one line of biotherapy (n=135, 47.9%), 84 (29.8%) had received 2 lines, 47 (16.7%) had received 3 lines and 16 (5.67%) had received ≥4 lines of biotherapy (Table 15).

Among the 3 disease cohorts, PsA patients generally received the fewest lines of biotherapy (mean of 1.50 lines), followed by AS patients (mean of 1.73 lines), with RA patients having received the most lines of biotherapy (mean of 2.44 lines, $p < .001$).

The number of biotherapies received per patient in each disease group is elaborated in Table 15. The three most often used prior biotherapies in the study cohort were etanercept (n=179, 63.5%), adalimumab (n=169, 59.9%) and infliximab (n=90, 31.9%). Etanercept and infliximab usage was similar between the 3 disease groups. However, adalimumab was prescribed to a significantly greater proportion of AS patients (67.4%) versus RA (44.1%) and PsA patients (47.2%, $p = .002$).

The main reason for discontinuing the above 3 biotherapies was secondary failure, defined as a decreasing responsiveness to a drug after an initial satisfactory response: 46.9% for etanercept, 45.0% for adalimumab, and 41.1% for infliximab. The second most frequent reason for discontinuation was primary non-response, for those who received etanercept (28.5%) and adalimumab (31.4%), and intolerance in those who received infliximab (32.2%). Primary non-response is defined as the lack of improvement of clinical signs and symptoms during induction therapy.

Other previously prescribed biotherapies and reasons for discontinuation are detailed in Table 15. The duration of use for each is also given in Table 15, and overall was mainly less than one year for these biotherapies.

Table 15 : Biotherapy history at baseline for RA, PsA and AS patients

	RA (n=169)	PsA (n=106)	AS (n=478)	Total (n=753)	*p*
Previous biotherapy	59 (34.9)	36 (34.0)	187 (39.1)	282 (37.5)	.453
No. of prior biotherapies per patient	n = 59	n = 36	n = 187	n = 282	< .001
1	23 (39.0)	22 (61.1)	90 (48.1)	135 (47.9)	
2	15 (25.4)	10 (27.8)	59 (31.6)	84 (29.8)	
3	7 (11.9)	4 (11.1)	36 (19.3)	47 (16.7)	
4 and more	14 (23.7)	0 (0)	2 (1.07)	16 (5.67)	
n	59	36	187	282	**< .001**
Mean (SD)	2.44 (1.63)	1.50 (0.70)	1.73 (0.81)	1.85 (1.07)	
Median	2.00	1.00	2.00	2.00	
Range	1.00 - 6.00	1.00 - 3.00	1.00 - 4.00	1.00 - 6.00	
	n = 59	n = 36	n = 187	n = 282	**< .001**
Abatacept	18 (30.5)	1 (2.78)	0 (0)	19 (6.74)	
Reason for withdrawal	n = 18	n = 1	n = 0	n = 19	
Primary non-response	3 (16.7)	1 (100)	-	4 (21.1)	
Intolerance	3 (16.7)	0 (0)	-	3 (15.8)	
Secondary failure	10 (55.6)	0 (0)	-	10 (52.6)	
Other reason	1 (5.56)	0 (0)	-	1 (5.26)	
Treatment duration	n = 15	n = 1	n = 0	n = 16	
Less than one year	8 (53.3)	1 (100)	0 (.)	9 (56.3)	
Between 1 and 2 years	4 (26.7)	0 (0)	0 (.)	4 (25.0)	
2 years and more	3 (20.0)	0 (0)	0 (.)	3 (18.8)	

	RA (n=169)	PsA (n=106)	AS (n=478)	Total (n=753)	*p*
	n = 59	n = 36	n = 187	n = 282	**.008**
Certolizumab	10 (16.9)	1 (2.78)	9 (4.81)	20 (7.09)	
Reason for withdrawal	n = 10	n = 1	n = 9	n = 20	
Primary non-response	3 (30.0)	0 (0)	4 (44.4)	7 (35.0)	
Intolerance	0 (0)	1 (100)	1 (11.1)	2 (10.0)	
Secondary failure	7 (70.0)	0 (0)	3 (33.3)	10 (50.0)	
Other reason	0 (0)	0 (0)	1 (11.1)	1 (5.00)	
Treatment duration	n = 9	n = 0	n = 7	n = 16	
Less than one year	5 (55.6)	-	6 (85.7)	11 (68.8)	
Between 1 and 2 years	3 (33.3)	-	0 (0)	3 (18.8)	
2 years and more	1 (11.1)	-	1 (14.3)	2 (12.5)	
	n = 59	n = 36	n = 187	n = 282	.160
Infliximab	13 (22.0)	11 (30.6)	66 (35.3)	90 (31.9)	
Reason for withdrawal	n = 13	n = 11	n = 66	n = 90	
Primary non-response	3 (23.1)	3 (27.3)	12 (18.2)	18 (20.0)	
Intolerance	5 (38.5)	3 (27.3)	21 (31.8)	29 (32.2)	
Secondary failure	5 (38.5)	4 (36.4)	28 (42.4)	37 (41.1)	
Other reason	0 (0)	2 (18.2)	6 (9.09)	8 (8.89)	
Treatment duration	n = 11	n = 9	n = 58	n = 78	
Less than one year	3 (27.3)	4 (44.4)	30 (51.7)	37 (47.4)	
Between 1 and 2 years	4 (36.4)	2 (22.2)	9 (15.5)	15 (19.2)	
2 years and more	4 (36.4)	3 (33.3)	19 (32.8)	26 (33.3)	
	n = 59	n = 36	n = 187	n = 282	**< .001**
Rituximab	13 (22.0)	0 (0)	2 (1.07)	15 (5.32)	
Reason for withdrawal	n = 13	n = 0	n = 2	n = 15	
Primary non-response	5 (38.5)	-	1 (50.0)	6 (40.0)	
Intolerance	4 (30.8)	-	0 (0)	4 (26.7)	
Secondary failure	3 (23.1)	-	1 (50.0)	4 (26.7)	
Treatment duration	n = 10	n = 0	n = 1	n = 11	
Less than one year	7 (70.0)	-	1 (100)	8 (72.7)	
Between 1 and 2 years	2 (20.0)	-	0 (0)	2 (18.2)	
2 years and more	1 (10.0)	-	0 (0)	1 (9.09)	
	n = 59	n = 36	n = 187	n = 282	**.002**
Adalimumab	26 (44.1)	17 (47.2)	126 (67.4)	169 (59.9)	
Reason for withdrawal	n = 26	n = 17	n = 126	n = 169	
Primary non-response	6 (23.1)	7 (41.2)	40 (31.7)	53 (31.4)	
Intolerance	7 (26.9)	4 (23.5)	19 (15.1)	30 (17.8)	
Secondary failure	10 (38.5)	5 (29.4)	61 (48.4)	76 (45.0)	
Other reason	3 (11.5)	2 (11.8)	12 (9.52)	17 (10.1)	
Treatment duration	n = 19	n = 15	n = 113	n = 147	
Less than one year	9 (47.4)	10 (66.7)	59 (52.2)	78 (53.1)	
Between 1 and 2 years	5 (26.3)	3 (20.0)	19 (16.8)	27 (18.4)	
2 years and more	5 (26.3)	2 (13.3)	35 (31.0)	42 (28.6)	
	n = 59	n = 36	n = 187	n = 282	.555
Etanercept	41 (69.5)	22 (61.1)	116 (62.0)	179 (63.5)	

	RA (n=169)	PsA (n=106)	AS (n=478)	Total (n=753)	*p*
Reason for withdrawal	n = 41	n = 22	n = 116	n = 179	
Primary non-response	12 (29.3)	3 (13.6)	36 (31.0)	51 (28.5)	
Intolerance	10 (24.4)	5 (22.7)	19 (16.4)	34 (19.0)	
Secondary failure	14 (34.1)	12 (54.5)	58 (50.0)	84 (46.9)	
Other reason	4 (9.76)	2 (9.09)	3 (2.59)	9 (5.03)	
Treatment duration	n = 32	n = 17	n = 96	n = 145	
Less than one year	18 (56.3)	7 (41.2)	41 (42.7)	66 (45.5)	
Between 1 and 2 years	5 (15.6)	3 (17.6)	15 (15.6)	23 (15.9)	
2 years and more	9 (28.1)	7 (41.2)	40 (41.7)	56 (38.6)	
	n = 59	n = 36	n = 187	n = 282	**< .001**
Tocilizumab	20 (33.9)	1 (2.78)	1 (0.53)	22 (7.80)	
Reason for withdrawal	n = 20	n = 1	n = 1	n = 22	
Primary non-response	5 (25.0)	0 (0)	0 (0)	5 (22.7)	
Intolerance	5 (25.0)	0 (0)	0 (0)	5 (22.7)	
Secondary failure	9 (45.0)	1 (100)	1 (100)	11 (50.0)	
Other reason	1 (5.00)	0 (0)	0 (0)	1 (4.55)	
Treatment duration	n = 18	n = 1	n = 1	n = 20	
Less than one year	10 (55.6)	1 (100)	0 (0)	11 (55.0)	
Between 1 and 2 years	2 (11.1)	0 (0)	0 (0)	2 (10.0)	
2 years and more	6 (33.3)	0 (0)	1 (100)	7 (35.0)	

13.5.6.2 Disease-Modifying Anti-Rheumatic Drug

Over half of the patients (53.4%) in the study cohort received disease-modifying anti-rheumatic drugs (DMARDs) prior to golimumab initiation. Data on the types of DMARDs received and their status in patients are presented in Table 16 below.

Significant differences in prior DMARDs use were found between disease groups: almost all RA patients and the majority of PsA patients, had been treated with DMARDs (91.8% and 79.2%, respectively), whereas only a third of AS patients had ever received DMARDs (34.1%, $p < .001$). These observations comply with standard clinical recommendations of prescribing DMARDs as a first line of treatment to RA and PsA patients.

Among patients who received DMARDs (n=403), MTX was most commonly prescribed (n=339, 84.1%), followed by sulfasalazine (n=130, 32.3%), leflunomide (n=79, 19.6%) and chloroquines (n=43, 10.7%). Only 1 patient with RA had received ciclosporine. DMARD prescription patterns and reasons for discontinuation were variable between disease groups.

- MTX (n=339): in patients who received DMARDs, all but 1 PsA patient (n=83, 98.8%) and almost all RA patients (n=146, 93.6%) received MTX, compared to two-thirds of AS patients (n=110, 67.5%, $p < .001$). A higher proportion of RA patients (61.6%) were continuing MTX at baseline compared to PsA (54.2%) and AS patients (41.8%, $p < .007$). The most common reason for stopping MTX was intolerance in RA and PsA patients (26.7% and 27.7%, respectively). Primary non-response was the most common reason for MTX discontinuation in the AS group, resulting in over a third of patients stopping treatment (34.5%); comparatively, primary non-response was lower in the PsA (16.9%) and RA groups (9.59%, $p < .001$).
- Sulfasalazine (n=130): A significantly higher proportion of AS patients (n=89, 54.6%) had a history of sulfasalazine use than PsA (n=16, 19.0%) and RA patients (n=25, 16.0%, $p < .001$).

Only 1 (6.25%) PsA, 10 (11.2%) AS, and 4 RA patients (16.0%) were continuing sulfasalazine at baseline. Primary non-response was the most frequent reason for discontinuation and was observed in 40.3% of patients who initiated sulfasalazine. A quarter of the patients stopped due to intolerance, and 18.5% discontinued due to secondary failure. Reasons for discontinuation were comparable among the three disease groups.

- Leflunomide (n=79): A greater proportion of RA patients (n=44, 28.2%) were on leflunomide compared to PsA (n=21, 25.0%) and AS patients (n=14, 8.59%, *p*< .001). Leflunomide was ongoing in 18 (40.9%) RA, 4 (19.0%) PsA and 1 (7.14%) AS patient(s) at baseline (*p* = .028). Intolerance was the most frequent reason for discontinuation, being reported in 32.9% of the study patients who initiated leflunomide. Nevertheless, primary non-response was the most common reason for discontinuation in AS patients (64.3%) compared to PsA (38.1%) and RA patients (11.4%, *p* < .001).
- Chloroquines (n=43): A greater proportion of RA patients received chloroquines (n=35, 22.4%), compared to PsA (n=4, 4.76%) and AS patients (n=4, 2.45%, *p*< .001). At baseline, the treatment was ongoing in 7 (20.0%) RA patients, 1 (25.0%) PsA and 1 (25.0%) AS patient. Primary non-response was the most common reason for stopping the treatment, and was observed in 44.2% of patients who received chloroquines.

Table 16 : Prior DMARD treatment history at baseline for RA, PsA and AS patients

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	p
Prior DMARD	156 (91.8)	84 (79.2)	163 (34.1)	403 (53.4)	**< .001**
	n = 156	n = 84	n = 163	n = 403	
MTX	**146 (93.6)**	**83 (98.8)**	**110 (67.5)**	**339 (84.1)**	**< .001**
	n = 146	n = 83	n = 110	n = 339	
Ongoing	*90 (61.6)*	*45 (54.2)*	*46 (41.8)*	*181 (53.4)*	***.007***
Reason for discontinuation					
Primary non-response	14 (9.59)	14 (16.9)	38 (34.5)	66 (19.5)	**<.001**
Intolerance	39 (26.7)	23 (27.7)	21 (19.1)	83 (24.5)	.274
Secondary failure	10 (6.85)	6 (7.23)	9 (8.18)	25 (7.37)	.920
Other reason	6 (4.11)	3 (3.61)	11 (10.0)	20 (5.90)	.108
	n = 156	n = 84	n = 163	n = 403	
Leflunomide	**44 (28.2)**	**21 (25.0)**	**14 (8.59)**	**79 (19.6)**	**< .001**
	n = 44	n = 21	n = 14	n = 79	
Ongoing	*18 (40.9)*	*4 (19.0)*	*1 (7.14)*	*23 (29.1)*	***.028***
Reason for discontinuation					
Primary non-response	5 (11.4)	8 (38.1)	9 (64.3)	22 (27.8)	**<.001**
Intolerance	14 (31.8)	7 (33.3)	5 (35.7)	26 (32.9)	1.000
Secondary failure	9 (20.5)	1 (4.76)	0 (0)	10 (12.7)	.075
Other reason	1 (2.27)	1 (4.76)	0 (0)	2 (2.53)	.693
	n = 156	n = 84	n = 163	n = 403	
Sulfasalazine	**25 (16.0)**	**16 (19.0)**	**89 (54.6)**	**130 (32.3)**	**< .001**
	n = 25	n = 16	n = 89	n = 130	
Ongoing	4 (16.0)	1 (6.25)	10 (11.2)	15 (11.5)	.692
Reason for discontinuation					
Primary non-response	8 (32.0)	6 (37.5)	39 (43.8)	53 (40.8)	.546
Intolerance	7 (28.0)	6 (37.5)	20 (22.5)	33 (25.4)	.410
Secondary failure	6 (24.0)	2 (12.5)	16 (18.0)	24 (18.5)	.650

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	p
Other reason	0 (0)	1 (6.25)	4 (4.49)	5 (3.85)	.483
Hydroxychloroquine/ Chloroquine	n = 156 **35 (22.4)**	n = 84 **4 (4.76)**	n = 163 **4 (2.45)**	n = 403 **43 (10.7)**	**<.001**
Ongoing	n = 35 *7 (20.0)*	n = 4 *1 (25.0)*	n = 4 *1 (25.0)*	n = 43 *9 (20.9)*	*1.000*
Reason for withdrawal					
Primary non-response	14 (40.0)	3 (75.0)	2 (50.0)	19 (44.2)	.520
Intolerance	7 (20.0)	0 (0)	0 (0)	7 (16.3)	1.000
Secondary failure	6 (17.1)	0 (0)	1 (25.0)	7 (16.3)	.791
Ciclosporine	n = 156 **1 (0.64)**	n = 84 **0 (0)**	n = 163 **0 (0)**	n = 403 **1 (0.25)**	.596
Reason for discontinuation	n = 1	n = 0	n = 0	n = 1	
Primary non-response	1 (100)	-	-	1 (100)	NA
Other DMARDs	n = 156 **9 (5.29)**	n = 84 **5 (4.72)**	n = 163 **1 (0.21)**	n = 403 **15 (1.99)**	NC
Ongoing	n = 9 *3 (33.3)*	n = 5 *2 (40.0)*	n = 1 *0 (0)*	n = 15 *5 (33.3)*	*1.000*
Reason for discontinuation					
Primary non-response	1 (11.1)	2 (40.0)	0 (0)	3 (20.0)	.604
Intolerance	3 (33.3)	1 (20.0)	0 (0)	4 (26.7)	1.000
Secondary failure	2 (22.2)	0 (0)	1 (100)	3 (20.0)	.123

13.5.6.3 Corticosteroids

A little under a third of the patients in the study cohort (n=224, 29.7%) had received long term corticosteroids. As per disease group, corticosteroid use was more common in RA patients (n=108, 63.5%) than in PsA (n=37, 34.9%) and AS patients (n=79, 16.5%, $p < .001$).

The most used corticosteroid was prednisone/prednisolone/methylprednisolone (in 66.5% of patients who received corticosteroids) with no significant difference between disease groups. It was ongoing at the time of inclusion in about half of the patients (51.0%), but mainly in RA patients (69.6%) and less frequently in AS patients (27.8%, $p < .001$). Prescription of Cortisone/Hydrocortisone was similar across all disease groups: it was prescribed to 35.3% of all patients who received corticosteroids, and it was ongoing in 38.0% of patients who initiated the treatment. A significantly lower proportion of AS patients (12.0%) were continuing the treatment compared to PsA and RA patients (50.0% each, $p = .003$).

For the 2 most commonly prescribed corticosteroids, reasons for discontinuation in the overall population were mostly “other” than primary non-response, intolerance or secondary failure. Further details are presented in Table 17. Overall, corticosteroid discontinuations were more common in AS patients, as observed from the significantly lower number of AS patients ongoing treatment at baseline, relative to RA and PsA patients. This was due to a higher frequency of primary non-responses in AS patients compared to RA and PsA patients.

Table 17 : Corticosteroid treatment history at baseline for RA, PsA and AS patients

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	*p*
Corticosteroids	108 (63.5)	37 (34.9)	79 (16.5)	224 (29.7)	**<.001**
	n = 108	n = 37	n = 79	n = 224	
Cortisone/hydrocortisone	**42 (38.9)**	**12 (32.4)**	**25 (31.6)**	**79 (35.3)**	**.548**
	n = 42	n = 12	n = 25	n = 79	
Ongoing	21 (50.0)	6 (50.0)	3 (12.0)	30 (38.0)	**.003**
Reason for discontinuation					
Primary non-response	5 (11.9)	0 (0)	10 (40.0)	15 (19.0)	**.006**
Intolerance	3 (7.14)	0 (0)	4 (16.0)	7 (8.86)	.345
Secondary failure	1 (2.38)	0 (0)	2 (8.00)	3 (3.80)	.728
Other reason	15 (35.7)	4 (33.3)	8 (32.0)	27 (34.2)	.948
	n = 108	n = 37	n = 79	n = 224	
Prednisone/prednisolone/ methylprednisolone	**69 (63.9)**	**26 (70.3)**	**54 (68.4)**	**149 (66.5)**	.709
	n = 69	n = 26	n = 54	n = 149	
Ongoing	48 (69.6)	13 (50.0)	15 (27.8)	76 (51.0)	**<.001**
Reason for discontinuation					
Primary non-response	2 (2.90)	3 (11.5)	14 (25.9)	19 (12.8)	**.001**
Intolerance	3 (4.35)	1 (3.85)	2 (3.70)	6 (4.03)	1.000
Secondary failure	3 (4.35)	0 (0)	2 (3.70)	5 (3.36)	.847
Other reason	17 (24.6)	6 (23.1)	21 (38.9)	44 (29.5)	.166
	n = 108	n = 37	n = 79	n = 224	
Triamcinolone/ paramethasone [a]	**0 (0)**	**0 (0)**	**4 (5.06)**	**4 (1.79)**	**.030**
	n = 0	n = 0	n = 4	n = 4	
Ongoing	-	-	0 (0)	0 (0)	NA
Reason for discontinuation					
Primary non-response	-	-	2 (50.0)	2 (50.0)	NA
Secondary failure	-	-	1 (25.0)	1 (25.0)	NA
Other reason	-	-	1 (25.0)	1 (25.0)	NA
Betamethasone/ Dexamethasone/cortivazol	**1 (0.93)**	**0 (0)**	**1 (1.27)**	**2 (0.89)**	1.000
	n = 1	n = 0	n = 1	n = 2	
Ongoing	0 (0)	-	0 (0)	0 (0)	NA
Reason for discontinuation					
Primary non-response	0 (0)	0 (.)	1 (100)	1 (50.0)	1.000
Other reason	1 (100)	0 (.)	0 (0)	1 (50.0)	1.000
Other corticosteroids [c]	**1 (0.93)**	**1 (2.70)**	**0 (0)**	**2 (0.89)**	.427
	n = 1	n = 1	n = 0	n = 2	
Ongoing	1 (100)	1 (100)	-	2 (100)	NA

13.5.6.4 NSAIDs/Analgesics

The majority of patients, particularly those with AS and PsA had received at least one NSAID/Analgesic (90.0% of AS patients and 86.8% of PsA patients versus 71.2% of RA patients, $p < .001$).

The most prescribed NSAID in the total cohort was paracetamol (61.6%), with a significantly higher proportion of RA patients (78.5%) having received the drug, compared to PsA (63.0%) and AS patients (56.5%, $p < .001$). Aspirin/ibuprofen/coxibs were used by 37.3% patients, and were prescribed to 42.1% of AS patients, 32.6% of PsA patients and 24.0% of RA patients ($p = .001$). Nefopam was mainly prescribed to patients in the AS group (16 AS patients out of 17 in the cohort who were prescribed Nefopam). Opioids and other NSAIDs/analgesics were received by 21.2% and 41.1% of the patients, respectively, with no significant difference between the disease groups. Further details are provided in Table 18.

It is worth noting that according to standard recommendations and clinical practice, AS patients should receive NSAIDs as a first line of treatment. In this study cohort, 48 AS patients (10.0%) did not report any prior NSAID/analgesic use. Of these, 14 had previously received biotherapy, 34 patients were nave to biotherapy and 25 patients were nave to both biotherapy and DMARDs.

Altogether, these data indicate that golimumab utilization conformed to the IFU in terms of prior NSAID treatment, particularly in AS patients.

Table 18 : NSAIDs/Analgesics treatment history for RA, PsA and AS patients

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	*p*
NSAIDs/Analgesics, Yes	121 (71.2)	92 (86.8)	430 (90.0)	643 (85.3)	**< .001**
n	121	92	430	643	
Paracetamol	95 (78.5)	58 (63.0)	243 (56.5)	396 (61.6)	**<.001**
Aspirin/ibuprofen/coxibs	29 (24.0)	30 (32.6)	181 (42.1)	240 (37.3)	**.001**
Opioid	23 (19.0)	15 (16.3)	98 (22.8)	136 (21.2)	.313
Nefopam	1 (0.83)	0 (0)	16 (3.72)	17 (2.64)	.055
Other NSAIDs/Analgesics	39 (32.2)	39 (42.4)	186 (43.3)	264 (41.1)	.090

13.5.6.5 Prior Local or surgical therapies

Almost one third of patients (27.9%) had a history of surgical therapies related to rheumatic disease (Table 19), with a significantly higher percentage of RA (38.8%) and PsA (39.6%) patients having undergone local surgery relative to AS patients (21.3%, $p < .001$). The main surgical procedure in this study cohort was joint injections (85.7% of all local surgeries), with differences between the three disease groups being non-significant.

Table 19 : Surgical treatment history for RA, PsA and AS patients

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	*p*
Local/surgical treatment, Yes	66 (38.8)	42 (39.6)	102 (21.3)	210 (27.9)	**< .001**
n	66	42	102	210	
Joint injections	54 (81.8)	38 (90.5)	88 (86.3)	180 (85.7)	.444
Synoviorthesis	8 (12.1)	0 (0)	7 (6.86)	15 (7.14)	**.042**
Synovectomy	4 (6.06)	0 (0)	2 (1.96)	6 (2.86)	.217
Bone fusion	5 (7.58)	2 (4.76)	3 (2.94)	10 (4.76)	.392

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	*p*
Joint replacement	6 (9.09)	4 (9.52)	7 (6.86)	17 (8.10)	.843
Other surgical procedure	9 (13.6)	4 (9.52)	12 (11.8)	25 (11.9)	.812

13.6 Initial golimumab prescription

Initial golimumab prescription was comparable between BT-n and BT-p patients across all three disease groups, followed the IFU in terms of unit dose and dosage frequency (50 mg once monthly) in most cases. The mean initial golimumab prescription duration was on average 5 months in all disease groups, and similar for BT-n and BT-p patients. Further details are presented in Table 20 below.

- **Rheumatoid arthritis**

Prior biotherapy information, as mentioned earlier, was available for 169 of the 170 RA patients included in the study and golimumab prescription data was available for 168 patients. Initial golimumab prescription was comparable between BT-p and BT-n patients, and generally in line with the IFU: only 2 RA patients (1.19%) were prescribed 100 mg golimumab, with the remaining 98.8% receiving the standard 50 mg dose. All RA patients were prescribed golimumab once a month. The mean and median prescription duration was 5.30 and 6.00 months, respectively, and ranged between 2 to 12 months (Table 20).

- **Psoriatic arthritis**

Initial golimumab prescription was comparable between BT-n and BT-p PsA patients, and in line with the IFU in most cases. Only 5 of 106 PsA patients (4.72%) were prescribed a 100 mg dose of golimumab, all of them BT-n, and only 1 patient (also BT-n) was prescribed golimumab 1.25 times a month. The average prescription duration was 5.17 months, median 6.00, and ranging between 1 to 12 months (Table 20).

- **Ankylosing spondylitis**

Initial golimumab prescription data was available for 471 of 478 AS patients. Golimumab was prescribed in accordance with the IFU in most cases: only 6 (1.27%) patients (5 BT-p and 1 BT-n patient) received 100 mg golimumab, and 4 (0.85%) patients (all BT-p) were prescribed golimumab 1.25 times a month. The average prescription duration was around 5.37 months, median 6.00 months, and ranging between 1 to 12 months. Further details are provided in Table 20 below.

Table 20 : Initial prescription of golimumab in patients with RA, PsA and AS by prior biotherapy

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169)	*p*
Dosage (mg)				1.000
n	110	58	168	
50	109 (99.1)	57 (98.3)	166 (98.8)	
100	1 (0.91)	1 (1.72)	2 (1.19)	
Dose /month				
n	110	58	168	
1	110 (100.0)	58 (100.0)	168 (100.0)	
Prescription duration (month)				.971
n	109	57	166	
Mean (SD)	5.33 (2.65)	5.23 (2.60)	5.30 (2.63)	
Median	6.00	6.00	6.00	
Range	2.00 - 12.0	2.00 - 12.0	2.00 - 12.0	

Psoriatic arthritis (PsA)	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)	*p*
Dosage (mg)				.164
n	70	36	106	
50	65 (92.9)	36 (100)	101 (95.3)	
100	5 (7.14)	0 (0)	5 (4.72)	
Dose /month				
n	70	36	106	1.000
1	69 (98.6)	36 (100)	105 (99.1)	
1.25	1 (1.43)	0 (0)	1 (0.94)	
Prescription duration (month)				.153
n	70	36	106	
Mean (SD)	4.93 (2.45)	5.64 (2.75)	5.17 (2.57)	
Median	4.00	6.00	6.00	
Range	1.00 - 12.0	3.00 - 12.0	1.00 - 12.0	
Ankylosing spondylitis (AS)	**AS BT-n (n=291)**	**AS BT-p (n=187)**	**Total AS (n=478)**	***p***
Dosage (mg)				**.036**
n	287	184	471	
50	286 (98.3)	179 (95.7)	465 (97.3)	
100	1 (0.35)	5 (2.72)	6 (1.27)	
Dose /month				**.023**
n	287	184	471	
1	287 (100)	180 (97.8)	467 (99.2)	
1.25	0 (0)	4 (2.17)	4 (0.85)	
Prescription duration (month)				.190
n	286	184	470	
Mean (SD)	5.30 (2.76)	5.46 (2.58)	5.37 (2.69)	
Median	6.00	6.00	6.00	
Range	1.00 - 12.0	2.00 - 12.0	1.00 - 12.0	

13.7 Concomitant treatments at baseline

At baseline, golimumab was prescribed in combination with other treatments to 633 patients in the cohort (84.1%): by disease group, 97.6% (n=165) of RA patients, 85.8% (n=91) of PsA patients and 78.9% (n=377) of AS patients received co-treatments at baseline. The data are elaborated in Table 21 below.

DMARDs: baseline co-prescription (n=285, 45.0%) was similar in BT-n and BT-p groups. Oral MTX was prescribed to 140 (49.1%) patients and parenteral MTX to 90 (31.6%) patients. DMARDs were co-prescribed more frequently to RA patients (86.7%) compared to PsA (65.9%) and AS patients (21.8%). This observation complies with the IFU for golimumab treatment associations for the three indications.

Corticosteroids: Corticosteroids prescriptions were similar in the BT-n and BT-p groups; it was prescribed with golimumab at baseline to 145 (22.9%) patients. Prednisone/prednisolone and cortisone/hydrocortisone were predominantly used (55.9% and 42.1%, respectively). Corticosteroids were prescribed in association with golimumab in over half of RA patients (54.5%), in under a third of PsA patients (29.7%) and in a minority of AS patients (7.43%).

NSAIDs/analgesics: NSAIDs/analgesics were co-prescribed with golimumab to 533 (84.2%) patients, particularly to 93.4% of AS patients, 85.7% of PsA patients and 62.4% of RA patients. Paracetamol was co-prescribed to 40.0% of patients, and more frequently to BT-p than BT-n patients (49.3% versus 33.9%, $p < .001$). Opioids, which were co-prescribed to 18.6% of patients, were more frequently given to BT-p than BT-n patients (24.6% versus 14.6%, respectively, $p = .004$). Unspecified "other" NSAIDs/analgesics were prescribed to most patients (62.7%), and more frequently to BT-n than BT-p patients (67.7% vs. 55.0%, $p = .003$).

Table 21: Concomitant treatments at baseline by prior biotherapy for the entire cohort

	BT-n patients (n=471)	BT-p patients (n=282)	Total (n=753)	*p*
Concomitant treatments	392 (83.2)	241 (85.5)	633 (84.1)	.418
	n = 392	n = 241	n = 633	
1) DMARDs	**184 (46.9)**	**101 (41.9)**	**285 (45.0)**	
	n = 184	n = 101	n = 285	
MTX (oral)	86 (46.7)	54 (53.5)	140 (49.1)	.277
MTX (parenteral)	62 (33.7)	28 (27.7)	90 (31.6)	.299
Sulfasalazine	13 (7.07)	8 (7.92)	21 (7.37)	.791
Leflunomide	22 (12.0)	7 (6.93)	29 (10.2)	.179
Hydroxychloroquine/ Chloroquine	3 (1.63)	3 (2.97)	6 (2.11)	.669
Other DMARDs	5 (2.72)	5 (4.95)	10 (3.51)	.333
	n = 392	n = 241	n = 633	
2) Corticosteroids	**96 (24.5)**	**49 (20.3)**	**145 (22.9)**	
	n = 96	n = 49	n = 145	
Cortisone/hydrocortisone	37 (38.5)	24 (49.0)	61 (42.1)	.228
Prednisone/prednisolone/methylprednisolone	57 (59.4)	24 (49.0)	81 (55.9)	.233
Other corticosteroids	4 (4.17)	2 (4.08)	6 (4.14)	1.000
	n = 392	n = 241	n = 633	
NSAIDs/analgesics	**322 (82.1)**	**211 (87.6)**	**533 (84.2)**	
	n = 322	n = 211	n = 533	
Ibuprofen	18 (5.59)	9 (4.27)	27 (5.07)	.495
Coxibs	38 (11.8)	17 (8.1)	55 (10.3)	.165
Paracetamol	109 (33.9)	104 (49.3)	213 (40.0)	**< .001**

	BT-n patients (n=471)	BT-p patients (n=282)	Total (n=753)	*p*
Opioids	47 (14.6)	52 (24.6)	99 (18.6)	**.004**
Nefopam	3 (0.93)	2 (0.95)	5 (0.94)	1.000
Other NSAIDs/analgesics	218 (67.7)	116 (55.0)	334 (62.7)	**.003**

13.7.1 Baseline concomitant treatments in RA patients

Almost all RA patients were prescribed other treatments with golimumab at baseline (n=165, 97.6%), of whom 143 (86.7%) were given DMARDs, 103 (62.4%) were prescribed NSAIDs/analgesics, and 90 (54.5%) were given corticosteroids. A higher proportion of BT-n than BT-p patients were co-prescribed DMARDs (90.8% vs. 78.6%) and corticosteroids (62.4% vs. 39.3%). Conversely, a greater proportion of BT-p RA patients received NSAIDs/analgesics (75.0%) compared to BT-n patients (56.0%).

Among patients who were co-prescribed DMARDs (n=143), 70 (49.0%) received oral MTX and 49 (34.3%) received parenteral MTX. Following MTX, leflunomide was the next most frequently co-prescribed DMARD in RA patients (n=19, 13.3%).

Of patients who received corticosteroids as co-treatment (n=90), 48 (53.3%) received prednisone/prednisolone/methylprednisolone and 44 (48.9%) received cortisone/hydrocortisone.

Among the 103 patients who were co-prescribed NSAIDs/analgesics, the majority were given paracetamol (n=62, 60.2%), followed by other NSAIDs/analgesics (n=49, 47.6%), opioids (n=17, 16.5%) and then ibuprofen (n=9, 8.74%).

Data on baseline concomitant treatments in the RA cohort by prior biotherapy is given in Table 22.

Table 22: Concomitant treatments at baseline by prior biotherapy for RA patients

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169)	*p*
Concomitant treatments	109 (99.1)	56 (94.9)	165 (97.6)	.123
	n = 109	n = 56	n = 165	
1) DMARDs	**99 (90.8)**	**44 (78.6)**	**143 (86.7)**	
	n = 99	n = 44	n = 143	
MTX (oral)	48 (48.5)	22 (50.0)	70 (49.0)	.867
MTX (parenteral)	38 (38.4)	11 (25.0)	49 (34.3)	.120
Sulfasalazine	1 (1.01)	4 (9.09)	5 (3.50)	**.031**
Leflunomide	13 (13.1)	6 (13.6)	19 (13.3)	.935
Hydroxychloroquine/ Chloroquine	2 (2.02)	3 (6.82)	5 (3.50)	.170
Other DMARDs	1 (1.01)	1 (2.27)	2 (1.40)	.522
	n = 109	n = 56	n = 165	
2) Corticosteroids	**68 (62.4)**	**22 (39.3)**	**90 (54.5)**	
	n = 68	n = 22	n = 90	
Cortisone/hydrocortisone	30 (44.1)	14 (63.6)	44 (48.9)	.111
Prednisone/prednisolone/ methylprednisolone	39 (57.4)	9 (40.9)	48 (53.3)	.179
	n = 109	n = 56	n = 165	
NSAIDs/analgesics	**61 (56.0)**	**42 (75.0)**	**103 (62.4)**	
	n = 61	n = 42	n = 103	
Ibuprofen	6 (9.84)	3 (7.14)	9 (8.74)	.735
Paracetamol	32 (52.5)	30 (71.4)	62 (60.2)	.053

Rheumatoid arthritis (RA)	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=169)	*p*
Opioids	8 (13.1)	9 (21.4)	17 (16.5)	.264
Other NSAIDs/analgesics	30 (49.2)	19 (45.2)	49 (47.6)	.694

13.7.2 Baseline concomitant treatments in PsA patients

The majority of PsA patients were prescribed other treatments with golimumab at baseline (n=91, 85.8%), of whom 78 (85.7%) received NSAIDs/analgesics, followed by 60 (65.9%) who received DMARDs and then 27 (29.7%) who received corticosteroids. A higher proportion of BT-p PsA patients received NSAIDs/analgesics (93.3%) compared to BT-n patients (82.0%).

Among patients who were co-prescribed DMARDs (n=60), 35 (58.3%) received oral MTX and 16 (26.7%) received parenteral MTX. Following MTX, leflunomide was the next most frequently co-prescribed DMARD (n=6, 10.0%). Of patients who received corticosteroids as co-treatment (n=27), 16 (59.3%) received prednisone/prednisolone/methylprednisolone, 12 (44.4%) received cortisone/ hydrocortisone, and 1 patient received other (unspecified) corticosteroid.

Of the 78 patients who were co-prescribed NSAIDs/analgesics, the majority were given other (unspecified) NSAIDs/analgesics (n=47, 60.3%), followed by paracetamol (n=26, 33.3%), opioids (n=15, 19.2%) and then coxibs (n=9, 11.5%). Baseline concomitant treatments in PsA patients by prior biotherapy are presented in Table 23.

Table 23: Concomitant treatments at baseline by prior biotherapy for PsA patients

Psoriatic arthritis (PsA)	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)	*p*
Concomitant treatments	61 (87.1)	30 (83.3)	91 (85.8)	.594
	n = 61	n = 30	n = 91	
1) DMARDs	**42 (68.9)**	**18 (60.0)**	**60 (65.9)**	
	n = 42	n = 18	n = 60	
MTX (oral)	21 (50.0)	14 (77.8)	35 (58.3)	**.046**
MTX (parenteral)	12 (28.6)	4 (22.2)	16 (26.7)	.755
Leflunomide	6 (14.3)	0 (0)	6 (10.0)	.165
Other DMARDs	2 (4.76)	0 (0)	2 (3.33)	1.000
	n = 61	n = 30	n = 91	
2) Corticosteroids	**18 (29.5)**	**9 (30.0)**	**27 (29.7)**	
	n = 18	**n = 9**	**n = 27**	
Cortisone/hydrocortisone	7 (38.9)	5 (55.6)	12 (44.4)	.448
Prednisone/prednisolone/ methylprednisolone	11 (61.1)	5 (55.6)	16 (59.3)	1.000
Other corticosteroids	1 (5.56)	0 (0)	1 (3.70)	1.000
	n = 61	n = 30	n = 91	
NSAIDs/analgesics	**50 (82.0)**	**28 (93.3)**	**78 (85.7)**	
	n = 50	**n = 28**	**n = 78**	
Coxibs	5 (10.0)	4 (14.3)	9 (11.5)	.715
Paracetamol	16 (32.0)	10 (35.7)	26 (33.3)	.739
Opioids	8 (16.0)	7 (25.0)	15 (19.2)	.333
Other NSAIDs/analgesics	33 (66.0)	14 (50.0)	47 (60.3)	.166

13.7.3 Baseline concomitant treatments in AS patients

Most AS patients were prescribed another treatment together with golimumab at baseline (n=377, 78.9%), a lower proportion compared to RA (97.6%) and PsA patients (85.8%) who were prescribed a concomitant treatment at baseline. Among AS patients who received co-treatment (n=377), the majority received NSAIDs (n=352, 93.4%), followed by about one-fifth of patients who received DMARDs (n=82, 21.8%), and then 28 (7.43%) who received corticosteroids.

In patients co-prescribed with DMARDs (n=82), 35 (42.7%) received oral MTX and 25 (30.5%) received parenteral MTX. Sulfasalazine was the next frequently co-prescribed DMARD (n=14, 17.1%). In patients who received corticosteroids as co-treatment (n=28), most (n=17, 60.7%) received prednisone/prednisolone/methylprednisolone, followed by 5 patients each (17.9%) who received cortisone/hydrocortisone and other (unspecified) corticosteroid.

Among those 352 patients co-prescribed with NSAIDs/analgesics, the majority received "other" NSAIDs/analgesics (n=238, 67.6%), followed by paracetamol (n=125, 35.5%), opioids (n=67, 19.0%), coxibs (n=44, 12.5%) and ibuprofen (n=18, 5.11%). A higher proportion of BT-p than BT-n patients were given paracetamol (45.4% vs. 28.9%, *p* = .002) and opioids (25.5% vs. 14.7%, *p* = .011). Conversely, a higher percentage of BT-n versus BT-p patients received "other" NSAIDs (73.5 vs. 58.9%, *p*= .004).

Baseline concomitant therapies in the AS cohort by prior biotherapy are given in Table 24 below.

Table 24: Concomitant treatments at baseline by prior biotherapy for AS patients

Ankylosing spondylitis (AS)	AS BT-n (n=291)	AS BT-p (n=187)	Total AS (n=478)	*p*
Concomitant treatments	222 (76.3)	155 (82.9)	377 (78.9)	.085
1) DMARDs	n = 222 **43 (19.4)**	n = 155 **39 (25.2)**	n = 377 **82 (21.8)**	
	n = 43	**n = 39**	**n = 82**	
MTX (oral)	17 (39.5)	18 (46.2)	35 (42.7)	.545
MTX (parenteral)	12 (27.9)	13 (33.3)	25 (30.5)	.594
Sulfasalazine	10 (23.3)	4 (10.3)	14 (17.1)	.118
Leflunomide	3 (6.98)	1 (2.56)	4 (4.88)	.617
Other DMARDs	2 (4.65)	4 (10.3)	6 (7.32)	.417
2) Corticosteroids	n = 222 **10 (4.50)**	n = 155 **18 (11.6)**	n = 377 **28 (7.43)**	
	n = 10	**n = 18**	**n = 28**	
Cortisone/hydrocortisone	0 (0)	5 (27.8)	5 (17.9)	.128
Prednisone/prednisolone/ methylprednisolone	7 (70.0)	10 (55.6)	17 (60.7)	.689
Other corticosteroids	3 (30.0)	2 (11.1)	5 (17.9)	.315
NSAIDs/analgesics	n = 222 **211 (95.0)**	n = 155 **141 (91.0)**	n = 377 **352 (93.4)**	
	n = 211	**n = 141**	**n = 352**	
Ibuprofen	12 (5.69)	6 (4.26)	18 (5.11)	.550
Coxibs	32 (15.2)	12 (8.51)	44 (12.5)	.064
Paracetamol	61 (28.9)	64 (45.4)	125 (35.5)	**.002**
Opioids	31 (14.7)	36 (25.5)	67 (19.0)	**.011**
Nefopam	3 (1.42)	2 (1.42)	5 (1.42)	1.000
Other NSAIDs/analgesics	155 (73.5)	83 (58.9)	238 (67.6)	**.004**

14 RESULTS PART II –ANALYSIS OF PATIENTS WITH 2 YEARS OF FOLLOW-UP

14.1 Baseline data for patients with 2-years follow-up

As explained previously in section 13.3, 391 patient CRFs were received at the end of the study after 2 years of follow-up. In this section, the baseline characteristics of these 391 patients will be described.

As performed for the entire study cohort at baseline in the previous section, the results in this section will also be presented according to the prior biotherapy status of patients: that is, BT-n versus BT-p patients in each disease cohort.

Among the 391 patients for whom data was available at 2 years, 98 (25.1%) had RA, 52 (13.3%) had PsA and 241 (61.6%) had AS. The majority of patients were biotherapy naïve (BT-n, n=265, 67.8%) and 125 (32.0%) had at least one biotherapy (BT-p) prior to golimumab initiation. The proportion of BT-p patients in each disease cohort was similar: 31.6% (n=31) in the RA group, 26.9% (n=14) in the PsA group and 33.2% (n=80) in the AS group (Table 25).

Table 25 : Rheumatic inflammatory disease distribution of patients by prior biotherapy

	Rheumatoid arthritis (RA) (n=98[a])	Psoriatic arthritis (PsA) (n=52)	Ankylosing spondylitis (AS) (n=241)	Total (n=391[a])
Prior biotherapy				
n	98[a]	52	241	391[a]
Biotherapy-naive patients	66 (67.3)	38 (73.1)	161 (66.8)	265 (67.8)
Biotherapy-pretreated patients	31 (31.6)	14 (26.9)	80 (33.2)	125 (32.0)

[a] Prior biotherapy data was missing for 1 patient

14.1.1 Baseline sociodemographic characteristics of patients with 2 years of follow-up

The mean age in the n=391 population was 46.4 years and 53.5% were female. The mean age was higher for patients in the RA cohort (54.5 years) compared to the PsA (48.9 years) and AS cohorts (42.7 years, $p < .001$). Additionally, the proportion of females in the RA group (73.5%) was significantly higher than in the PsA (57.7%) and AS groups (44.4%, $p< .001$). It may be of interest to note that the gender ratio in the AS group was majority female in the total study cohort (54.6% female, Table 5), but majority male in this n=391 population.

Most patients in the n=391 cohort had a normal BMI (42.6%) and 22.5% were obese. Contrarily, the majority of patients in the PsA group were obese (40.4%) and only 25.0% had a normal BMI (Table 26).

Most patients were full-time or part time employees (60.4%), 15.3% were retired, 10.2% were unemployed and 6.91% presented with an incapacity to work. Corresponding to the mean age of patients in each disease cohort, a higher proportion of AS patients worked full-time (53.9%) compared to PsA (34.6%) and RA patients (30.6%) and a higher proportion of RA patients were retired (30.6%) compared to PsA (21.2%) and AS patients (7.88%).

Baseline sociodemographic characteristics are presented for the n=391 population by disease group in Table 26.

Table 26 : Baseline sociodemographic characteristics for patients with 2 years of follow-up

	Rheumatoid arthritis (RA) (n=98)	Psoriatic arthritis (PsA) (n=52)	Ankylosing spondylitis (AS) (n=241)	Total (n=391)	*p*
Age					**< .001**
n	97	52	241	390	
Mean (SD)	54.5 (12.8)	48.9 (13.6)	42.7 (11.7)	46.4 (13.2)	
Median	56.0	47.5	41.0	45.0	
Range	22.0 - 82.0	23.0 - 77.0	21.0 - 79.0	21.0 - 82.0	
Gender					**<.001**
n	98	52	241	391	
Male	26 (26.5)	22 (42.3)	134 (55.6)	182 (46.5)	
Female	72 (73.5)	30 (57.7)	107 (44.4)	209 (53.5)	
BMI					NC
n	97	52	238	387	
< 18.5 Kg/m^2	3 (3.09)	1 (1.92)	6 (2.52)	10 (2.58)	
18.5 - 24.9 Kg/m^2	39 (40.2)	13 (25.0)	113 (47.5)	165 (42.6)	
25 - 29.9 Kg/m^2	35 (36.1)	17 (32.7)	73 (30.7)	125 (32.3)	
>30 Kg/m^2	20 (20.6)	21 (40.4)	46 (19.3)	87 (22.5)	
Socio-professional category (SPC) categories					NC
n	98	52	241	391	
Part-time	11 (11.2)	11 (21.2)	36 (14.9)	58 (14.8)	
Full-time	30 (30.6)	18 (34.6)	130 (53.9)	178 (45.5)	
Student	1 (1.02)	0 (0)	4 (1.66)	5 (1.28)	
Retired	30 (30.6)	11 (21.2)	19 (7.88)	60 (15.3)	
Unemployed	12 (12.2)	5 (9.62)	23 (9.54)	40 (10.2)	
Male/Housewife	3 (3.06)	3 (5.77)	9 (3.73)	15 (3.84)	
Disability/Incapacity for work	7 (7.14)	4 (7.69)	16 (6.64)	27 (6.91)	
2 SPCs given	4 (4.08)	0 (0)	4 (1.66)	8 (2.05)	

14.1.2 Baseline sociodemographic characteristics at baseline by biotherapy history in the n=391 population

Rheumatoid arthritis (RA): among patients with RA (n=98), 66 patients (67.3%) were BT-n, 31 (31.6%) were BT-p and biotherapy history was missing for 1 patient (1.02%). As seen in Table 27 below, mean age was comparable between BT-n and BT-p RA patients. However, a significantly higher proportion of BT-p patients were female (90.3%) compared to BT-n patients (65.2%, *p*= .009). Also, a higher percentage of BT-p RA patients were obese (29.0%) than BT-n RA patients (15.4%); correspondingly 44.6% of BT-n RA patients were of normal BMI compared to 32.3% of BT-p patients (Table 27).

Psoriatic arthritis (PsA): in the PsA group (n=52), 38 patients (73.1%) were BT-n and 14 (26.9%) were BT-p. Mean age was significantly higher for BT-p versus BT-n patients (55.7 vs. 46.4 years, *p*= .029). Although not statistically significant (possibly owing due to the smaller sample size of PsA patients in the n=391 population), there was a higher proportion of females in the BT-n than in the BT- p group (63.2% vs. 42.9%). A higher proportion of BT-n PsA patients were working part-time or full-time (63.2%) compared to BT-p patients (35.7%), and higher proportion of BT-p versus BT-n PsA patients were retired (35.7% vs. 15.8%) or unable to work (21.4% vs. 2.63%). These data are presented in Table 27.

Ankylosing spondylitis (AS): among AS patients (n=241), 161 patients (66.8%) were BT-n and 80 (33.2%) were BT-p. Mean age was significantly higher for BT-p versus BT-n patients (46.6 vs. 40.7 years, $p < .001$), and the ratio of females was higher in the BT-p than in the BT-n group (55.0% vs. 39.1%, $p = .020$). BMI and SPC distribution were similar between the BT-n and BT-p groups. These results are presented in Table 27 below.

Table 27 : Baseline sociodemographic characteristics of patients with RA, PsA and AS by prior biotherapy, for whom 2 years of follow-up was available

Rheumatoid arthritis (RA)	RA BT-n (n=66)	RA BT-p (n=31)	Total RA (n=97*)	*p*
Age				.389
n	66	30	96	
Mean (SD)	54.9 (12.6)	53.0 (13.1)	54.3 (12.7)	
Median	56.0	54.5	56.0	
Range	24.0 - 80.0	22.0 - 82.0	22.0 - 82.0	
Gender				**.009**
n	66	31	97	
Male	23 (34.8)	3 (9.68)	26 (26.8)	
Female	43 (65.2)	28 (90.3)	71 (73.2)	
BMI				.389
n	65	31	96	
< 18.5 Kg/m2	2 (3.08)	1 (3.23)	3 (3.13)	
18.5 - 24.9 Kg/m2	29 (44.6)	10 (32.3)	39 (40.6)	
25 - 29.9 Kg/m2	24 (36.9)	11 (35.5)	35 (36.5)	
>30 Kg/m2	10 (15.4)	9 (29.0)	19 (19.8)	
Socio-professional category (SPC)				.581
n	66	31	97	
Part-time employment	8 (12.1)	3 (9.68)	11 (11.3)	
Full-time employment	23 (34.8)	7 (22.6)	30 (30.9)	
Student	1 (1.52)	0 (0)	1 (1.03)	
Retired	20 (30.3)	9 (29.0)	29 (29.9)	
Unemployed	6 (9.09)	6 (19.4)	12 (12.4)	
Male/Housewife	2 (3.03)	1 (3.23)	3 (3.09)	
Disability/Incapacity for work	3 (4.55)	4 (12.9)	7 (7.22)	
2 SPCs given	3 (4.55)	1 (3.23)	4 (4.12)	
Psoriatic arthritis (PsA)	**PsA BT-n (n=38)**	**PsA BT-p (n=14)**	**Total PsA (n=52)**	**p**
Age				**.029**
n	38	14	52	
Mean (SD)	46.4 (13.4)	55.7 (12.1)	48.9 (13.6)	
Median	45.0	56.5	47.5	
Range	23.0 - 77.0	36.0 - 73.0	23.0 - 77.0	
Gender				.189
n	38	14	52	
Male	14 (36.8)	8 (57.1)	22 (42.3)	
Female	24 (63.2)	6 (42.9)	30 (57.7)	

Psoriatic arthritis (PsA)	PsA BT-n (n=38)	PsA BT-p (n=14)	Total PsA (n=52)	p
BMI				.081
n	38	14	52	
< 18.5 Kg/m2	1 (2.63)	0 (0)	1 (1.92)	
18.5 - 24.9 Kg/m2	12 (31.6)	1 (7.14)	13 (25.0)	
25 - 29.9 Kg/m2	9 (23.7)	8 (57.1)	17 (32.7)	
>30 Kg/m2	16 (42.1)	5 (35.7)	21 (40.4)	
Socio-professional category (SPC)				.122
n	38	14	52	
Part-time employment	9 (23.7)	2 (14.3)	11 (21.2)	
Full-time employment	15 (39.5)	3 (21.4)	18 (34.6)	
Student	0 (0)	0 (0)	0 (0)	
Retired	6 (15.8)	5 (35.7)	11 (21.2)	
Unemployed	4 (10.5)	1 (7.14)	5 (9.62)	
Male/Housewife	3 (7.89)	0 (0)	3 (5.77)	
Disability/Incapacity for work	1 (2.63)	3 (21.4)	4 (7.69)	
2 SPCs given	0 (0)	0 (0)	0 (0)	

Ankylosing spondylitis (AS)	AS BT-n (n=161)	AS BT-p (n=80)	Total AS (n=241)	*p*
Age				**<.001**
n	161	80	241	
Mean (SD)	40.7 (11.1)	46.6 (11.8)	42.7 (11.7)	
Median	39.0	47.5	41.0	
Range	21.0 - 75.0	23.0 - 79.0	21.0 - 79.0	
Gender				**.020**
n	161	80	241	
Male	98 (60.9)	36 (45.0)	134 (55.6)	
Female	63 (39.1)	44 (55.0)	107 (44.4)	
BMI				.126
n	158	80	238	
< 18.5 Kg/m2	4 (2.53)	2 (2.50)	6 (2.52)	
18.5 - 24.9 Kg/m2	77 (48.7)	36 (45.0)	113 (47.5)	
25 - 29.9 Kg/m2	53 (33.5)	20 (25.0)	73 (30.7)	
>30 Kg/m2	24 (15.2)	22 (27.5)	46 (19.3)	
Socio-professional categories (SPC)				.424
n	161	80	241	
Part-time employment	21 (13.0)	15 (18.8)	36 (14.9)	
Full-time employment	91 (56.5)	39 (48.8)	130 (53.9)	
Student	4 (2.48)	0 (0)	4 (1.66)	
Retired	10 (6.21)	9 (11.3)	19 (7.88)	
Unemployed	17 (10.6)	6 (7.50)	23 (9.54)	
Male/Housewife	5 (3.11)	4 (5.00)	9 (3.73)	
Disability/Incapacity for work	11 (6.83)	5 (6.25)	16 (6.64)	
2 SPCs given	2 (1.24)	2 (2.50)	4 (1.66)	

14.1.3 Baseline medical history and comorbidities in patients with 2 years of follow-up

Table 28 : Medical history and co-morbidities at baseline for patients with 2 years of follow-up

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
Number of co-morbidities					**.010**
n	98	52	241	391	
0	15 (15.3)	2 (3.85)	44 (18.3)	61 (15.6)	
1	26 (26.5)	8 (15.4)	60 (24.9)	94 (24.0)	
2	24 (24.5)	16 (30.8)	62 (25.7)	102 (26.1)	
3	21 (21.4)	18 (34.6)	33 (13.7)	72 (18.4)	
4 or more	12 (12.2)	8 (15.4)	42 (17.4)	62 (15.9)	
At least one comorbidity	83 (84.7)	50 (96.2)	197 (81.7)	330 (84.4)	**.034**
Tobacco consumption	n = 87 39 (44.8)	n = 50 16 (32.0)	n = 204 104 (51.0)	n = 341 159 (46.6)	.051
Psoriasis	n = 83 6 (7.23)	n = 50 47 (94.0)	n = 202 48 (23.8)	n = 335 101 (30.1)	**< .001**
Hypertension	n = 85 27 (31.8)	n = 49 12 (24.5)	n = 202 30 (14.9)	n = 336 69 (20.5)	**.004**
Uveitis	n = 84 1 (1.19)	n = 48 1 (2.08)	n = 203 51 (25.1)	n = 335 53 (15.8)	**< .001**
Depressive disorder	n = 84 8 (9.52)	n = 49 2 (4.08)	n = 201 23 (11.4)	n = 334 33 (9.88)	.344
Thyroid disease	n = 86 14 (16.3)	n = 50 5 (10.0)	n = 200 12 (6.00)	n = 336 31 (9.23)	**.026**
Gastrointestinal disease	n =86 4 (4.65)	n = 50 2 (4.00)	n = 199 15 (7.54)	n = 335 21 (6.27)	.588
Asthma	n = 83 2 (2.41)	n = 49 1 (2.04)	n = 200 12 (6.00)	n = 332 15 (4.52)	.384
Type I or II diabetes	n = 84 7 (8.33)	n = 49 6 (12.2)	n = 200 10 (5.00)	n = 333 23 (6.91)	.153
Inflammatory bowel disease (IBD)	n = 84 0 (0)	n = 49 1 (2.04)	n = 198 25 (12.6)	n = 331 26 (7.85)	**< .001**
Lung disease	n = 84 9 (10.7)	n = 49 3 (6.12)	n = 199 8 (4.02)	n = 332 20 (6.02)	.093
Prior surgery	n = 87 50 (57.5)	n = 49 27 (55.1)	n = 204 93 (45.6)	n = 340 170 (50.0)	.133
Other physical illness	n = 84 5 (5.95)	n = 49 1 (2.04)	n = 199 9 (4.52)	n = 332 15 (4.52)	.603

Baseline comorbidities with over a 5% prevalence in the n=391 population are detailed in Table 28.

Most patients had at least 1 comorbidity at baseline (84.4%); in particular, a higher proportion of PsA patients had at least one comorbidity (96.2%), compared to RA (84.7%) or AS patients (81.7%, *p*= .034). In the n=391 population, most patients had 2 comorbidities at baseline (26.1%), followed by 1 comorbidity (24.0%), 3 comorbidities (18.4%) and 4 or more comorbidities (15.9%); 15.6% of the

patients had no comorbidities. Prior surgery was reported in 50.0% of the population, followed by tobacco consumption (46.6%), psoriasis (30.1%), hypertension (20.5%) and uveitis (15.8%).

Among RA patients, the majority had 1 comorbidity at baseline (26.5%), in PsA the majority had 3 comorbidities (34.6%) and in AS the majority had 2 comorbidities at baseline (25.7%, p= .010)

Psoriasis (30.1%) was significantly more common in PsA patients (94.0%) than in AS (23.8%) and RA patients (7.23%, p < .001), representing the bulk of the n=391 population suffering from psoriasis. Uveitis was found in a higher proportion of AS patients (15.8%) compared to PsA (2.08%) and RA patients (1.19%, p< .001) – uveitis is a common extra-articular manifestation in AS. IBD, another extra-articular manifestation in AS, was also common in AS patients (12.6%), with no RA patients and only 1 PsA patients suffering from the condition (p < .001).

Hypertension and thyroid disease were more frequent in RA patients compared to PsA and AS patients: 31.8%, 24.5% and 14.9%, respectively with hypertension (p= .004) and 16.3%, 10.0% and 6.00%, respectively with thyroid disease (p= .026). The distribution of the other comorbidities in the 3 disease groups were rather similar (Table 28).

The prevalence of comorbidities between BT-n and BT-p patients in the RA and PsA groups were also similar. However, in the AS group, a higher proportion of BT-p than BT-n patients suffered from IBD (20.0% vs. 9.02%, p= .029), hypertension (23.9% vs. 10.4%, p= .011), lung disease (9.09% vs. 1.50%, p= .017), depression (19.4% vs. 7.46%, p= .012) and gastrointestinal disease (13.8% vs. 4.48%, p=.041). Also, a higher proportion of BT-p AS patients (63.2%) underwent surgery than BT-n AS patients (36.8%, p < .001).

14.1.4 Baseline rheumatic disease characteristics for patients with 2 years of follow-up

As presented earlier, in the n=391 population, 98 (25.1%) patients had RA, 52 (13.3%) had PsA and 241 (61.6%) had AS. The duration since rheumatic disease diagnosis was missing for 20 patients, and the mean duration for the n=391 cohort was 7.73 years. Mean duration since disease diagnosis was the highest in RA patients (8.24 years), followed by AS patients (7.85 years) and the lowest in PsA patients (6.15 years), as in Table 29 below. Most patients were BT-n at baseline (n=265, 67.8%).

Table 29: Chronic rheumatic inflammatory disease classification and duration

	Rheumatoid arthritis (RA) (n=98 [a])	Psoriatic arthritis (PsA) (n=52)	Ankylosing spondylitis (AS) (n=241)	Total (n=391 [a])
Duration since diagnosis				
n	95	48	228	371
Mean (SD)	8.24 (9.80)	6.15 (7.33)	7.85 (9.22)	7.73 (9.15)
Median	5.02	2.89	4.31	4.30
Range	0.23 - 63.3	0.068 - 34.2	0.030 - 45.1	0.030 - 63.3
Prior biotherapy				
n	98 [a]	52	241	391 [a]
Biotherapy-naive patients	66 (67.3)	38 (73.1)	161 (66.8)	265 (67.8)
Biotherapy-pretreated patients	31 (31.6)	14 (26.9)	80 (33.2)	125 (32.0)

[a] Biotherapy data missing for one patient with RA

14.1.4.1 Rheumatoid arthritis (RA)

The baseline clinical characteristics of RA patients with 2 years of follow-up are summarized in Table 30. On average, BT-p patients had a longer disease duration at baseline than BT-n patients (13.8 vs. 5.55 years, $p < .001$). Rheumatoid factors and CCP antibodies were present in the majority of patients (73.2% and 65.3%, respectively). The mean ESR was 19.5 mm/h and mean CRP was 10.2 mg/l, and for BT-n and BT-p RA patients these means were comparable.

Disease activity at baseline was assessed with the DAS28 questionnaire and in combination with the CRP and ESR results for each patient. DAS28-ESR was available for 83 RA patients, and the mean score was 4.42. DAS28-CRP was available for 92 patients and the mean score was 4.19. Average DAS28 scores were similar between BT-n and BT-p RA patients.

Radiological results (n=97): Imaging results detected bone erosion and joint space loss in 54.6% and 39.2% of patients, respectively. Bone demineralization and complete fusion of joints were noted in 33.0% and 1.03% of patients. Overall, bone and joint lesions were reported in 79 RA patients (81.4%), of which 23 (29.1%) had 2 lesions and 11 (13.9%) had 3 or more lesions (Table 30).

Extra-articular manifestations (n=97) were observed in 13 RA patients (13.4%), of which 5 suffered from pleuro-pulmonary complications (Table 30).

Table 30: Baseline disease characteristics of RA patients with 2 years of follow-up by prior biotherapy

Rheumatoid arthritis (RA)	RA BT-n (n=66)	RA BT-p (n=31)	Total RA (n=97 [a])	*p*
Duration since diagnosis (years)				**< .001**
n	64	31	95	
Mean (SD)	5.55 (6.94)	13.8 (12.3)	8.24 (9.80)	
Median	2.81	10.4	5.02	
Range	0.23 - 39.8	2.34 - 63.3	0.23 - 63.3	
	n=66	n=31	n=97	.186
Presence of rheumatoid factors	51 (77.3)	20 (64.5)	71 (73.2)	
	n=64	n=31	n=95	
Presence of CCP antibodies	46 (71.9)	16 (51.6)	62 (65.3)	.052
ESR (mm/h)				0.241
n	58	28	86	
Mean (SD)	19.8 (16.8)	19.0 (9.91)	19.5 (14.8)	
Median	15.0	18.0	16.0	
Range	1.00 - 67.0	3.00 - 45.0	1.00 - 67.0	
CRP (mg/l)				0.311
n	64	31	95	
Mean (SD)	11.1 (15.5)	8.34 (10.6)	10.2 (14.0)	
Median	5.62	4.00	5.00	
Range	0 - 95.0	0 - 44.3	0 - 95.0	
DAS 28 (ESR)				0.644
n	56	27	83	
Mean (SD)	4.37 (1.43)	4.52 (1.07)	4.42 (1.32)	
Median	4.47	4.63	4.57	
Range	0.68 - 7.14	1.88 - 6.41	0.68 - 7.14	

Rheumatoid arthritis (RA)	RA BT-n (n=66)	RA BT-p (n=31)	Total RA (n=97 [a])	*p*
DAS 28 (CRP)				0.977
n	62	30	92	
Mean (SD)	4.21 (1.18)	4.15 (1.08)	4.19 (1.15)	
Median	4.08	4.20	4.15	
Range	1.72 - 7.18	1.41 - 6.11	1.41 - 7.18	
Radiological characteristics				
Type of lesion	n=66	n=31	n=97	
Bone demineralization	19 (28.8)	13 (41.9)	32 (33.0)	0.199
Bone erosion	38 (57.6)	15 (48.4)	53 (54.6)	0.397
Loss of joint space	26 (39.4)	12 (38.7)	38 (39.2)	0.949
Ossification/complete fusion	0 (0)	1 (3.23)	1 (1.03)	0.320
Patients with lesions, Yes	54 (81.8)	25 (80.6)	79 (81.4)	
Number of lesions per patient				
n	54	25	79	.359
1	33 (61.1)	12 (48.0)	45 (57.0)	
2	13 (24.1)	10 (40.0)	23 (29.1)	
3 or more	8 (14.8)	3 (12.0)	11 (13.9)	
Extra-articular manifestations				
No. of extra-articular manifestations	n=66	n=31	n=97	1.000
0	57 (86.4)	27 (87.1)	84 (86.6)	
1	8 (12.1)	4 (12.9)	12 (12.4)	
3 and more	1 (1.52)	0 (0)	1 (1.03)	
Type of extra-articular manifestation				
n	9	4	13	
Pleuro-pulmonary complications	4 (44.4)	1 (25.0)	5 (38.5)	
Cardiac complications	1 (11.1)	0 (0)	1 (7.69)	
Vascular complications	1 (11.1)	0 (0)	1 (7.69)	
Hepatic complications	1 (11.1)	0 (0)	1 (7.69)	
Hematological manifestations	1 (11.1)	0 (0)	1 (7.69)	
Felty's syndrome	1 (11.1)	0 (0)	1 (7.69)	
Others	6 (66.7)	3 (75.0)	9 (69.2)	

14.1.4.2 Psoriatic arthritis (PsA)

The baseline clinical characteristics of PsA patients with 2 years of follow-up are given in Table 31. The mean duration of PsA illness was significantly longer in BT-p than in BT-n patients (10.4 vs. 4.38 years, *p* =.007). Rheumatoid factors were present in only 1 BT-n patient. Mean ESR was 23.1 mm/h and mean CRP was 11.1 mg/l, and for BT-n and BT-p PsA patients these means were similar. DAS28-ESR was available for 45 PsA patients, and mean score was 4.03. DAS28-CRP was available for 48 patients and mean score was 3.95. Mean DAS28 for BT-n and BT-p patients were similar.

Skin manifestations (n=52): cutaneous psoriasis was present in most PsA patients (n=43, 82.7%), with it being significantly more common in BT-n than BT-p patients (89.5% vs. 64.3%, *p* = .048). Among the

43 patients with skin manifestations, scaly or erythematous plaques were observed in the majority (n=40, 93.0%), affected nails in 4 patients (9.30%) and oral or genital lesions in 4 patients (9.30%).

Radiological results (n=52): Bone erosion and joint space loss was observed in 32.7% and 38.5% of patients, respectively. Bone demineralization and complete fusion of joints were noted in 13.5% and 7.69% of patients. Bone and joint lesions were present in 31 (59.6%) PsA patients, of whom 10 (32.3%) had two lesions and 3 (9.68%) had three or more lesions.

Clinical forms of PsA (n=52): the clinical forms observed were similar between BT-n and BT-p groups. Peripheral forms were reported in the majority of patients (90.4%); more specifically 20 (38.5%) had enthesitis and 42 (80.8%) had an affected peripheral joint. Peripheral joint afflictions included active synovitis in 28 patients (66.7%) followed by affected distal interphalangeal joints in 16 (38.1%), dactylitis in 15 (35.7%) and affected hips in 4 patients (9.52%). Axial forms of PsA were found in 23 (44.2%) patients; 19 (36.5%) had sacroiliac joint involvement and 14 (26.9%) had axial skeleton involvement. Both axial and peripheral forms of the disease were found in 19 (36.5%) PsA patients.

Extra-articular manifestations (n=50) were found in 4 (8.00%) PsA patients.

Table 31: Baseline disease characteristics of PsA patients with 2 years of follow-up by prior biotherapy

Psoriatic arthritis (PsA)	PsA BT-n (n=38)	PsA BT-p (n=14)	Total PsA (n=52)	*p*
Duration since diagnosis (years)				**.007**
n	34	14	48	
Mean (SD)	4.38 (5.52)	10.4 (9.43)	6.15 (7.33)	
Median	2.10	7.18	2.89	
Range	0.19 - 20.3	0.068 - 34.2	0.068 - 34.2	
	n=38	n=13	n=51	1.000
Presence of rheumatoid factors	1 (2.63)	0 (0)	1 (1.96)	
ESR (mm/h)				.559
n	36	12	48	
Mean (SD)	21.5 (21.4)	28.1 (34.5)	23.1 (25.1)	
Median	13.5	9.00	13.0	
Range	2.00 - 95.0	2.00 - 100	2.00 - 100	
CRP (mg/l)				.767
n	38	12	50	
Mean (SD)	12.2 (15.7)	7.52 (6.37)	11.1 (14.2)	
Median	5.50	5.75	5.75	
Range	0.70 - 77.0	1.56 - 20.8	0.70 - 77.0	
DAS 28 (ESR)				.591
n	35	10	45	
Mean (SD)	3.98 (1.07)	4.21 (1.54)	4.03 (1.17)	
Median	3.92	4.57	4.02	
Range	0.53 - 6.43	1.71 - 6.23	0.53 - 6.43	
DAS 28 (CRP)				.275
n	37	11	48	
Mean (SD)	3.88 (0.82)	4.20 (1.20)	3.95 (0.92)	
Median	3.91	4.40	4.09	
Range	1.65 - 5.16	1.65 - 5.80	1.65 - 5.80	
Skin manifestations				

Psoriatic arthritis (PsA)	PsA BT-n (n=38)	PsA BT-p (n=14)	Total PsA (n=52)	*p*
	n = 38	n = 14	n = 52	
Personal or family history of psoriasis	25 (65.8)	11 (78.6)	36 (69.2)	.506
Presence of skin psoriasis	34 (89.5)	9 (64.3)	43 (82.7)	**.048**
Type of psoriasis	n = 34	n = 9	n = 43	
Scaly or erythematous plaques	32 (94.1)	8 (88.9)	40 (93.0)	.515
Erythematous oral or genital lesions	4 (11.8)	0 (0)	4 (9.30)	.564
Nails	3 (8.82)	1 (11.1)	4 (9.30)	1.000
Radiological characteristics				
Type of lesion	n = 38	n = 14	n = 52	
Bone demineralization	4 (10.5)	3 (21.4)	7 (13.5)	.370
Bone erosion	12 (31.6)	5 (35.7)	17 (32.7)	1.000
Loss of joint space	13 (34.2)	7 (50.0)	20 (38.5)	.299
Ossification/complete fusion	2 (5.26)	2 (14.3)	4 (7.69)	.291
Patients with lesions, Yes	22 (57.9)	9 (64.3)	31 (59.6)	NC
Number of lesions per patient				.299
n	22	9	31	
1	14 (63.6)	4 (44.4)	18 (58.1)	
2	7 (31.8)	3 (33.3)	10 (32.3)	
3 or more	1 (4.55)	2 (22.2)	3 (9.68)	

Clinical forms of PsA	n=38	n=14	n=52	
1) Axial forms	18 (47.4)	5 (35.7)	23 (44.2)	.453
- Sacroiliac joints	16 (42.1)	3 (21.4)	19 (36.5)	.170
- Axial skeleton	11 (28.9)	3 (21.4)	14 (26.9)	.732
2) Axial and Peripheral forms	14 (36.8)	5 (35.7)	19 (36.5)	.940
3) Peripheral forms	34 (89.5)	13 (92.9)	47 (90.4)	1.000
Enthesis	16 (42.1)	4 (28.6)	20 (38.5)	.374
Insertions of quadricipital and patellar tendons	3 (18.8)	1 (25.0)	4 (20.0)	1.000
Insertions of calcaneal tendon and superficial plantar facia	11 (68.8)	4 (100)	15 (75.0)	.530
Chest	5 (31.3)	1 (25.0)	6 (30.0)	1.000
Affected peripheral joint	31 (81.6)	11 (78.6)	42 (80.8)	1.000
Hips	3 (9.68)	1 (9.09)	4 (9.52)	1.000
Distal interphalangeal joints	10 (32.3)	6 (54.5)	16 (38.1)	.281
Dactylitis	12 (38.7)	3 (27.3)	15 (35.7)	.717
Active synovitis	21 (67.7)	7 (63.6)	28 (66.7)	1.000
Type of Peripheral involvement				.659
n	31	12	43	
Unilateral	5 (16.1)	1 (8.33)	6 (14.0)	
Bilateral	26 (83.9)	11 (91.7)	37 (86.0)	
Extra-articular manifestations				
Number of extra-articular manifestations	n = 38	n = 12	n = 50	.240

Psoriatic arthritis (PsA)	PsA BT-n (n=38)	PsA BT-p (n=14)	Total PsA (n=52)	*p*
0	36 (94.7)	10 (83.3)	46 (92.0)	
1	2 (5.26)	2 (16.7)	4 (8.00)	
Type of extra-articular manifestation				
n	2	2	4	
Cardiac complications	0 (0)	1 (50.0)	1 (25.0)	
Other extra-articular manifestations	2 (100)	1 (50.0)	3 (75.0)	

14.1.4.3 Ankylosing spondylitis (AS)

Baseline clinical characteristics of AS patients with 2 years of follow-up are given in Table 32 below. Similar to the RA and PsA cohorts, mean rheumatic disease duration in AS patients was longer in BT-p than in BT-n participants (10.3 vs. 6.65 years, *p* <.001); 69.2% of patients were HLA-B27 positive and mean ESR was 16.6 mm/h. The mean CRP was significantly higher for BT-n patients than BT-p patients (13.7 mg/L vs. 10.7 mg/L, *p*= .013). The mean ASDAS ESR (available for 199 AS patients) was 2.87. The mean ASDAS CRP (available for 226 patients) was 3.15.

Radiological results (n=241): bone demineralization, complete fusion of joints and joint space loss was detected in 12.9%, 20.3% and 24.5% of patients, respectively. Bone erosion (34.9%) was found in a significantly greater proportion of BT-n than BT-p patients (41.0% vs. 22.5%, *p* = .005).

Clinical forms of AS (n=241): axial forms were observed in the majority of AS patients (95.4%): 159 had axial skeleton involvement (66.0%) and 206 had sacroiliac joint involvement (85.5%), the latter being more prevalent in BT-n than in BT-p patients (88.8% vs. 78.8%, *p*= .037).

Peripheral forms of AS occurred in a significantly higher proportion of BT-p than BT-n patients (66.3% vs. 47.8%, *p*= .007); enthesitis was also found in a greater percentage of BT-p than BT-n patients (48.8% vs. 31.1%, *p*= .007). Peripheral joint complications occurred in 35.3% of patients. Details of the types of peripheral joint afflictions are elaborated in Table 32. Both axial and peripheral forms of the disease were found together in a significantly higher proportion of BT-p versus BT-n participants (61.3% vs. 44.1%, *p*= .012). Extra-articular manifestations (n=241) were found in 75 AS patients (31.1%), of whom 48 (64.0%) had acute anterior uveitis and 21 (28.0%) had IBD.

Table 32: Baseline disease characteristics of AS patients with 2 years of follow-up by prior biotherapy

Ankylosing spondylitis (AS)	AS BT-n (n=161)	AS BT-p (n=80)	Total AS (n=241)	*p*
Duration since diagnostic (years)				**<.001**
n	152	76	228	
Mean (SD)	6.65 (8.62)	10.3 (9.95)	7.85 (9.22)	
Median	2.91	6.28	4.31	
Range	0.030 - 45.1	0.58 - 44.7	0.030 - 45.1	
Presence of HLA-B27 antibodies	n=161	n=79	n=240	
Yes, n (%)	116 (72.0)	50 (63.3)	166 (69.2)	.340
ESR (mm/h)				.596
n	141	67	208	
Mean (SD)	17.1 (17.0)	15.5 (16.8)	16.6 (16.9)	
Median	11.0	11.0	11.0	
Range	1.00 - 81.0	2.00 - 85.0	1.00 - 85.0	
CRP (mg/l)				**.013**

Ankylosing spondylitis (AS)	AS BT-n (n=161)	AS BT-p (n=80)	Total AS (n=241)	*p*
n	160	76	236	
Mean (SD)	13.7 (16.8)	10.7 (15.4)	12.7 (16.4)	
Median	6.80	4.00	6.00	
Range	0.50 - 88.0	0.22 - 73.0	0.22 - 88.0	
ASDAS (ESR)				.269
n	135	64	199	
Mean (SD)	2.83 (0.77)	2.95 (0.70)	2.87 (0.75)	
Median	2.84	2.87	2.84	
Range	0.96 - 5.16	1.05 - 4.78	0.96 - 5.16	
ASDAS (CRP)				.687
n	153	73	226	
Mean (SD)	3.16 (0.79)	3.12 (0.77)	3.15 (0.79)	
Median	3.18	3.17	3.18	
Range	1.35 - 5.39	1.35 - 5.33	1.35 - 5.39	
Radiological characteristics				
Type of radiological manifestation	n = 161	n = 80	n = 241	
Bone demineralization	18 (11.2)	13 (16.3)	31 (12.9)	.268
Bone erosion	66 (41.0)	18 (22.5)	84 (34.9)	**.005**
Loss of joint space	42 (26.1)	17 (21.3)	59 (24.5)	.411
Ossification/complete fusion	33 (20.5)	16 (20.0)	49 (20.3)	.928
Patients with lesions, Yes	107 (66.5)	47 (58.8)	154 (63.9)	NC
Number of lesions per patient				.416
n	107	47	154	
1	62 (57.9)	30 (63.8)	92 (59.7)	
2	40 (37.4)	17 (36.2)	57 (37.0)	
3 or more	5 (4.67)	0 (0)	5 (3.25)	
Clinical forms for AS	n = 161	n = 80	n = 241	
1) Axial forms	155 (96.3)	75 (93.8)	230 (95.4)	.513
- Sacroiliac joints	143 (88.8)	63 (78.8)	206 (85.5)	**.037**
- Axial skeleton	105 (65.2)	54 (67.5)	159 (66.0)	.725
2) Axial and peripheral forms	71 (44.1)	49 (61.3)	120 (49.8)	**.012**
3) Peripheral forms	77 (47.8)	53 (66.3)	130 (53.9)	**.007**
- Enthesitis	50 (31.1)	39 (48.8)	89 (36.9)	**.007**
Insertions of quadricipital and patellar tendons	5 (10.0)	10 (25.6)	15 (16.9)	.050
Insertions of calcaneal tendon and superficial plantar facia	27 (54.0)	25 (64.1)	52 (58.4)	.337
Chest	27 (54.0)	24 (61.5)	51 (57.3)	.476
- Affected peripheral joint	53 (32.9)	32 (40.0)	85 (35.3)	.279
Hips	16 (30.2)	14 (43.8)	30 (35.3)	.205
Distal interphalangeal joints	10 (18.9)	4 (12.5)	14 (16.5)	.443
Dactylitis	10 (18.9)	7 (21.9)	17 (20.0)	.737

Ankylosing spondylitis (AS)	AS BT-n (n=161)	AS BT-p (n=80)	Total AS (n=241)	*p*
Active synovitis	20 (37.7)	12 (37.5)	32 (37.6)	.983
Type of Peripheral involvement				.364
n	54	35	89	
Unilateral	18 (33.3)	15 (42.9)	33 (37.1)	
Bilateral	36 (66.7)	20 (57.1)	56 (62.9)	
Extra-articular manifestations				
Number of extra-articular manifestations	n = 161	n = 80	n = 241	**.026**
0	119 (73.9)	47 (58.8)	166 (68.9)	
1	38 (23.6)	27 (33.8)	65 (27.0)	
2	4 (2.48)	6 (7.50)	10 (4.15)	
Type of extra-articular manifestation				
n	42	33	75	
Acute anterior uveitis	26 (61.9)	22 (66.7)	48 (64.0)	
Inflammatory bowel disease	9 (21.4)	12 (36.4)	21 (28.0)	
Other	11 (26.2)	5 (15.2)	16 (21.3)	

14.1.5 Prior treatments at baseline for patients with 2 years of follow-up

14.1.5.1 Biotherapies

As mentioned above, 125 patients (32.1%) in the n=391 population had received at least one biotherapy prior to study initiation. Of these, the majority had received one line of biotherapy (n=60, 48.0%), 43 (34.4%) had received 2 lines, 15 (12.0%) had received 3 lines and 7 (5.60%) had received ≥4 lines of biotherapy (Table 33).

Among the 3 disease cohorts, PsA patients generally received the fewest lines of biotherapy (mean 1.57 ± 0.65 lines), followed by AS patients (mean 1.66 ± 0.71 lines), with RA patients having received the most lines of biotherapy (mean 2.26 ± 1.61 lines, *p*= .015).

The number of biotherapies received per patient in each disease group is presented in Table 33. The three most used prior biotherapies in the study cohort was etanercept (n=80, 64.0%), adalimumab (n=76, 60.8%) and infliximab (n=36, 28.8%). The main reason for discontinuing these 3 biotherapies was secondary failure: 52.5% for etanercept, 51.3% for adalimumab, and 50.0% for infliximab. The second most frequent reason for discontinuation was primary non-response for those who received etanercept (21.3%) and adalimumab (22.4%), and intolerance in those who received infliximab (30.6%).

Other previously prescribed biotherapies and reasons for discontinuation are detailed in Table 33. The duration of use was mostly less than one year for all biotherapies.

Table 33: Prior biotherapies at baseline for RA, PsA and AS patients with 2-years of follow-up

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
Previous biotherapy	31 (32.0)	14 (26.9)	80 (33.2)	125 (32.1)	0.679
No. of prior biotherapies per patient	n = 31	n = 14	n = 80	n = 125	.002
1	15 (48.4)	7 (50.0)	38 (47.5)	60 (48.0)	
2	6 (19.4)	6 (42.9)	31 (38.8)	43 (34.4)	
3	3 (9.68)	1 (7.14)	11 (13.8)	15 (12.0)	
4 and more	7 (22.6)	0 (0)	0 (0)	7 (5.60)	

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
n	31	14	80	125	**.015**
Mean (SD)	2.26 (1.61)	1.57 (0.65)	1.66 (0.71)	1.80 (1.03)	
Median	2.00	1.50	2.00	2.00	
Range	1.00 - 6.00	1.00 - 3.00	1.00 - 3.00	1.00 - 6.00	
	n = 59	n = 36	n = 187	n = 282	**< .001**
Abatacept	8 (25.8)	1 (7.14)	0 (0)	9 (7.20)	
Reason for withdrawal	n = 8	n = 1	n = 0	n = 9	
Primary non-response	2 (25.0)	1 (100)	-	3 (33.3)	
Intolerance	1 (12.5)	0 (0)	-	1 (11.1)	
Secondary failure	4 (50.0)	0 (0)	-	4 (44.4)	
Other reason	1 (12.5)	0 (0)	-	1 (11.1)	
Treatment duration	n = 8	n = 1	n = 0	n = 9	
Less than one year	5 (62.5)	1 (100)	-	6 (66.7)	
Between 1 and 2 years	2 (25.0)	0 (0)	-	2 (22.2)	
2 years and more	1 (12.5)	0 (0)	-	1 (11.1)	
	n = 31	n = 14	n = 80	n = 125	.262
Certolizumab	4 (12.9)	0 (0)	4 (5.00)	8 (6.40)	
Reason for withdrawal	n = 4	n = 0	n = 4	n = 8	
Primary non-response	0 (0)	0 (.)	1 (25.0)	1 (12.5)	
Intolerance	0 (0)	0 (.)	1 (25.0)	1 (12.5)	
Secondary failure	4 (100)	0 (.)	2 (50.0)	6 (75.0)	
Treatment duration	n = 4	n = 0	n = 3	n = 7	
Less than one year	1 (25.0)	0 (.)	3 (100)	4 (57.1)	
Between 1 and 2 years	2 (50.0)	0 (.)	0 (0)	2 (28.6)	
2 years and more	1 (25.0)	0 (.)	0 (0)	1 (14.3)	
	n = 31	n = 14	n = 80	n = 125	.423
Infliximab	6 (19.4)	4 (28.6)	26 (32.5)	36 (28.8)	
Reason for withdrawal	n = 6	n = 4	n = 26	n = 36	
Primary non-response	0 (0)	2 (50.0)	1 (3.85)	3 (8.33)	
Intolerance	2 (33.3)	2 (50.0)	7 (26.9)	11 (30.6)	
Secondary failure	4 (66.7)	0 (0)	14 (53.8)	18 (50.0)	
Other reason	0 (0)	1 (25.0)	4 (15.4)	5 (13.9)	
Treatment duration	n = 5	n = 3	n = 22	n = 30	
Less than one year	1 (20.0)	0 (0)	11 (50.0)	12 (40.0)	
Between 1 and 2 years	1 (20.0)	1 (33.3)	5 (22.7)	7 (23.3)	
2 years and more	3 (60.0)	2 (66.7)	6 (27.3)	11 (36.7)	
	n = 31	n = 14	n = 80	n = 125	**.002**
Rituximab	5 (16.1)	0 (0)	0 (0)	5 (4.00)	
Reason for withdrawal	n = 5	n = 0	n = 0	n = 5	
Primary non-response	2 (40.0)	-	-	2 (40.0)	
Intolerance	1 (20.0)	-	-	1 (20.0)	
Secondary failure	2 (40.0)	-	-	2 (40.0)	
Treatment duration	n = 4	n = 0	n = 0	n = 4	
Less than one year	3 (75.0)	-	-	3 (75.0)	
Between 1 and 2 years	1 (25.0)	-	-	1 (25.0)	

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
	n = 31	n = 14	n = 80	n = 125	.249
Adalimumab	16 (51.6)	7 (50.0)	53 (66.3)	76 (60.8)	
Reason for withdrawal	n = 16	n = 7	n = 53	n = 76	
Primary non-response	2 (12.5)	3 (42.9)	12 (22.6)	17 (22.4)	
Intolerance	5 (31.3)	0 (0)	5 (9.43)	10 (13.2)	
Secondary failure	6 (37.5)	2 (28.6)	31 (58.5)	39 (51.3)	
Other reason	3 (18.8)	2 (28.6)	8 (15.1)	13 (17.1)	
Treatment duration	n = 12	n = 6	n = 44	n = 62	
Less than one year	6 (50.0)	5 (83.3)	22 (50.0)	33 (53.2)	
Between 1 and 2 years	2 (16.7)	0 (0)	8 (18.2)	10 (16.1)	
2 years and more	4 (33.3)	1 (16.7)	14 (31.8)	19 (30.6)	
	n = 31	n = 14	n = 80	n = 125	.260
Etanercept	23 (74.2)	10 (71.4)	47 (58.8)	80 (64.0)	
Reason for withdrawal	n = 23	n = 10	n = 47	n = 80	
Primary non-response	4 (17.4)	1 (10.0)	12 (25.5)	17 (21.3)	
Intolerance	6 (26.1)	2 (20.0)	7 (14.9)	15 (18.8)	
Secondary failure	9 (39.1)	6 (60.0)	27 (57.4)	42 (52.5)	
Other reason	3 (13.0)	1 (10.0)	1 (2.13)	5 (6.25)	
Treatment duration	n = 17	n = 8	n = 35	n = 60	
Less than one year	8 (47.1)	3 (37.5)	16 (45.7)	27 (45.0)	
Between 1 and 2 years	4 (23.5)	1 (12.5)	5 (14.3)	10 (16.7)	
2 years and more	5 (29.4)	4 (50.0)	14 (40.0)	23 (38.3)	
	n = 31	n = 14	n = 80	n = 125	**< .001**
Tocilizumab	6 (19.4)	0 (0)	0 (0)	6 (4.80)	
Reason for withdrawal	n = 6	n = 0	n = 0	n = 6	
Intolerance	3 (50.0)	-	-	3 (50.0)	
Secondary failure	3 (50.0)	-	-	3 (50.0)	
Treatment duration	n = 6	n = 0	n = 0	n = 6	
Less than one year	2 (33.3)	-	-	2 (33.3)	
Between 1 and 2 years	1 (16.7)	-	-	1 (16.7)	
2 years and more	3 (50.0)	-	-	3 (50.0)	

14.1.5.2 DMARDs

DMARDs were prescribed to almost half the patients (n=194, 49.6%) in the n=391 cohort prior to golimumab initiation. Data on the types of DMARDs received and their status in patients are presented in Table 34 below.

Significant differences in prior DMARDs use were found between disease groups: the majority of RA and PsA patients, had been treated with DMARDs (85.7% and 76.9%, respectively), whereas less than a third of AS patients received DMARDs (29.0%, $p < .001$). These observations comply with standard clinical recommendations for prescribing DMARDs as a first line of treatment to RA and PsA patients.

Among patients who received DMARDs (n=194), MTX was most commonly prescribed (n=162, 83.5%), followed by sulfasalazine (n=64, 33.0%), leflunomide (n=37, 19.1%) and chloroquines (n=17, 8.76%). DMARD prescription patterns and reasons for discontinuation were variable between disease groups.

- MTX (n=162): in patients who received DMARDs, all PsA patients and almost all RA patients (n=78, 92.9%) received MTX, compared to 62.9% (n=44) of AS patients ($p < .001$). Overall,

56.2% of patients were continuing MTX at baseline, with no significant differences between disease groups. The most common reason for stopping MTX was intolerance in RA and PsA patients (24.4% and 22.5%, respectively). Primary non-response was the most common reason for MTX discontinuation in the AS group, resulting in over a third of patients stopping treatment (38.6%); comparatively, primary non-response was significantly lower in the PsA (17.5%) and RA groups (10.3%, *p*= .001).

- Sulfasalazine (n=64): A significantly higher proportion of AS patients (n=42, 60.0%) had a history of sulfasalazine use than PsA (n=8, 20.0%) and RA patients (n=14, 16.7%, *p* < .001).

  Only 1 PsA, 2 RA and 6 AS patients were continuing sulfasalazine at baseline. Primary non-response was the most frequent reason for discontinuation and was observed in 39.1% of patients who initiated sulfasalazine. A quarter of the patients stopped due to secondary failure, and 18.8% discontinued due to intolerance. Reasons for discontinuation were comparable among the three disease groups.
- Leflunomide (n=37): A higher proportion of PsA (n=11, 27.5%) and RA patients (n=21, 25.0%) were on leflunomide compared to AS patients (n=5, 7.14%, *p*= .006). At baseline, leflunomide was ongoing in 8 RA and 3 PsA and none of the AS patients were continuing the treatment. Intolerance was the most frequent reason for discontinuation (23.5%). Nevertheless, primary non-response was the most common reason for discontinuation in AS patients (38.6%) compared to PsA (17.5%) and RA patients (10.3%, *p*= .001).
- Chloroquines (n=17): A greater proportion of RA patients received chloroquines (n=13, 15.5%), compared to PsA (n=2, 5.00%) and AS patients (n=2, 2.86%, *p*= .017). At baseline, the treatment was ongoing in only 3 RA patients. Primary non-response was the most common reason for stopping the treatment, and was observed in almost half of the patients who received chloroquines.

Table 34: DMARDs treatment history at baseline for RA, PsA and AS patients with 2-years of follow-up

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
Prior DMARD	84 (85.7)	40 (76.9)	70 (29.0)	194 (49.6)	**< .001**
	n = 84	n = 40	n = 70	n = 194	
MTX	**78 (92.9)**	**40 (100)**	**44 (62.9)**	**162 (83.5)**	**< .001**
	n = 78	n = 40	n = 44	n = 162	
Ongoing	50 (64.1)	22 (55.0)	19 (43.2)	91 (56.2)	*0.081*
Reason for discontinuation					
Primary non-response	8 (10.3)	7 (17.5)	17 (38.6)	32 (19.8)	0.001
Intolerance	19 (24.4)	9 (22.5)	10 (22.7)	38 (23.5)	0.966
Secondary failure	7 (8.97)	3 (7.50)	3 (6.82)	13 (8.02)	1.000
Other reason	3 (3.85)	2 (5.00)	4 (9.09)	9 (5.56)	0.452
	n = 84	n = 40	n = 70	n = 194	
Leflunomide	**21 (25.0)**	**11 (27.5)**	**5 (7.14)**	**37 (19.1)**	**0.006**
	n = 21	n = 11	n = 5	n = 37	
Ongoing	8 (38.1)	3 (27.3)	0 (0)	11 (29.7)	0.360
Reason for discontinuation					
Primary non-response	2 (9.52)	4 (36.4)	3 (60.0)	9 (24.3)	0.032
Intolerance	7 (33.3)	2 (18.2)	2 (40.0)	11 (29.7)	0.600
Secondary failure	3 (14.3)	1 (9.09)	0 (0)	4 (10.8)	1.000
Other reason	1 (4.76)	1 (9.09)	0 (0)	2 (5.41)	1.000

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
	n = 84	n = 40	n = 70	n = 194	
Sulfasalazine	**14 (16.7)**	**8 (20.0)**	**42 (60.0)**	**64 (33.0)**	**< .001**
	n = 14	n = 8	n = 42	n = 64	
Ongoing	2 (14.3)	1 (12.5)	6 (14.3)	9 (14.1)	1.000
Reason for discontinuation					
Primary non-response	4 (28.6)	3 (37.5)	18 (42.9)	25 (39.1)	0.696
Intolerance	4 (28.6)	1 (12.5)	7 (16.7)	12 (18.8)	0.621
Secondary failure	4 (28.6)	2 (25.0)	10 (23.8)	16 (25.0)	0.911
Other reason	0 (0)	1 (12.5)	3 (7.14)	4 (6.25)	0.419
	n = 84	n = 40	n = 70	n = 194	
Hydroxychloroquine/ Chloroquine	**13 (15.5)**	**2 (5.00)**	**2 (2.86)**	**17 (8.76)**	**0.017**
	n = 13	n = 2	n = 2	n = 17	
Ongoing	3 (23.1)	0 (0)	0 (0)	3 (17.6)	1.000
Reason for withdrawal					
Primary non-response	4 (30.8)	2 (100)	2 (100)	8 (47.1)	0.029
Intolerance	2 (15.4)	0 (0)	0 (0)	2 (11.8)	1.000
Secondary failure	3 (23.1)	0 (0)	0 (0)	3 (17.6)	1.000
	n = 84	n = 40	n = 70	n = 194	
Other DMARDs	**3 (3.57)**	**4 (10.0)**	**0 (0)**	**7 (3.61)**	**0.018**
	n = 9	n = 5	n = 1	n = 15	
Ongoing	2 (66.7)	2 (50.0)	0 (.)	4 (57.1)	1.000
Reason for discontinuation					
Primary non-response	0 (0)	1 (25.0)	0 (.)	1 (14.3)	1.000
Intolerance	0 (0)	1 (25.0)	0 (.)	1 (14.3)	1.000
Secondary failure	1 (33.3)	0 (0)	0 (.)	1 (14.3)	0.429

14.1.5.3 Corticosteroids

A little under a third of the patients in the n=391 cohort (n=117, 29.9%) had received long term corticosteroids. As per disease group, corticosteroid use was more common in RA patients (n=61, 62.2%) than in PsA (n=20, 38.5%) and AS patients (n=36, 14.9%, $p < .001$).

The most used corticosteroid was prednisone/prednisolone/methylprednisolone (in 69.2% of patients who received corticosteroids) with no significant difference between disease groups. It was ongoing at the time of inclusion in about half of the patients (48.1%), but mainly in RA patients (66.7%) and less frequently in AS patients (16.7%, $p < .001$).

Prescription of Cortisone/Hydrocortisone was similar across all disease groups: it was prescribed to 31.6% of overall patients and was ongoing in 35.1% of patients who initiated the treatment. A lower proportion of AS patients (11.1%) were continuing the treatment compared to RA and PsA patients (38.1% and 57.1%, respectively).

For the 2 most commonly prescribed corticosteroids, reasons for discontinuation in the overall population were mostly “other” than primary non-response, intolerance or secondary failure. Further details are presented in Table 35.

Overall, corticosteroid discontinuations were more common in AS patients, as observed from the significantly lower number of AS patients ongoing treatment at baseline, relative to RA and PsA patients.

This was due to a higher frequency of primary non-responses in AS patients compared to RA and PsA patients.

Table 35: Corticosteroid treatment history at baseline for RA, PsA and AS patients with 2-years of follow-up

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
Corticosteroids	61 (62.2)	20 (38.5)	36 (14.9)	117 (29.9)	**<.001**
	n = 61	n = 20	n = 36	n = 117	
Cortisone/hydrocortisone	**21 (34.4)**	**7 (35.0)**	**9 (25.0)**	**37 (31.6)**	.589
	n = 21	n = 7	n = 9	n = 37	
Ongoing	8 (38.1)	4 (57.1)	1 (11.1)	13 (35.1)	.141
Reason for discontinuation					
Primary non-response	1 (4.76)	0 (0)	3 (33.3)	4 (10.8)	.065
Intolerance	3 (14.3)	0 (0)	2 (22.2)	5 (13.5)	.563
Secondary failure	1 (4.76)	0 (0)	0 (0)	1 (2.70)	1.000
Other reason	9 (42.9)	1 (14.3)	3 (33.3)	13 (35.1)	.465
	n = 61	n = 20	n = 36	n = 117	
Prednisone/prednisolone/ methylprednisolone	**42 (68.9)**	**15 (75.0)**	**24 (66.7)**	**81 (69.2)**	.807
	n = 42	n = 15	n = 24	n = 81	
Ongoing	28 (66.7)	7 (46.7)	4 (16.7)	39 (48.1)	**<.001**
Reason for discontinuation					
Primary non-response	2 (4.76)	3 (20.0)	7 (29.2)	12 (14.8)	**.017**
Intolerance	3 (7.14)	1 (6.67)	0 (0)	4 (4.94)	.401
Secondary failure	2 (4.76)	0 (0)	2 (8.33)	4 (4.94)	.648
Other reason	9 (21.4)	3 (20.0)	11 (45.8)	23 (28.4)	.092
	n = 61	n = 20	n = 36	n = 117	
Triamcinolone/ paramethasone	**0 (0)**	**0 (0)**	**3 (8.33)**	**3 (2.56)**	.058
	n = 0	n = 0	n = 3	n = 3	
Ongoing	-	-	0 (0)	0 (0)	NA
Reason for discontinuation					
Primary non-response	-	-	1 (33.3)	1 (33.3)	NA
Secondary failure	-	-	1 (33.3)	1 (33.3)	NA
Other reason	-	-	1 (33.3)	1 (33.3)	NA
	n = 61	n = 20	n = 36	n = 117	
Betamethasone/ Dexamethasone/cortivazol	**0 (0)**	**0 (0)**	**1 (2.78)**	**1 (0.85)**	.479
	n = 0	n = 0	n = 1	n = 1	
Ongoing	0 (0)	-	0 (0)	0 (0)	NA
Reason for discontinuation					
Primary non-response	0 (.)	0 (.)	1 (100)	1 (100)	NA

14.1.5.4 NSAIDs/analgesics

The majority of patients, particularly those with AS and PsA had received at least one NSAID/Analgesic at baseline (90.0% of AS patients, 86.5% of PsA patients and 73.5% of RA patients, *p*= .001).

The most prescribed NSAID in the total cohort was paracetamol (59.6%), with a significantly higher proportion of RA patients (79.2%) having received the drug, compared to PsA (60.0%) and AS patients (53.0%, *p* < .001). Aspirin/ibuprofen/coxibs were used in 35.3% patients, and were prescribed to 41.0% of AS patients, 26.7% of PsA patients and 23.6% of RA patients (*p*= .012). Nefopam was mainly prescribed to patients in the AS group (5 AS patients out of 6 in the cohort who were prescribed Nefopam). Opioids were received by 17.4% of the patients. A higher proportion of PsA patients (53.3%) were prescribed other NSAIDs/analgesics compared to AS (48.8%) and RA patients (31.9%, *p*= .025).

According to standard recommendations and clinical practice, AS patients should receive NSAIDs as a first line of treatment. In this study cohort, 24 AS patients (9.96%) did not report any prior NSAID/analgesic use. Of these, 4 had previously received biotherapy, 20 patients were naïve to biotherapy and 17 patients were naïve to both biotherapy and DMARDs.

Altogether, these data indicate that golimumab utilization conformed to the IFU in terms of prior NSAID treatment, particularly in AS patients.

Table 36: NSAID and analgesic treatment history at baseline for RA, PsA and AS patients with 2-years of follow-up

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
NSAIDs/Analgesics, Yes	72 (73.5)	45 (86.5)	217 (90.0)	334 (85.4)	**.001**
n	72	45	217	334	
Paracetamol	57 (79.2)	27 (60.0)	115 (53.0)	199 (59.6)	**< .001**
Aspirin/ibuprofen/coxibs	17 (23.6)	12 (26.7)	89 (41.0)	118 (35.3)	**.012**
Opioid	14 (19.4)	6 (13.3)	38 (17.5)	58 (17.4)	.694
Nefopam	1 (1.39)	0 (0)	5 (2.30)	6 (1.80)	.842
Other NSAIDs/Analgesics	23 (31.9)	24 (53.3)	106 (48.8)	153 (45.8)	**.025**

14.1.5.5 Prior surgical treatment

Local surgery history at baseline for the n=391 population is presented in Table 37. Almost one third of patients (26.9%) had a history of surgical therapies related to rheumatic disease, with a significantly higher percentage of RA (38.8%) and PsA (44.2%) patients having undergone local surgery relative to AS patients (18.3%, *p*< .001). The main surgical procedure in this study cohort was joint injections (85.7% of all local surgeries), with differences between the three disease groups being non-significant.

Table 37: Surgical treatment history at baseline for RA, PsA and AS patients with 2-years of follow-up

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
Local/surgical treatment, Yes	38 (38.8)	23 (44.2)	44 (18.3)	105 (26.9)	**< .001**
n	38	23	44	105	
Joint injections	32 (84.2)	20 (87.0)	38 (86.4)	90 (85.7)	1.000
Synoviorthesis	3 (7.89)	0 (0)	5 (11.4)	8 (7.62)	.288
Synovectomy	3 (7.89)	0 (0)	1 (2.27)	4 (3.81)	.345

	RA (n=98)	PsA (n=52)	AS (n=241)	Total (n=391)	*p*
Bone fusion	4 (10.5)	1 (4.35)	0 (0)	5 (4.76)	.072
Joint replacement	4 (10.5)	3 (13.0)	3 (6.82)	10 (9.52)	.698
Other surgical procedure	4 (10.5)	3 (13.0)	4 (9.09)	11 (10.5)	.919

14.2 Initial Golimumab prescription in patients with 2-years of follow-up

Initial golimumab prescription in the n=391 population was similar between BT-n and BT-p patients in all three disease groups, and in most cases, was in line with the IFU in terms of unit dose and dosage frequency (50 mg once a month). The mean initial golimumab prescription duration was around 5 months in all disease groups, and similar for BT-n and BT-p patients. Further details are presented in Table 38 below.

- **Rheumatoid arthritis**

Prior biotherapy information was available for 97 of the 98 RA patients in the n=391 population. All patients in the RA cohort were prescribed golimumab 50 mg once a month, as per the IFU. The mean and median duration of prescription was 5.19 and 6.00 months, respectively, and ranged between 2 to 12 months (Table 38).

- **Psoriatic arthritis**

Initial golimumab prescription was comparable between BT-n and BT-p PsA patients, and in line with the IFU in most cases. Only 2 of 52 PsA patients (3.85%) were prescribed a 100 mg dose of golimumab, all of them BT-n. As for golimumab dosage frequency, this was once a month in all PsA patients. The average prescription duration was 5.23 months, median 4.00, and ranging between 1 to 12 months (Table 38).

- **Ankylosing spondylitis**

Initial golimumab prescription data was available for 235 of 241 AS patients with 2 years of follow-up. Golimumab was prescribed in accordance with the IFU in most cases: only 2 (0.85%) BT-p patients received 100 mg golimumab. As for golimumab dosage frequency, this was once a month in all AS patients. The average prescription duration was 5.31 months, median 6.00 months, and ranging between 2 to 12 months. Further details are provided in Table 38 below.

Table 38 : Initial prescription of golimumab in RA, PsA and AS patients with 2 years of follow-up by prior biotherapy

Rheumatoid arthritis (RA)	RA BT-n (n=66)	RA BT-p (n=31)	Total RA (n=97 [a])	*p*
Dosage (mg)				NA
n	66	31	97	
50	66 (100)	31 (100)	97 (100)	
Dose /month				NA
n	66	31	97	
1	66 (100)	31 (100)	97 (100)	
Prescription duration (month)				.626
n	66	31	97	
Mean (SD)	5.14 (2.60)	5.29 (2.66)	5.19 (2.60)	
Median	5.50	6.00	6.00	
Range	2.00 - 12.0	2.00 - 12.0	2.00 - 12.0	

Psoriatic arthritis (PsA)	PsA BT-n (n=38)	PsA BT-p (n=14)	Total PsA (n=52)	*p*
Dosage (mg)				1.000
n	38	14	52	
50	36 (94.7)	14 (100)	50 (96.2)	
100	2 (5.26)	0 (0)	2 (3.85)	
Dose /month				
n	38	14	52	NA
1	38 (100)	14 (100)	52 (100)	
Prescription duration (month)				0.142
n	38	14	52	
Mean (SD)	4.97 (2.81)	5.93 (2.87)	5.23 (2.83)	
Median	4.00	6.00	4.00	
Range	1.00 - 12.0	3.00 - 12.0	1.00 - 12.0	
Ankylosing spondylitis (AS)	**AS BT-n (n=161)**	**AS BT-p (n=80)**	**Total AS (n=241)**	***p***
Dosage (mg)				.109
n	157	78	235	
50	157 (100)	76 (97.4)	233 (99.1)	
100	0 (0)	2 (2.56)	2 (0.85)	
Dose /month				NA
n	157	78	235	
1	157 (100)	78 (100)	235 (100)	
Prescription duration (month)				.547
n	156	78	234	
Mean (SD)	5.31 (2.80)	5.29 (2.40)	5.31 (2.67)	
Median	6.00	6.00	6.00	
Range	2.00 - 12.0	2.00 - 12.0	2.00 - 12.0	

14.3 Baseline concomitant treatments in patients with 2 years of follow-up

Other treatments co-prescribed with initial golimumab prescriptions in the n=391 population are presented in Table 39 below. Golimumab was prescribed in combination with other treatments to 325 (83.3%) patients in the n=391 population: by disease group, 95.9% (n=93) of RA patients, 84.6% (n=44) of PsA patients and 78.0% (n=188) of AS patients received co-treatments at baseline.

DMARDs: DMARDs were co-prescribed to 157 (48.3%) patients in the n=391 population at baseline, and similarly between BT-n and BT-p groups. Among them, oral MTX was prescribed to 77 (49.0%) patients and parenteral MTX to 51 (32.5%) patients. DMARDs were co-prescribed more frequently to RA patients (92.5%) compared to PsA (72.7%) and AS patients (20.7%). This observation complies with the IFU for golimumab treatment associations in the three indications.

NSAIDs/analgesics: NSAIDs/analgesics were co-prescribed with golimumab to 271 (83.4%) patients in the n=391 population, and similarly between BT-n and BT-p patients. Other NSAIDs/analgesics were used in most patients (64.2%), followed by paracetamol (39.1%), opioids (13.3%), coxibs (10.7%), ibuprofen (4.80%) and nefopam in only 2 (0.74%) patients. NSAIDs/analgesics were co-prescribed to a higher proportion of PsA (73.1%) and AS patients (72.2%), compared to RA patients (60.8%).

Corticosteroids: Corticosteroid prescriptions were similar in the BT-n and BT-p groups; it was prescribed with golimumab at baseline to 72 (22.2%) patients. Prednisone/prednisolone and cortisone/hydrocortisone were predominantly used (61.1% and 38.9%, respectively). Corticosteroids were prescribed in association with golimumab almost half of RA patients (48.4%), in a third of PsA patients (34.1%) and in a minority of AS patients (6.38%).

Table 39: Concomitant treatments at baseline by prior biotherapy for the entire cohort with 2 years of follow-up

	Biotherapy-naive patients (n=265)	Bio-pretreated patients (n=125)	Total (n=390 [a])	*p*
Concomitant treatments	223 (84.2)	102 (81.6)	325 (83.3)	.528
	n = 223	n = 102	n = 325	
1) DMARDs	**111 (49.8)**	**46 (45.1)**	**157 (48.3)**	
	n = 111	n = 46	n = 157	
MTX (oral)	51 (45.9)	26 (56.5)	77 (49.0)	.228
MTX (parenteral)	38 (34.2)	13 (28.3)	51 (32.5)	.467
Sulfasalazine	10 (9.01)	3 (6.52)	13 (8.28)	.757
Leflunomide	12 (10.8)	2 (4.35)	14 (8.92)	.236
Hydroxychloroquine/ Chloroquine	2 (1.80)	1 (2.17)	3 (1.91)	1.000
Other DMARDs	2 (1.80)	2 (4.35)	4 (2.55)	.581
	n = 223	n = 102	n = 325	
2) Corticosteroids	**51 (22.9)**	**21 (20.6)**	**72 (22.2)**	
	n = 51	n = 21	n = 72	
Cortisone/hydrocortisone	18 (35.3)	10 (47.6)	28 (38.9)	.330
Prednisone/prednisolone/ methylprednisolone	32 (62.7)	12 (57.1)	44 (61.1)	.658
Other corticosteroids	2 (3.92)	1 (4.76)	3 (4.17)	1.000
	n = 223	n = 102	n = 325	
NSAIDs/analgesics	**182 (81.6)**	**89 (87.3)**	**271 (83.4)**	
	n = 182	n = 89	n = 271	
Ibuprofen	9 (4.95)	4 (4.49)	13 (4.80)	1.000
Coxibs	21 (11.5)	8 (8.99)	29 (10.7)	.524
Paracetamol	64 (35.2)	42 (47.2)	106 (39.1)	.057
Opioids	20 (11.0)	16 (18.0)	36 (13.3)	.111
Nefopam	1 (0.55)	1 (1.12)	2 (0.74)	.550
Other NSAIDs/analgesics	123 (67.6)	51 (57.3)	174 (64.2)	.097

[a] Prior biotherapy data was missing for 1 patient in n=391

14.3.1 Baseline concomitant treatments in RA patients with 2 years of follow-up

Data on baseline concomitant treatments in the RA cohort by prior biotherapy is given in Table 40 below.

Almost all RA patients in the n=391 population were prescribed other treatments with golimumab at baseline (n=93, 95.9%), of whom 86 (92.5%) were given DMARDs, 59 (63.4%) were prescribed NSAIDs/analgesics, and 45 (48.4%) were given corticosteroids. A higher proportion of BT-n than BT-p patients were co-prescribed DMARDs (96.9% vs. 82.1%) and corticosteroids (53.8% vs. 35.7%).

Conversely, a greater proportion of BT-p RA patients received NSAIDs/analgesics (78.6%) compared to BT-n patients (56.9%).

Among patients who were co-prescribed DMARDs (n=86), 44 (51.2%) received oral MTX, 31 (36.0%) received parenteral MTX, and 8 (9.30%) received leflunomide. Among the 59 patients who were prescribed NSAIDs/analgesics, the majority were given paracetamol (n=34, 57.6%), followed by "other" (unspecified) NSAIDs/analgesics (n=30, 50.8%), opioids (n=8, 13.6%) and then ibuprofen (n=5, 8.47%).

Of patients who were given corticosteroids (n=45), 27 (60.0%) received prednisolone/ methylprednisolone and 20 (44.4%) received cortisone/hydrocortisone.

Table 40: Concomitant treatments at baseline by prior biotherapy for RA patients with 2 years of follow-up

Rheumatoid arthritis (RA)	Biotherapy-naive patients (n=66)	Bio-pretreated patients (n=31)	Total (n=97 [a])	*p*
Concomitant treatments	65 (98.5)	28 (90.3)	93 (95.9)	.095
	n = 65	n = 28	n = 93	
1) DMARDs	**63 (96.9)**	**23 (82.1)**	**86 (92.5)**	
	n = 63	n = 23	n = 86	
MTX (oral)	30 (47.6)	14 (60.9)	44 (51.2)	.277
MTX (parenteral)	25 (39.7)	6 (26.1)	31 (36.0)	.245
Sulfasalazine	1 (1.59)	1 (4.35)	2 (2.33)	.466
Leflunomide	7 (11.1)	1 (4.35)	8 (9.30)	.676
Hydroxychloroquine/ Chloroquine	2 (3.17)	1 (4.35)	3 (3.49)	1.000
Other DMARDs	1 (1.59)	0 (0)	1 (1.16)	1.000
	n = 65	n = 28	n = 93	
2) Corticosteroids	**35 (53.8)**	**10 (35.7)**	**45 (48.4)**	
	n = 35	n = 10	n = 45	
Cortisone/hydrocortisone	14 (40.0)	6 (60.0)	20 (44.4)	.301
Prednisone/prednisolone/ methylprednisolone	22 (62.9)	5 (50.0)	27 (60.0)	.489
	n = 65	n = 28	n = 93	
NSAIDs/analgesics	**37 (56.9)**	**22 (78.6)**	**59 (63.4)**	
	n = 37	n = 22	n = 59	
Ibuprofen	3 (8.11)	2 (9.09)	5 (8.47)	1.000
Paracetamol	20 (54.1)	14 (63.6)	34 (57.6)	.471
Opioids	4 (10.8)	4 (18.2)	8 (13.6)	.455
Other NSAIDs/analgesics	18 (48.6)	12 (54.5)	30 (50.8)	.661

[a] Prior biotherapy data was missing for 1 patient with RA (n=98)

14.3.2 Baseline concomitant treatments in PsA patients with 2 years of follow-up

The majority of PsA patients were prescribed other treatments with golimumab at baseline (n=44, 84.6%), of whom 38 (86.4%) received NSAIDs/analgesics, followed by 32 (72.7%) who received DMARDs and then 15 (34.1%) who received corticosteroids.

All BT-p PsA patients were co-prescribed NSAIDs/analgesics at baseline, compared to 4 of 5 BT-n PsA patients (81.3%). Of the 38 patients who were co-prescribed NSAIDs/analgesics, the majority were

given other NSAIDs/analgesics (n=26, 68.4%), followed by paracetamol (n=12, 31.6%), coxibs (n=5, 13.2%) and then opioids (n=3, 7.89%).

Among patients who were co-prescribed DMARDs (n=32), 16 (50.0%) received oral MTX and 10 (31.3%) received parenteral MTX. Leflunomide was co-prescribed to 4 (12.5%) patients.

Of the 15 patients who were co-prescribed corticosteroids, 9 (60.0%) received prednisolone/ methylprednisolone and 7 (46.7%) received cortisone/hydrocortisone. Baseline concomitant treatments in PsA patients with 2 years of follow-up are presented in Table 41.

Table 41: Concomitant treatments at baseline by prior biotherapy for PsA patients with 2 years of follow-up

Psoriatic arthritis (PsA)	Biotherapy-naive patients (n=38)	Bio-pretreated patients (n=14)	Total (n=52)	*p*
Concomitant treatments	32 (84.2)	12 (85.7)	44 (84.6)	1.000
	n = 32	**n = 12**	**n = 44**	
1) DMARDs	25 (78.1)	7 (58.3)	32 (72.7)	
	n = 25	**n = 7**	**n = 32**	
MTX (oral)	12 (48.0)	4 (57.1)	16 (50.0)	1.000
MTX (parenteral)	7 (28.0)	3 (42.9)	10 (31.3)	.648
Leflunomide	4 (16.0)	0 (0)	4 (12.5)	.552
	n = 32	**n = 12**	**n = 44**	
2) Corticosteroids	11 (34.4)	4 (33.3)	15 (34.1)	
	n = 11	**n = 4**	**n = 15**	
Cortisone/hydrocortisone	4 (36.4)	3 (75.0)	7 (46.7)	.282
Prednisone/prednisolone/ methylprednisolone	7 (63.6)	2 (50.0)	9 (60.0)	1.000
	n = 32	**n = 12**	**n = 44**	
NSAIDs/analgesics	26 (81.3)	12 (100.0)	38 (86.4)	
	n = 26	**n = 12**	**n = 38**	
Coxibs	3 (11.5)	2 (16.7)	5 (13.2)	.643
Paracetamol	8 (30.8)	4 (33.3)	12 (31.6)	1.000
Opioids	3 (11.5)	0 (0)	3 (7.89)	.538
Other NSAIDs/analgesics	18 (69.2)	8 (66.7)	26 (68.4)	1.000

14.3.3 Baseline concomitant treatments in AS patients with 2 years of follow-up

Most AS patients were prescribed other treatments with golimumab at baseline (n=188, 78.0%); however, they were lower than the proportion of RA (95.9%) and PsA patients (84.6%) who were co-prescribed a treatment at baseline. Among AS patients who received another co-treatment (n=188), the majority got NSAIDs (n=174, 92.6%), followed by a fifth of patients who received DMARDs (n=39, 20.7%), and then 12 (6.38%) who received corticosteroids. A higher proportion of BT-p than BT-n patients were co-prescribed corticosteroids (11.3% vs. 3.97%).

Among 174 patients co-prescribed with NSAIDs/analgesics, the majority received other NSAIDs/analgesics (n=118, 67.8%), followed by paracetamol (n=60, 34.5%), opioids (n=25, 14.4%), coxibs (n=24, 13.8%) and ibuprofen (n=8, 4.60%). A significantly higher percentage of BT-n versus BT-p patients received “other” (unspecified) NSAIDs (73.1 vs. 56.4%, *p*= .028).

In patients who were co-prescribed DMARDs (n=39), 17 (43.6%) and 10 (25.6%) patients received oral and parenteral MTX, respectively. Sulfasalazine was the next frequently co-prescribed DMARD (n=9, 23.1%). In patients who received corticosteroids as co-treatment (n=12), most (n=8, 66.7%) received prednisolone/ methylprednisolone, followed by 3 patients (25.0%) who received "other" unspecified corticosteroids, and 1 patient who was co-prescribed cortisone/ hydrocortisone.

Baseline concomitant therapies in AS patients with 2 years of follow-up are given in Table 42 below.

Table 42: Concomitant treatments at baseline by prior biotherapy for AS patients with 2-years of follow-up

Ankylosing spondylitis (AS)	Biotherapy-naive patients (n=161)	Bio-pretreated patients (n=80)	Total (n=241)	*p*
Concomitant treatments	126 (78.3)	62 (77.5)	188 (78.0)	.893
	n = 126	**n = 62**	**n = 188**	
1) DMARDs	23 (18.3)	16 (25.8)	39 (20.7)	
	n = 23	**n = 16**	**n = 39**	
MTX (oral)	9 (39.1)	8 (50.0)	17 (43.6)	.501
MTX (parenteral)	6 (26.1)	4 (25.0)	10 (25.6)	1.000
Sulfasalazine	7 (30.4)	2 (12.5)	9 (23.1)	.262
Leflunomide	1 (4.35)	1 (6.25)	2 (5.13)	1.000
Other DMARDs	1 (4.35)	2 (12.5)	3 (7.69)	.557
	n = 126	**n = 62**	**n = 188**	
2) Corticosteroids	5 (3.97)	7 (11.3)	12 (6.38)	
	n = 5	**n = 7**	**n = 12**	
Cortisone/hydrocortisone	0 (0)	1 (14.3)	1 (8.33)	1.000
Prednisone/prednisolone/ methylprednisolone	3 (60.0)	5 (71.4)	8 (66.7)	1.000
Other corticosteroids	2 (40.0)	1 (14.3)	3 (25.0)	.523
	n = 126	**n = 62**	**n = 188**	
NSAIDs/analgesics	119 (94.4)	55 (88.7)	174 (92.6)	
	n = 119	**n = 55**	**n = 174**	
Ibuprofen	6 (5.04)	2 (3.64)	8 (4.60)	1.000
Coxibs	18 (15.1)	6 (10.9)	24 (13.8)	.453
Paracetamol	36 (30.3)	24 (43.6)	60 (34.5)	.084
Opioids	13 (10.9)	12 (21.8)	25 (14.4)	.179
Nefopam	1 (0.84)	1 (1.82)	2 (1.15)	.534
Other NSAIDs/analgesics	87 (73.1)	31 (56.4)	118 (67.8)	**.028**

14.4 Comparison of patients continuing golimumab at 2 years with those who discontinued after 1 year

A higher proportion of PsA patients (18.9%) had discontinued golimumab after 1 year compared to AS (11.9%) and RA patients (8.24%). Golimumab was ongoing in 52.4% of RA, 47.7% of AS and 42.5% of PsA patients at 2 years. These results are shown in Table 43.

Table 43: Number of participants who stopped golimumab treatment after 1 year and those continuing treatment at 2 years by pathology

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)
Golimumab discontinued after 1 year	14 (8.24)	20 (18.9)	57 (11.9)	91 (12.1)
Golimumab persisting at 2 years	89 (52.4)	45 (42.5)	228 (47.7)	362 (48.0) [a]

a: Percentage of patients persisting on golimumab corresponds to the worse-case scenario, shown in section 15.1

14.4.1 Baseline sociodemographic characteristics

Table 44: Sociodemographic characteristics of patients who stopped golimumab after a year versus those who continued at 2 years in the total cohort

	GLM discontinued after 1 year (n=91)	GLM persisting at 2 years (n=362)	*p*
Age			.503
n	90	362	
Mean (SD)	45.2 (12.7)	46.2 (13.3)	
Median	46.0	45.0	
Range	19.0 - 76.0	21.0 - 82.0	
Gender, n (%)			**.001**
n	91	362	
Male	25 (27.5)	171 (47.2)	
Female	66 (72.5)	191 (52.8)	
BMI, n (%)			.293
n	90	358	
< 18.5 kg/m^2	6 (6.67)	9 (2.51)	
18.5 - 24.9 kg/m^2	36 (40.0)	155 (43.3)	
25 - 29.9 kg/m^2	29 (32.2)	115 (32.1)	
>30 Kg/m^2	19 (21.1)	79 (22.1)	
Socio-professional category (SPC)			
n	91	362	NC
Part-time employment	13 (14.3)	55 (15.2)	
Full-time employment	41 (45.1)	165 (45.6)	
Student	0 (0)	5 (1.38)	
Retired	12 (13.2)	54 (14.9)	
Unemployed	8 (8.79)	40 (11.0)	
Stay-at-home husband/wife	0 (0)	13 (3.59)	
Disability/ unable to work	14 (15.4)	23 (6.35)	
2 SPCs provided	3 (3.30)	7 (1.93)	

GLM = golimumab

Sociodemographic characteristics of patients who withdrew from golimumab therapy after a year and those who continued up to 2 years are compared in Table 44 above.

Mean age of patients in both subgroups were comparable: for those who stopped golimumab after a year, 45.2 years and for the latter 46.2 years. The proportion of females who discontinued golimumab after a year were significantly higher than the proportion persisting on treatment at 2 years (72.5% vs. 52.8%, *p*= .001). BMI and SPC distributions were comparable between the two patient groups.

14.4.2 Comorbidities at baseline

The prevalence of co-morbidities in the two patient groups were similar, as detailed in Table 45. The majority of patients suffered from at least one co-morbidity (86.8% in the golimumab discontinuation group and 84.3% in the golimumab persistence group). Also, most patients had 2 comorbidities at baseline (25.3% of patients who discontinued after a year and 26.5% of patients who persisted on golimumab at 2 years).

The following baseline co-morbidities were significantly more common in patients who discontinued golimumab after a year compared to those who persisted with golimumab up to 2 years: asthma (13.2% vs. 4.87%, *p*= .016), thyroid disease (17.8% vs. 8.01%, *p*= .012), gastrointestinal disease (16.4% vs. 5.48%, *p*= .001) and malignant disease (8.11% vs. 2.58%, *p*= .034).

Table 45: Medical history and co-morbidities at baseline for patients stopping golimumab after a year versus those persisting on the treatment at 2 years

	GLM discontinued after 1 year (n=91)	GLM persisting at 2 years (n=362)	*p*
Number of co-morbidities	n = 91	n = 362	.222
0	12 (13.2)	57 (15.7)	
1	15 (16.5)	90 (24.9)	
2	23 (25.3)	96 (26.5)	
3	21 (23.1)	64 (17.7)	
4 or more	20 (22.0)	55 (15.2)	
At least one comorbidity	79 (86.8)	305 (84.3)	.544
Tobacco consumption	n = 75	n = 316	.817
	36 (48.0)	147 (46.5)	
IBD	n = 74	n = 307	.992
	6 (8.11)	25 (8.14)	
Uveitis	n = 73	n = 311	.389
	9 (12.3)	51 (16.4)	
Psoriasis	n = 77	n = 311	.249
	28 (36.4)	92 (29.6)	
Hypertension	n = 75	n = 312	.239
	19 (25.3)	60 (19.2)	
Type I or II diabetes	n = 74	n = 309	.309
	7 (9.46)	19 (6.15)	
Asthma	n = 76	n = 308	**.016**
	10 (13.2)	15 (4.87)	
Lung disease	n = 73	n = 308	.142

	GLM discontinued after 1 year (n=91)	GLM persisting at 2 years (n=362)	*p*
	1 (1.37)	18 (5.84)	
Liver disease	n = 74	n = 307	.342
	5 (6.76)	12 (3.91)	
Thyroid disease	n = 73	n = 312	**.012**
	13 (17.8)	25 (8.01)	
Gastrointestinal disease	n = 73	n = 310	**.001**
	12 (16.4)	17 (5.48)	
Malignant disease	n = 74	n = 310	**.034**
	6 (8.11)	8 (2.58)	
Depressive disorder	n = 75	n = 310	.610
	9 (12.0)	31 (10.0)	
Prior surgery	n = 76	n = 315	.076
	46 (60.5)	155 (49.2)	
Other physical illness	n = 76	n = 308	.167
	7 (9.21)	15 (4.87)	

14.4.3 Baseline disease characteristics in RA, PsA and AS patients

- **Rheumatoid arthritis (RA)**

Of 170 RA patients included in the study, 14 (8.24%) discontinued golimumab after a year and 89 (52.4%) persisted on the treatment at 2 years. Baseline disease characteristics for RA patients who discontinued golimumab after a year versus those who persisted on it at 2 years were comparable: including duration since disease diagnosis, presence of rheumatoid factors and ani-CCP, mean ESR and CRP, mean DAS ESR and DAS CPR, radiological characteristics and extra-articular manifestations. These are presented in Table 46 below.

Table 46: Baseline clinical characteristics of RA patients who discontinued golimumab after 1 year versus those persisting on the treatment at 2 years

Rheumatoid arthritis (RA)	GLM discontinued after 1 year (n=14)	GLM persisting at 2 years (n=89)	Total (n=103)	*p*
Duration since diagnosis (years)	n = 14	n = 87	n = 101	0.988
Mean (SD)	7.57 (6.56)	8.32 (10.1)	8.22 (9.65)	
Median	5.22	5.02	5.02	
Range	0.53 - 19.1	0.23 - 63.3	0.23 - 63.3	
Presence of rheumatoid factors	n = 14	n = 89	n = 103	.753
	11 (78.6)	64 (71.9)	75 (72.8)	
Presence of CCP antibodies	n = 14	n = 87	n = 101	.369
	11 (78.6)	55 (63.2)	66 (65.3)	
ESR (mm/h)	n = 14	n = 78	n = 92	.948
Mean (SD)	20.1 (17.6)	18.9 (14.1)	19.1 (14.6)	
Median	16.0	16.0	16.0	

Rheumatoid arthritis (RA)	GLM discontinued after 1 year (n=14)	GLM persisting at 2 years (n=89)	Total (n=103)	*p*
Range	1.00 - 67.0	2.00 - 60.0	1.00 - 67.0	
CRP (mg/l)	n = 13	n = 88	n = 101	.776
Mean (SD)	15.6 (25.7)	9.42 (11.2)	10.2 (13.9)	
Median	4.30	5.03	5.00	
Range	1.00 - 95.0	0 - 62.0	0 - 95.0	
DAS 28 (ESR)	n = 14	n = 75	n = 89	.625
Mean (SD)	4.25 (1.65)	4.44 (1.29)	4.41 (1.35)	
Median	4.78	4.57	4.57	
Range	0.68 - 6.64	1.53 - 7.14	0.68 - 7.14	
DAS 28 (CRP)	n = 13	n = 85	n = 98	.802
Mean (SD)	4.30 (1.08)	4.19 (1.16)	4.21 (1.15)	
Median	4.33	4.20	4.24	
Range	2.09 - 6.30	1.41 - 7.18	1.41 - 7.18	
Radiological characteristics				
Type of radiological manifestation	n = 14	n = 89	n = 103	
Bone demineralization	4 (28.6)	28 (31.5)	32 (31.1)	1.000
Bone erosion	7 (50.0)	48 (53.9)	55 (53.4)	0.784
Loss of joint space	4 (28.6)	36 (40.4)	40 (38.8)	0.397
Ossification/complete fusion	0 (0)	1 (1.12)	1 (0.97)	1.000
Patients with lesions, Yes	11 (78.6)	71 (79.8)	82 (79.6)	
Number of lesions per patient	n = 11	n = 71	n = 82	.473
1	7 (63.6)	40 (56.3)	47 (57.3)	
2	4 (36.4)	20 (28.2)	24 (29.3)	
3 or more	0 (0)	11 (15.5)	11 (13.4)	
Extra-articular manifestations				
Number of extra-articular manifestations	n = 14	n = 89	n = 103	1.000
1	2 (14.3)	11 (12.4)	13 (12.6)	
Type of extra-articular manifestation	n = 2	n = 11	n = 13	
Pleuro-pulmonary complications	0 (0)	4 (36.4)	4 (30.8)	1.000
Others	2 (100)	7 (63.6)	9 (69.2)	1. 000

- **Psoriatic arthritis (PsA)**

Of 106 RA patients included in the study, 19 (18.9%) discontinued golimumab after 1 year and 45 (42.5%) were continuing the treatment at 2 years. Most baseline disease characteristics for PsA patients in both treatment duration groups were similar, including duration since disease diagnosis, rheumatoid factors, mean DAS ESR and DAS CPR, skin manifestations, radiological characteristics, clinical forms and extra-articular manifestations. These are detailed in Table 47 below.

Table 47: Baseline clinical characteristics of PsA patients who discontinued golimumab after 1 year versus those persisting on the treatment at 2 years

Psoriatic arthritis (PsA)	Discontinuation after 1 year (n=20)	Persisting at 2 years (n=45)	Total (n=65)	*p*
Duration since diagnosis (years)	n = 19	n = 41	n = 60	.348
Mean (SD)	6.69 (6.15)	6.27 (7.53)	6.40 (7.07)	
Median	4.08	2.87	2.96	
Range	0.64 - 19.7	0.068 - 34.2	0.068 - 34.2	
Presence of rheumatoid factors	n = 20	n = 44	n = 64	.087
	3 (15.0)	1 (2.27)	4 (6.25)	
ESR (mm/h)	n = 20	n = 41	n = 61	.096
Mean (SD)	15.7 (24.0)	22.7 (25.0)	20.4 (24.7)	
Median	8.50	13.0	10.0	
Range	2.00 - 103	2.00 - 100	2.00 - 103	
CRP (mg/l)	n = 20	n = 43	n = 63	.062
Mean (SD)	5.59 (5.97)	10.0 (11.1)	8.62 (9.93)	
Median	3.85	5.50	5.00	
Range	0.14 - 20.0	1.00 - 47.0	0.14 - 47.0	
DAS 28 (ESR)	n = 19	n = 39	n = 58	.242
Mean (SD)	3.48 (1.42)	3.90 (1.23)	3.76 (1.30)	
Median	3.48	3.89	3.79	
Range	1.22 - 6.39	0.53 - 6.43	0.53 - 6.43	
DAS 28 (CRP)	n = 19	n = 42	n = 61	.336
Mean (SD)	3.49 (1.32)	3.83 (0.93)	3.73 (1.07)	
Median	3.71	3.90	3.89	
Range	1.11 - 5.80	1.27 - 5.38	1.11 - 5.80	
Radiological characteristics				
Type of radiological manifestation	n = 20	n = 45	n = 65	
Bone demineralization	4 (20.0)	4 (8.89)	8 (12.3)	0.238
Bone erosion	5 (25.0)	15 (33.3)	20 (30.8)	0.502
Loss of joint space	4 (20.0)	16 (35.6)	20 (30.8)	0.210
Ossification/complete fusion	2 (10.0)	3 (6.67)	5 (7.69)	0.639
Patients with lesions, Yes	10 (50.0)	25 (55.6)	35 (53.8)	
Number of lesions per patient	n = 10	n = 25	n = 35	.744
1	7 (70.0)	14 (56.0)	21 (60.0)	
2	2 (20.0)	9 (36.0)	11 (31.4)	
3 or more	1 (10.0)	2 (8.00)	3 (8.57)	

Psoriatic arthritis (PsA)	**Discontinuation after 1 year (n=20)**	**Persisting at 2 years (n=45)**	**Total (n=65)**	***p***
	Skin manifestations			
	n = 20	n = 45	n = 65	
Presence of skin psoriasis	16 (80.0)	37 (82.2)	53 (81.5)	1.000
Type of psoriasis	n = 16	n = 37	n = 53	
Scaly or erythematous plaques	16 (100)	34 (91.9)	50 (94.3)	0.545
Erythematous oral or genital lesions	1 (6.25)	3 (8.11)	4 (7.55)	1.000
Nails	1 (6.25)	3 (8.11)	4 (7.55)	1.000
Clinical forms of PsA	n=20	n=45	n=65	
1) Axial forms	14 (70.0)	20 (44.4)	34 (52.3)	0.057
- Sacroiliac joints	10 (50.0)	16 (35.6)	26 (40.0)	0.273
- Axial skeleton	7 (35.0)	13 (28.9)	20 (30.8)	0.622
2) Axial and Peripheral forms	10 (50.0)	16 (35.6)	26 (40.0)	0.273
3) Peripheral forms	15 (75.0)	41 (91.1)	56 (86.2)	0.120
- Enthesitis	9 (45.0)	17 (37.8)	26 (40.0)	0.583
Insertions of quadricipital and patellar tendons	*1 (11.1)*	*3 (17.6)*	*4 (15.4)*	*1.000*
Insertions of calcaneal tendon and superficial plantar facia	*7 (77.8)*	*14 (82.4)*	*21 (80.8)*	*1.000*
Chest	*4 (44.4)*	*5 (29.4)*	*9 (34.6)*	*0.667*
- Affected peripheral joint	12 (60.0)	37 (82.2)	49 (75.4)	0.068
Hips	*3 (25.0)*	*3 (8.11)*	*6 (12.2)*	*0.148*
Distal interphalangeal joints	*7 (58.3)*	*13 (35.1)*	*20 (40.8)*	*0.189*
Dactylitis	*2 (16.7)*	*13 (35.1)*	*15 (30.6)*	*0.298*
Active synovitis	*5 (41.7)*	*26 (70.3)*	*31 (63.3)*	*0.094*
Type of Peripheral involvement	n = 12	n = 28	n = 50	.379
Unilateral	3 (25.0)	5 (13.2)	8 (16.0)	
Bilateral	9 (75.0)	33 (86.8)	42 (84.0)	
	Extra-articular manifestations			
Number of extra-articular manifestations	n = 19	n = 43	n = 62	1.000
1	1 (5.26)	3 (6.98)	4 (6.45)	
Type of extra-articular manifestation	n = 1	n = 3	n = 4	
Cardiac complications	0 (0)	1 (33.3)	1 (25.0)	1.000
Others	1 (100)	2 (66.7)	3 (75.0)	1. 000

- **Ankylosing spondyltis (AS)**

Of 478 AS patients included in the study, 57 (11.9%) discontinued golimumab after a year and 228 (47.7%) persisted on the treatment at 2 years.

Like observed for the previous two disease cohorts, baseline disease characteristics for AS patients who discontinued golimumab after a year of treatment versus those persisting at 2 years were also similar. The only exception being that patients who discontinued after 1 year had a higher prevalence of ethesitis than those who were continuing golimumab for 2 years (50.9% vs. 35.5%, p = .033). Also, a higher proportion of patients who continued golimumab at 2 years presented with bone and joint lesions (64.0%) compared to those who discontinued after 1 year (40.4%). These characteristics are detailed in Table 48 below

Table 48: Baseline clinical characteristics of AS patients who discontinued golimumab after 1 year versus those persisting on the treatment at 2 years

Ankylosing spondylitis (AS)	Discontinuation after 1 year (n=57)	Persisting at 2 years (n=228)	Total (n=285)	*p*
Duration since diagnosis (years)	n = 54	n = 216	n = 270	0.474
Mean (SD)	6.44 (7.72)	8.01 (9.37)	7.70 (9.07)	
Median	3.63	4.43	4.26	
Range	0.10 - 35.7	0.030 - 45.1	0.030 - 45.1	
HLA-B27 antigen positive	n = 57	n = 227	n = 284	.331
	35 (61.4)	161 (70.9)	196 (69.0)	
ESR (mm/h)	n = 48	n = 196	n = 244	.541
Mean (SD)	15.4 (16.5)	16.8 (17.2)	16.5 (17.0)	
Median	9.50	11.0	10.0	
Range	2.00 - 82.0	1.00 - 85.0	1.00 - 85.0	
CRP (mg/l)	n = 55	n = 223	n = 278	.170
Mean (SD)	7.79 (8.83)	12.9 (16.4)	11.9 (15.4)	
Median	5.00	6.00	5.40	
Range	0.20 - 51.0	0.22 - 88.0	0.20 - 88.0	
ASDAS 28 (ESR)	n = 47	n = 187	n = 234	.608
Mean (SD)	2.82 (0.96)	2.86 (0.74)	2.86 (0.79)	
Median	2.82	2.84	2.84	
Range	1.05 - 5.25	0.96 - 5.16	0.96 - 5.25	
ASDAS 28 (CRP)	n = 53	n = 213	n = 266	.363
Mean (SD)	3.03 (0.83)	3.14 (0.78)	3.12 (0.79)	
Median	2.91	3.15	3.12	
Range	1.17 - 5.13	1.35 - 5.39	1.17 - 5.39	
Radiological characteristics				
Type of radiological manifestation	n = 57	n = 228	n = 285	
Bone demineralization	3 (5.26)	30 (13.2)	33 (11.6)	0.096
Bone erosion	13 (22.8)	80 (35.1)	93 (32.6)	0.077
Loss of joint space	9 (15.8)	56 (24.6)	65 (22.8)	0.158
Ossification/complete fusion	6 (10.5)	46 (20.2)	52 (18.2)	0.092
Patients with lesions, Yes	23 (40.4)	146 (64.0)	169 (59.3)	

Ankylosing spondylitis (AS)	**Discontinuation after 1 year (n=57)**	**Persisting at 2 years (n=228)**	**Total (n=285)**	***p***
Number of lesions per patient	n = 23	n = 146	n = 169	.475
1	16 (69.6)	87 (59.6)	103 (60.9)	
2	6 (26.1)	54 (37.0)	60 (35.5)	
3 or more	1 (4.35)	5 (3.42)	6 (3.55)	
Clinical forms of PsA	n=57	n=228	n=285	
1) Axial forms	55 (96.5)	217 (95.2)	272 (95.4)	1.000
- Sacroiliac joints	51 (89.5)	195 (85.5)	246 (86.3)	0.438
- Axial skeleton	35 (61.4)	149 (65.4)	184 (64.6)	0.577
2) Axial and Peripheral forms	34 (59.6)	112 (49.1)	146 (51.2)	0.155
3) Peripheral forms	36 (63.2)	122 (53.5)	158 (55.4)	0.190
- Enthesitis	29 (50.9)	81 (35.5)	110 (38.6)	**0.033**
Insertions of quadricipital and patellar tendons	13 (44.8)	13 (16.0)	26 (23.6)	**0.002**
Insertions of calcaneal tendon and superficial plantar facia	19 (65.5)	45 (55.6)	64 (58.2)	0.351
Chest	13 (44.8)	49 (60.5)	62 (56.4)	0.144
- Affected peripheral joint	22 (38.6)	79 (34.6)	101 (35.4)	0.577
Hips	7 (31.8)	28 (35.4)	35 (34.7)	0.752
Distal interphalangeal joints	8 (36.4)	14 (17.7)	22 (21.8)	0.080
Dactylitis	5 (22.7)	16 (20.3)	21 (20.8)	0.773
Active synovitis	6 (27.3)	29 (36.7)	35 (34.7)	0.411
Type of Peripheral involvement	n = 26	n = 82	n = 108	.243
Unilateral	6 (23.1)	29 (35.4)	35 (32.4)	
Bilateral	20 (76.9)	53 (64.6)	73 (67.6)	
Extra-articular manifestations				
Number of extra-articular manifestations	n = 57	n = 228	n = 285	.101
1	11 (19.3)	63 (27.6)	74 (26.0)	
2	0 (0)	10 (4.39)	10 (3.51)	
Type of extra-articular manifestation	n = 11	n = 73	n = 84	
Acute anterior uveitis	8 (72.7)	47 (64.4)	55 (65.5)	0.741
Autoimmune enterocolopathy	2 (18.2)	20 (27.4)	22 (26.2)	0.720
Others	1 (9.09)	16 (21.9)	17 (20.2)	0.448

15 RESULTS PART III –ANALYSIS OF STUDY OUTCOMES

15.1 Primary Objective: Golimumab treatment persistence at 2 years

The persistence of golimumab at 2 years after initial prescription was assessed for the 391 patients for whom CRFs were available at the year-2 visit. At the end of the 2nd year, and since initial prescription, 340 patients in the cohort discontinued golimumab and 362 patients persisted on the treatment. A total of 52 patients were lost to follow-up after inclusion of which 9 RA, 7 PsA and 36 AS participants. According to biotherapy history, 40 of the 52 patients lost to follow-up were BT-n, 11 were BT-p, and prior biotherapy status was unknown for 1 patient.

Taken together, base case analyses were carried out for 702 patients with available data at 2 years using descriptive statistics. A sensitivity analysis was performed applying two assumptions for patients lost to follow-up: “the best case and the worst case”:

- Worst case: all patients lost to follow-up have discontinued golimumab definitively
- Best case: all patients lost to follow-up are still continuing treatment with golimumab at 2 years

15.1.1 Base case

Among 702 patients with assessable data at 24 months, 340 stopped the treatment during the follow-up period (183 BT-n and 157 BT-p), consisting of 72 (44.7%) RA, 54 (54.5%) PsA and 214 (48.4%) AS patients. At 24 months, overall treatment persistence was 51.6% (n=362). Of these, 248 (57.5%) were BT-n and 114 (42.1%) were BT-p (Table 49). Golimumab persistence at 2 years was similar between the 3 disease groups. However, a significantly larger proportion of BT-n patients were continuing golimumab at 2 years, than the BT-p group, in particular for AS (Table 49).

Table 49 : Base case – percentage of patients persisting on golimumab therapy at 2 years (24 months) by disease and by prior biotherapy

	Persistence at 24 months, n (%)	*p*
Overall (n=702)	**362 (51.6%)**	
Biotherapy-naïve (n=431)	248 (57.5%)	**< .001**
Biotherapy pre-treated (n=271)	114 (42.1%)	
Rheumatoid arthritis (RA) (n=161)	**89(55.3%) [a]**	
Biotherapy-naïve (n=103)	61 (59.2%)	.180
Biotherapy pre-treated (n=58)	28 (48.3%)	
Psoriatic arthritis (PsA) (n=99)	**45/99 (45.5%) [a]**	
Biotherapy-naïve (n=64)	33 (51.6%)	.099
Biotherapy pre-treated (n=35)	12 (34.3%)	
Ankylosing spondylitis (AS) (n=442)	**228 (51.6%) [a]**	
Biotherapy-naïve (n=264)	154 (58.3%)	**.001**
Biotherapy pre-treated (n=178)	74 (41.6%)	

[a] *p*= .306 for the comparison of golimumab persistence among the total RA, PsA and AS cohorts

15.1.2 Worst case scenario

This scenario assumes that patients lost to follow-up (n=52) discontinued golimumab permanently. It is estimated that 392 patients out of 754 (52.0%) would have stopped golimumab in the course of the 24-month follow-up period, comprising 223 (47.3%) BT-n and 168 (59.6%) BT-p participants.

As shown in Table 50, overall treatment persistence at 2 years would be 48.0% for the total cohort, and 52.7% and 40.4% for BT-n and BT-p patients, respectively (*p* = .001). Golimumab persistence at 2 years seems to be similar and non-significant among the 3 disease groups. However, persistence would be significantly higher in BT-n compared to BT-p patients, especially in the AS group (Table 50).

Table 50 : Worst case scenario – percentage of patients persisting on golimumab therapy at 2 years (24 months) by disease and by prior biotherapy

	Persistence at 24 months, n (%)	*p*
Overall (n=754 [a])	**362 (48.0%)**	
Biotherapy-naïve (n=471 [a])	248 (52.7%)	**.001**
Biotherapy pre-treated (n=282 [a])	114 (40.4%)	
Rheumatoid arthritis (RA) (n=170 [b])	**89/170 (52.7%) [c]**	
Biotherapy-naïve (n=110 [b])	61 (55.5%)	.321
Biotherapy pre-treated (n=59 [b])	28 (47.5%)	
Psoriatic arthritis (PsA) (n=106)	**45/106 (42.5%) [c]**	
Biotherapy-naïve (n=70)	33 (47.1%)	.173
Biotherapy pre-treated (n=36)	12 (33.3%)	
Ankylosing spondylitis (AS) (n=478)	**228/478 (47.7%) [c]**	
Biotherapy-naïve (n=291)	154 (52.9%)	**.004**
Biotherapy pre-treated (n=187)	74 (39.6%)	

[a] Sum of BT-n (n = 471) and BT-p (n = 282) patients is 793; prior biotherapy data missing for 1 patient

[b] Sum of BT-n (n = 110) and BT-p (n = 59) patients is 169; prior biotherapy data missing for 1 patient

[c] *p*= .271 for the comparison of golimumab persistence among RA, PsA and AS cohorts

15.1.3 Best case scenario

The best-case scenario assumes that patients lost to follow-up (n=52) continue to be treated with golimumab. It is thus estimated that 414 of 754 patients would be persisting on golimumab at 2 years, comprising 288 BT-n (69.6%) and 125 (30.2%) BT-p patients. Overall treatment persistence at 2 years would be 54.9%: 61.1% in BT-n and 44.3% in BT-p patients, respectively (Table 51).

Golimumab treatment continuity at 2 years appears to be comparable between the 3 disease groups. However, persistence would be significantly higher in BT-n than in BT-p patients, especially in the AS group (Table 51).

Table 51 : Best case – percentage of patients persisting on golimumab therapy at 2 years (24 months) by disease and by prior biotherapy

	Persistence at 24 months, n (%)	*p*
Overall (n=754 [a])	**414 (54.9%)**	
Biotherapy-naïve (n=471 [a])	288 (61.1%)	**< .001**
Biotherapy pre-treated (n=282 [a])	125 (44.3%)	
Rheumatoid arthritis (RA) (n=170 [b])	**98 (57.6%) [c]**	
Biotherapy-naïve (n=110 [b])	68 (61.8%)	.112
Biotherapy pre-treated (n=59 [b])	29 (49.2%)	
Psoriatic arthritis (PsA) (n=106)	**52 (49.1%) [c]**	
Biotherapy-naïve (n=70)	39/70 (55.7%)	.056
Biotherapy pre-treated (n=36)	13/36 (36.1%)	
Ankylosing spondylitis (AS) (n=478)	**264 (55.2%) [c]**	
Biotherapy-naïve (n=291)	181/291 (62.2%)	**< .001**
Biotherapy pre-treated (n=187)	83/187 (44.4%)	

[a] Sum of BT-n (n = 471) and BT-p (n = 282) patients is 793; prior biotherapy data missing for 1 patient

[b] Sum of BT-n (n = 110) and BT-p (n = 59) patients is 169; prior biotherapy data missing for 1 patient

[c] *p*= .368 for the comparison of golimumab persistence among the RA, PsA and AS cohorts

15.1.4 Summary: Golimumab persistence at 2 years of follow-up

The base case results indicate that golimumab persistence at 2 years was 51.6% in the overall population. Applying sensitivity analyses (for best and worst-case scenarios) for patients lost to follow-up at 2 years, the persistence varies between 48.0% for the worst case and 54.9% for the best-case scenarios.

In RA patients, overall treatment persistence at 2 years was 55.3%, ranging in sensitivity from 52.7% (worst case) to 57.6% (best case). In PsA patients, overall treatment persistence at 2 years was 45.5%, ranging in sensitivity from 42.5% to 49.1% in the worst-case and best-case scenarios, respectively. In AS patients, golimumab persistence at 2 years was 51.6%, ranging in sensitivity from 47.7% to 55.2%, for the worst-case and the best-case situations.

Altogether, these results indicate that our estimation regarding golimumab persistence has low uncertainties based on a low variation in persistence results between scenarios. It turns out that patients with a PsA seem to discontinue the treatment earlier than RA or AS patients.

15.2 Golimumab treatment persistence at 1 year

Among 715 patients with assessable data at 12 months, 249 stopped the treatment before year 1, of which 129 (51.8%) were BT-n and 120 (48.2%) were BT-p. A total of 39 patients were lost to follow-up between inclusion and 12 months.

Overall treatment persistence at year-1 was 65.2% (466 of 715 patients continuing golimumab). Of these, 310 (66.5%) were BT-n, 155 (33.3%) were BT-p, and prior biotherapy data was missing for 1 patient (Table 52). A larger proportion of BT-n patients were continuing golimumab at 2 years, than in the BT-p group (Table 52).

Table 52 : Base case – percentage of patients persisting on golimumab therapy at 3, 6, 9 and 12 months by disease and by prior biotherapy

	3 months	6 months	9 months	12 months
Overall [a] (n=754)	**680/726 (93.7%)**	**584/725 (80.6%)**	**508/721 (70.5%)**	**466/715 (65.2%)**
Biotherapy-naïve [a] (n=471)	425/449 (94.7%)	373/448 (83.3%)	339/445 (76.2%)	310/439 (70.6%)
Biotherapy pre-treated [a] (n=282)	254/276 (92.0%)	210/276 (76.1%)	168/275 (61.1%)	155/275 (56.4%)
Rheumatoid arthritis (RA) [a] (n=170)	**154/167 (92.2%)**	**134/167 (80.2%)**	**120/166 (72.3%)**	**108/166 (65.1%)**
Biotherapy-naïve [a] (n=110)	104/109 (95.4%)	93/109 (85.3%)	84/108 (77.8%)	74/107 (69.2%)
Biotherapy pre-treated [a] (n=59)	50/58 (86.2%)	41/58 (70.7%)	36/58 (62.1%)	33/58 (56.9%)
Psoriatic arthritis (PsA) (n=106)	**96/100 (96.0%)**	**86/100 (86.0%)**	**73/100 (73.0%)**	**65 (65.7%)**
Biotherapy-naïve (n=70)	62/65 (95.4%)	57/65 (87.7%)	51/65 (78.5%)	46/65 (71.9%)
Biotherapy pre-treated (n=36)	34/35 (97.1%)	29/35 (82.9%)	22/35 (62.9%)	19/35 (54.3%)
Ankylosing spondylitis (AS) (n=478)	**429/458 (93.7%)**	**363/457 (79.4%)**	**314/454 (69.2%)**	**293/450 (65.1%)**
Biotherapy-naïve (n=291)	259/275 (94.2%)	223/274 (81.4%)	204/272 (75.0%)	190/268 (70.9%)
Biotherapy pre-treated (n=187)	170/183 (92.9%)	140/183 (76.5%)	110/182 (60.4%)	103/182 (56.6%)

[a] Prior biotherapy data was missing for 1 patient with RA

15.3 Cumulative persistence of golimumab over time

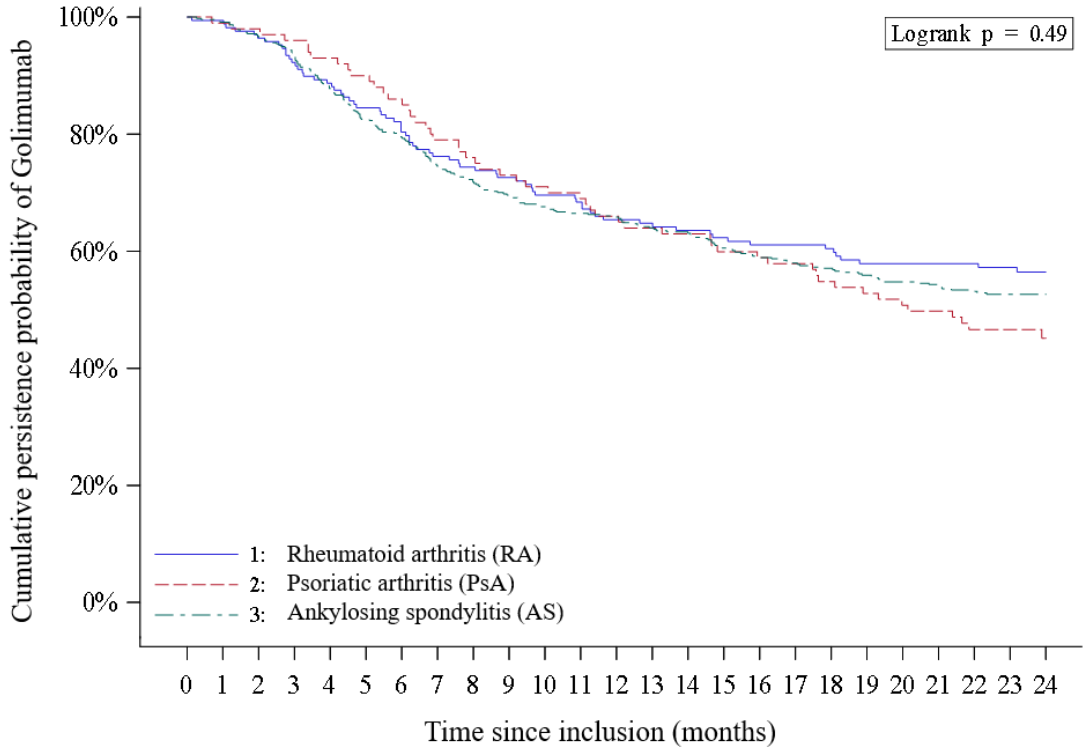
Cumulative persistence probabilities were obtained from Kaplan-Meier curves for each disease cohort, and are summarized in Table 53 and depicted in Figure 3. The difference in persistence rates at year-1 and year-2 among disease groups are shown to be non-significant (p = .490).

For the total study cohort, the cumulative persistence of golimumab was 65.7% at year-1 and 52.4% at year-2. For RA patients, it was 65.4% at year-1 and 56.5% at year-2. In the PsA group, golimumab cumulative persistence was 66.0% at year-1 and 45.1% at year-2 and in the AS group it was 65.8% at year-1 and 52.6% at the end of the 2nd year of follow-up. The median duration of golimumab persistence in PsA patients was estimated to be 20.1 months. The median duration could not be calculated for RA and AS patients, as more than half were continuing golimumab therapy at 2 years.

Table 53: Cumulative persistence of golimumab over time for RA, PsA and AS patients at 1-year and 2-year timepoints from Kaplan-Meier estimates

Cumulative persistence probability of golimumab (%)	1 year	2 years	*p*
Rheumatoid arthritis (RA)	65.4%	56.5%	
Psoriatic arthritis (PsA)	66.0%	45.1%	.490
Ankylosing spondylitis	65.8%	52.6%	
Total study population	**65.7%**	**52.4%**	

Figure 3: Kaplan-Meier curve showing the cumulative persistence probability of golimumab in the RA, PsA and AS cohorts from treatment initiation up to 2 years.



15.3.1 Cumulative persistence probability of golimumab by prior biotherapy

Kaplan-Meier curves depicting the cumulative persistence of golimumab over time were prepared for BT-n and BT-p patients in each disease cohort up to 24 months. Golimumab persistence at 2 years was lower for BT-p patients than for BT-n patients in all disease groups and in the total cohort.

RA patients (Figure 4): golimumab persistence at 1-year was 69.6% for BT-n patients and 56.9% for BT-p patients; persistence at 2 years was 60.6% in BT-n patients and 48.2% in BT-p patients. However, this difference was found to be statistically non-significant (p = .06). The median duration of golimumab persistence was calculable only for BT-p patients with RA, which was 20.4 months. The median duration could not be calculated for BT-n RA participants, as more than half were continuing golimumab therapy beyond the 2-year follow-up period.

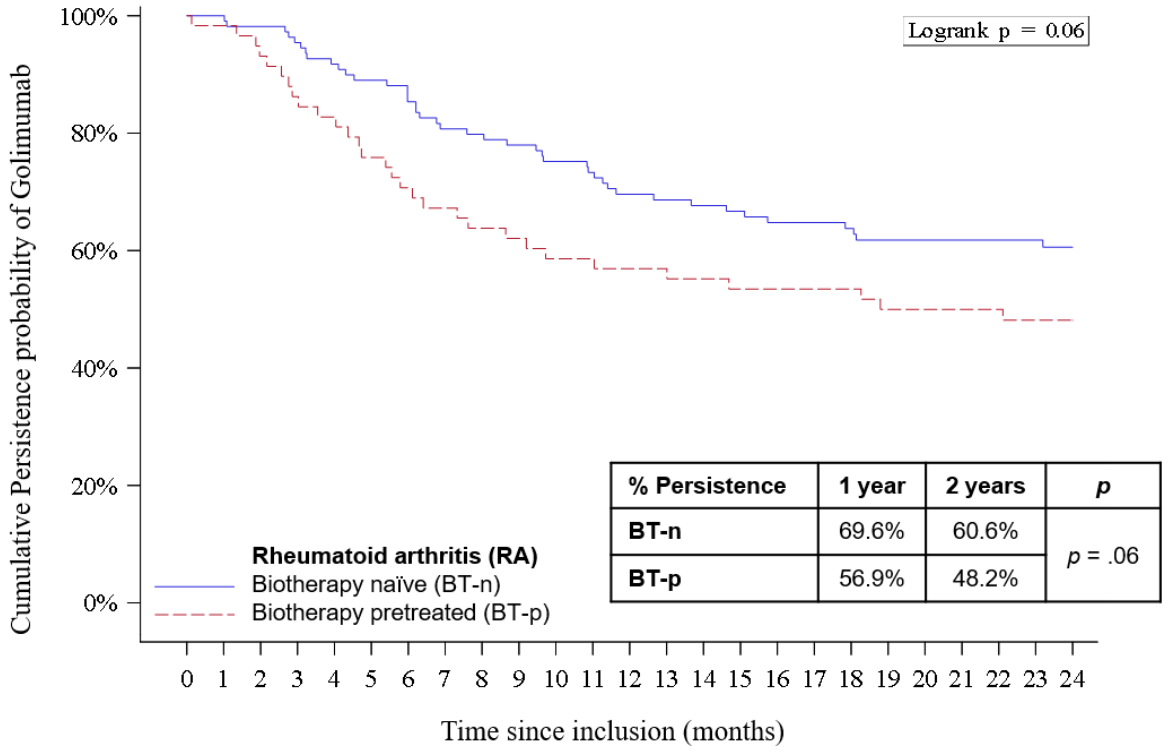
PsA patients (Figure 5): golimumab persistence at 1-year was 72.3% in BT-n patients and 54.3% in BT-p patients; persistence at 2 years was 56.9% in BT-n patients and 34.1% in BT-p patients. Nevertheless, the difference in golimumab persistence between BT-p and BT-n patients was found to be non-significant (p = .06). Median duration of golimumab persistence for BT-p patients was 14.8 months. The median duration of therapy persistence was calculable for BT-n PsA patients by extrapolation and was estimated to be 25.3 months.

AS patients (Figure 6): the difference in golimumab persistence over time was significant for AS patients (BT-n 59.2% vs BT-p 42.7% at 2 years, p < .01), implying that AS patients who are BT-n have an increased probability of persisting on golimumab treatment over time compared to AS patients who previously had biotherapy. Median duration of golimumab persistence among BT-n AS patients was estimated to be 15.2 months.

Total population: at 1-year, golimumab persisted among 71.2% of BT-n patients and 56.8% of BT-p patients, and at 2 years, golimumab persistence was 58.3% in BT-n patients and 42.7% in BT-p patients. The difference in golimumab persistence over time between BT-n and BT-p groups was statistically

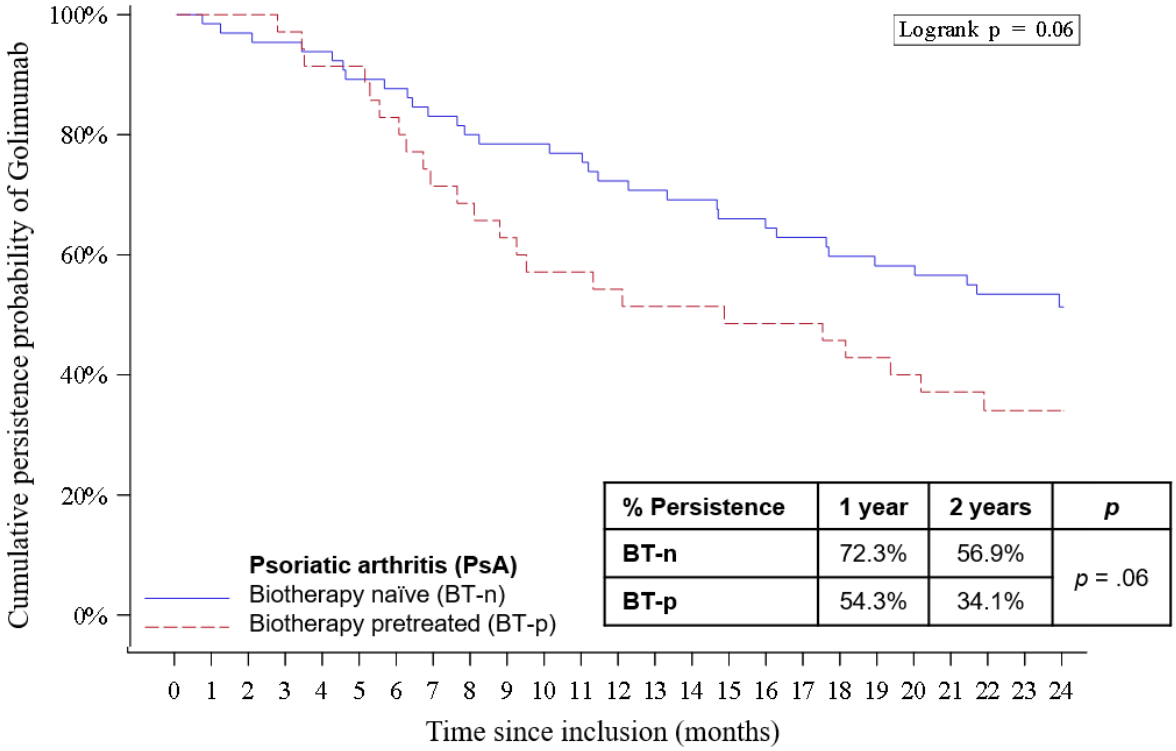
significant (p < .01). The median duration of golimumab persistence was calculable only for BT-p patients, and was 16.7 months.

Figure 4: Kaplan-Meier curve of the cumulative persistence probability of golimumab in RA patients by prior biotherapy, from treatment initiation up to 2 years.



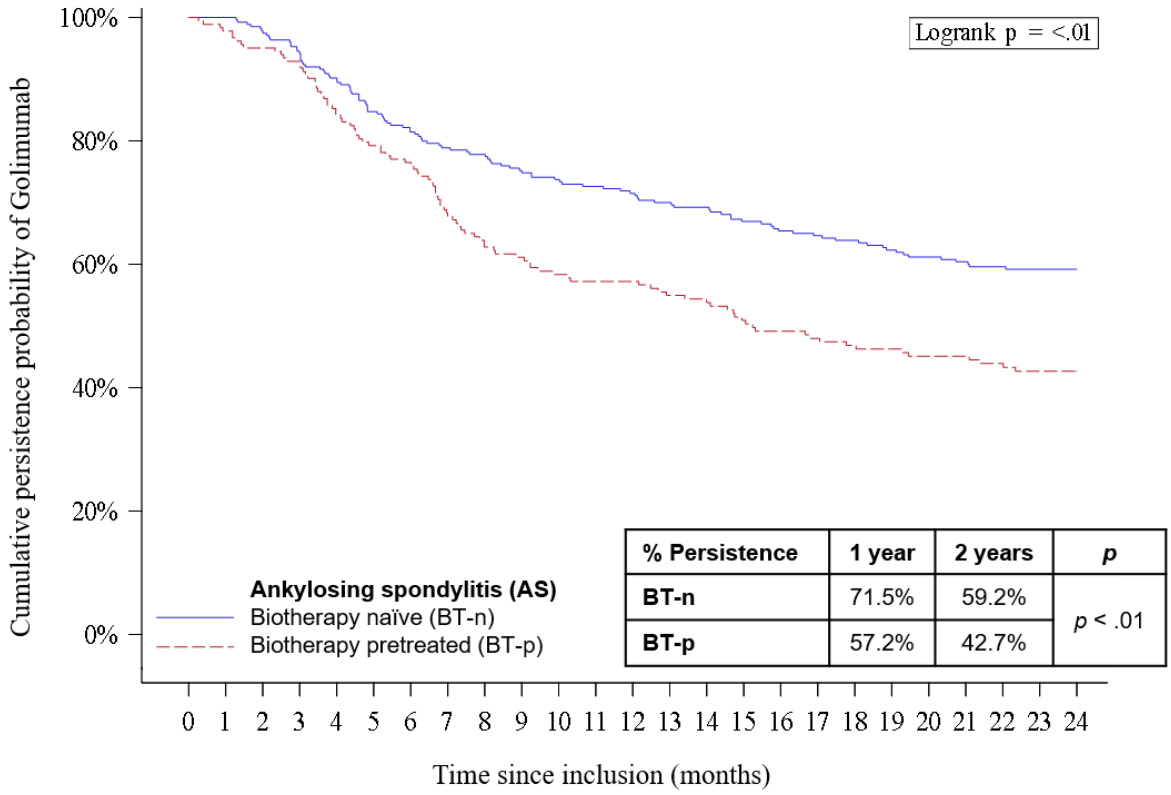
% Persistence	1 year	2 years	*p*
BT-n	69.6%	60.6%	*p* = .06
BT-p	56.9%	48.2%	

Figure 5: Kaplan-Meier curve of the cumulative persistence probability of golimumab in PsA patients by prior biotherapy, from treatment initiation up to 2 years.



% Persistence	1 year	2 years	*p*
BT-n	72.3%	56.9%	*p* = .06
BT-p	54.3%	34.1%	

Figure 6: Kaplan-Meier curve of the cumulative persistence probability of golimumab in AS patients by prior biotherapy, from treatment initiation up to 2 years.



% Persistence	1 year	2 years	*p*
BT-n	71.5%	59.2%	*p* < .01
BT-p	57.2%	42.7%	

15.4 Golimumab prescription patterns and co-treatments

15.4.1 Golimumab prescription renewals

Prescription renewal data was available for 523 out of 557 patients at year 1 and 373 of 391 patients at year two. Prescription renewal data by disease-type is provided below. There were no significant differences in prescription patterns between BT-n and BT-p patients.

- **Rheumatoid arthritis (RA)**

Golimumab prescription was renewed in the vast majority of patients followed-up at 1 year and 2 years. At year 1 (n=119), 106 RA patients (89.1%) had renewed prescriptions and at year 2 (n=93), 84 patients (90.3%) got their golimumab prescriptions renewed. For most patients, golimumab prescription renewal was consistent with the IFU in terms of dosage (50 mg) and frequency (100%), with the exception of 2 patients at year 1 and 4 patients at year 2 who were prescribed golimumab more than once a month (Table 54). The average prescription duration was around 7 months at both timepoints. There were no significant differences in any elements between BT-n and BT-p patients.

- **Psoriatic arthritis (PsA)**

Golimumab prescription was renewed in the majority of PsA patients who attended the 1-year and 2-year follow-ups. At year-1 (n=78) golimumab was re-prescribed to 62 PsA patients (79.5%), and at year-2 (n=48), golimumab was re-prescribed to 41 patients (85.4%). The dosage of golimumab was 50 mg and once a month in most cases. The average duration of prescription was shorter in year-1 (6.66 months) than in year-2 (7.78 months). Details on the prescription renewal of golimumab in PsA patients

are provided in Table 55. There were no significant differences in any aspects of renewal between BT-n and BT-p patients.

- **Ankylosing spondylitis (AS)**

Golimumab prescription was renewed in the vast majority of AS patients at 1-year and 2-year follow-ups. At year 1 (n=325) golimumab was re-prescribed to 283 AS patients (87.1%), and to 213 patients (91.8%) at year 2 (n=232). Golimumab was renewed at 50 mg and once a month in most patients. The average duration of prescription was slightly shorter at year 1 (7.57 months) than at year 2 (8.06 months). Details on golimumab prescription renewal are given in Table 56. No significant differences in re-prescription characteristics were noted between BT-n and BT-p AS patients.

Table 54 : Renewal of golimumab prescription in RA patients at each year

	Year 1 (n=123)	Year 2 (n=98)
Yearly renewal		
n	119	93
No	13 (10.9)	9 (9.68)
If Yes		
Dosage (mg)		
n	105	85
50	105 (100)	85 (100)
Injections /month		
n	105	85
0.66	1 (0.95)	2 (2.35)
0.75	1 (0.95)	2 (2.35)
1	103 (98.1)	81 (95.3)
Prescription duration (month)		
n	104	83
Mean (SD)	7.04 (2.78)	7.10 (2.96)
Median	6.00	6.00
Range	3.00 - 12.0	2.00 - 12.0

Table 55 : Renewal of golimumab prescription in PsA patients at each year

	Year 1 (n=84)	Year 2 (n=52)
Yearly renewal		
n	78	48
No	16 (20.5)	7 (14.6)
Yes	62 (79.5)	41 (85.4)
If Yes		
Dosage (mg)		
n	62	41
100	6 (9.68)	4 (9.76)
50	56 (90.3)	37 (90.2)
Injections /month		
n	62	41
0.8	1 (1.61)	0 (0)
1	60 (96.8)	41 (100)
1.33	1 (1.61)	0 (0)
Prescription duration (month)		
n	62	41
Mean (SD)	6.66 (2.91)	7.78 (3.07)
Median	6.00	6.00
Range	3.00 - 12.0	3.00 - 12.0

Table 56 : Renewal of golimumab prescription in AS patients at each year

	Year 1 (n=350)	Year 2 (n=241)
Yearly renewal		
n	325	232
No	42 (12.9)	19 (8.19)
Yes	283 (87.1)	213 (91.8)
If Yes		
Dosage (mg)		
n	283	213
100	15 (5.28)	24 (11.3)
50	268 (94.4)	189 (88.7)
Injections /month		
n	283	213
0.5 – 0.8	4 (1.41)	9 (4.22)
1	276 (97.5)	197 (92.5)
1.25 – 1.50	1 (0.35)	3 (1.41)
3	0 (0)	1 (0.47)
4	1 (0.35)	3 (1.41)
Unknown	1 (0.35)	0 (0)
Prescription duration (month)		
n	282	211
Mean (SD)	7.57 (3.04)	8.06 (3.10)
Median	6.00	6.00
Range	1.00 - 12.0	3.00 - 12.0

15.4.2 Change in golimumab prescription

Data on golimumab prescription change was available for 296 patients (39.3% of the cohort) of which 63 RA patients, 9 PsA patients and 36 AS patients. Prescription changes were made for 25 patients of the 296 (8.45%), comprising of 2 RA patients, 9 PsA patients and 14 AS patients.

"Other" reasons were cited as the main reason for prescription change (n=11, 44.0%), followed by secondary failure (n=8, 32.0%). Further details are provided in Table 57.

Table 57: Change in golimumab prescription by rheumatic disease

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)	*p*
Change in golimumab prescription					.019
n	63	49	184	296	
No	61 (96.8)	40 (81.6)	170 (92.4)	271 (91.6)	
Yes	2 (3.17)	9 (18.4)	14 (7.61)	25 (8.45)	
If Yes, new dosage					.103
n	2	8	13	23	
50	2 (100)	1 (12.5)	4 (30.8)	7 (30.4)	
100	0 (0)	6 (75.0)	9 (69.2)	15 (65.2)	
300	0 (0)	1 (12.5)	0 (0)	1 (4.35)	
Number of injections per month					.195
n	2	8	14	24	
1	1 (50.0)	8 (100)	10 (71.4)	19 (79.2)	
1.25	1 (50.0)	0 (0)	4 (28.6)	5 (20.8)	
Prescription duration (months)					.927
n	2	8	14	24	
1	0 (0)	0 (0)	1 (7.14)	1 (4.17)	
2	0 (0)	1 (12.5)	0 (0)	1 (4.17)	
3	0 (0)	1 (12.5)	2 (14.3)	3 (12.5)	
4	0 (0)	1 (12.5)	1 (7.14)	2 (8.33)	
6	2 (100)	5 (62.5)	8 (57.1)	15 (62.5)	
12	0 (0)	0 (0)	2 (14.3)	2 (8.33)	
Reason for change					
n	2	8	14	24	
Intolerance	0 (0)	0 (0)	1 (7.14)	1 (4.00)	
Primary non-response	0 (0)	2 (22.2)	2 (14.3)	4 (16.0)	
Secondary failure	0 (0)	3 (33.3)	5 (35.7)	8 (32.0)	
Patient request	0 (0)	1 (11.1)	0 (0)	1 (4.00)	
Change in body weight	0 (0)	0 (0)	1 (7.14)	1 (4.00)	
Other	2 (100)	3 (33.3)	6 (42.9)	11 (44.0)	

15.4.3 Permanent discontinuation of golimumab

Permanent golimumab discontinuation was reported in nearly half the patients included in this study (n=340, 45.1%), including 72 RA patients, 54 PsA patients and 214 AS patients.

Primary non-response was the most frequent reason, occurring in 129 (37.9%) patients who discontinued golimumab. A quarter of the patients (n=87, 25.6%) discontinued due to secondary failure

and almost 1 in 5 (n=67, 19.7%) discontinued due to intolerance. Details on the reasons for permanent golimumab discontinuation are given in Table 58.

Table 58: Permanent golimumab discontinuation by disease over the 2-year follow-up period

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)
Golimumab persisting at year-2				
Yes [a]	89 (52.4)	45 (42.5)	228 (47.7)	362 (48.0)
No [b]	**72 (42.4)**	**54 (50.9)**	**214 (44.8)**	**340 (45.1)**
Lost to follow-up	9 (5.29)	7 (6.60)	36 (7.53)	52 (6.90)
Reason for withdrawal				
n	72	54	214	340
Intolerance	13 (18.1)	8 (14.8)	46 (21.5)	67 (19.7)
Primary non-response	30 (41.7)	19 (35.2)	80 (37.4)	129 (37.9)
Secondary failure	15 (20.8)	19 (35.2)	53 (24.8)	87 (25.6)
Patient's request	15 (20.8)	6 (11.1)	22 (10.3)	43 (12.6)
Other reason	6 (8.33)	5 (9.26)	27 (12.6)	38 (11.2)

[a] Golimumab treatment was confirmed to be ongoing at year-2 follow-up

[b] Golimumab treatment was indicated as "discontinued" at the year-2 or year-1 visit, at an intermediate visit, or in the treatment discontinuation form.

- **Rheumatoid arthritis (RA)**

Golimumab was permanently discontinued in 42.4% of RA patients (n=72). A higher proportion of BT-p patients (50.8%) discontinued relative to BT-n patients (38.2%). Most frequent reasons for discontinuation were primary non-response (41.7%), secondary failure (20.8%) and patient request (20.8%); 18.1% discontinued golimumab due to intolerance. These results are presented in Table 59.

Table 59: Permanent golimumab discontinuation in RA patients by prior biotherapy

	RA BT-n (n=110)	RA BT-p (n=59)	Total RA (n=170 [c])
Golimumab persisting at year-2			
Yes [a]	61 (55.5)	28 (47.5)	89 (52.4)
No [b]	**42 (38.2)**	**30 (50.8)**	**72 (42.4)**
Lost to follow-up	7 [c] (6.36)	1 [c] (1.69)	9 [c] (5.29)
Reason for withdrawal			
n	42	30	72
Intolerance	9 (21.4)	4 (13.3)	13 (18.1)
Primary non-response	17 (40.5)	13 (43.3)	30 (41.7)
Secondary failure	9 (21.4)	6 (20.0)	15 (20.8)
Patient's request	10 (23.8)	5 (16.7)	15 (20.8)
Other reason	1 (2.38)	5 (16.7)	6 (8.33)

[a] Golimumab treatment was confirmed to be ongoing at year-2 follow-up

[b] Golimumab treatment was indicated as "discontinued" at the year-2 or year-1 visit, or at an intermediate visit, or in the treatment discontinuation form.

[c] 1 patient less due to missing biotherapy data

- **Psoriatic arthritis (PsA)**

Golimumab was permanently discontinued in over a half of PsA patients (n=54, 50.9%). A higher proportion of BT-p patients (63.9%) discontinued compared to BT-n patients (44.3%). The main reasons for discontinuation were primary non-response (35.2%) and secondary failure (35.2%); 8 PsA patients (14.8%) discontinued due to intolerance. Further details are provided in Table 60.

Table 60: Permanent golimumab discontinuation in PsA patients by prior biotherapy

	PsA BT-n (n=70)	PsA BT-p (n=36)	Total PsA (n=106)
Golimumab persisting at year-2			
Yes [a]	33 (47.1)	12 (33.3)	45 (42.5)
No [b]	**31 (44.3)**	**23 (63.9)**	**54 (50.9)**
Lost to follow-up	6 (8.57)	1 (2.77)	7 (6.60)
Reason for withdrawal			
n	31	23	54
Intolerance	5 (16.1)	3 (13.0)	8 (14.8)
Primary non-response	8 (25.8)	11 (47.8)	19 (35.2)
Secondary failure	13 (41.9)	6 (26.1)	19 (35.2)
Patient's request	3 (9.68)	3 (13.0)	6 (11.1)
Other reason	2 (6.45)	3 (13.0)	5 (9.26)

[a] Golimumab treatment was confirmed to be ongoing at year-2 follow-up

[b] Golimumab treatment was indicated as "discontinued" at the year-2 or year-1 visit, or at an intermediate visit, or in the treatment discontinuation form.

- **Ankylosing spondylitis (AS)**

Permanent golimumab discontinuation was reported in 44.8% of AS patients (n=214). A greater percentage of BT-p patients (55.6%) discontinued golimumab than BT-n patients (37.8%). As for other CIRDs, primary non-response was the main reason for discontinuation (37.4%), and in AS patients it was cited for a higher proportion of BT-n (43.6%) than BT-p patients (30.8%). Secondary failure was reported for 24.8% and intolerance for 21.5% of AS patients. Further details are provided in Table 61.

Table 61: Permanent golimumab discontinuation in AS patients by prior biotherapy

	AS BT-n (n=291)	AS BT-p (n=187)	Total AS (n=478)
Golimumab persisting at year-2			
Yes [a]	154 (52.9)	74 (39.6)	228 (47.7)
No [b]	**110 (37.8)**	**104 (55.6)**	**214 (44.8)**
Lost to follow-up	27 (9.28)	9 (4.81)	36 (7.53)
Reason for withdrawal			
n	110	104	214
Intolerance	18 (16.4)	28 (26.9)	46 (21.5)
Primary non-response	48 (43.6)	32 (30.8)	80 (37.4)
Secondary failure	24 (21.8)	29 (27.9)	53 (24.8)
Patient's request	8 (7.27)	14 (13.5)	22 (10.3)
Other reason	16 (14.5)	11 (10.6)	27 (12.6)

[a] Golimumab treatment was confirmed to be ongoing at year-2 follow-up

[b] Golimumab treatment was indicated as "discontinued" at the year-2 or year-1 visit, or at an intermediate visit, or in the treatment discontinuation form.

15.4.4 Concomitant treatments at 1-year follow-up visit

Concomitant treatments with initial golimumab prescription for the global population (n=754) and for patients with 2 years of follow-up (n=391) have been described earlier in sections 13.7 and 14.3, respectively. Treatments that were co-prescribed with golimumab at the year 1 follow-up visit are presented in Table 62 for the total cohort by prior biotherapy status.

Data on concomitant treatments were available for 339 BT-n patients and 179 BT-p patients. At year 1, concomitant treatments were prescribed to less than two-thirds of patients (n=314, 60.6%), and to a higher proportion of BT-p patients (66.5% vs 57.5% of BT-n patients, p = .047). Co-treatments were mostly NSAIDs/analgesics (71.7%), followed by DMARDs (58.9%) and Corticosteroids (15.0%). Only 23 patients (7.32%) were prescribed local or surgical treatment.

- **Disease-modifying antirheumatic drugs (DMARDs)**

At the 1-year follow-up visit, DMARDs were co-prescribed to more than half (n = 185, 58.9%) of patients receiving a concomitant treatment, and more frequently to BT-n (63.1%) than BT-p patients (52.1%). The most used was oral MTX (n = 100, 54.1%), followed by parenteral MTX (n = 52, 28.1%). Leflunomide was given to 9.73% of patients (n=18). No significant differences were observed in the types of DMARDs prescribed to BT-n and BT-p patients.

- **NSAIDs/analgesics**

NSAIDs/analgesics were co-prescribed to most patients (n = 225, 71.7%), and more frequently to BT-p patients (79.8%) than BT-n patients (66.7%). “Other” (unspecified) NSAIDs/analgesics were most commonly prescribed (n = 137, 60.9%); paracetamol was given to 39.1% of patients (n = 88) and opioids to 20.9% of patients (n = 47). No significant differences were observed in the types of NSAIDs/analgesics prescribed to BT-n and BT-p patients.

- **Corticosteroids**

At the 1-year follow-up visit, corticosteroids were co-prescribed to merely 15.0% of patients (n = 47) who received a concomitant treatment, with no significant difference between BT-n and BT-p patients. Cortisone/hydrocortisone and prednisolone/ methylprednisolone were predominantly prescribed (51.1% and 48.9%, respectively).

- **Local/surgical treatment**

Local/surgical treatments were prescribed in addition to golimumab to 23 patients (7.32%). They were mainly intra-articular injections (n=17, 73.9%), followed by joint replacement in a fifth of the patients (n=5, 21.7%). Further information is presented in Table 62.

Table 62: Co-prescriptions for the total cohort at the year-1 visit by prior biotherapy (n = 539)

Total cohort	Biotherapy-naive patients (n=353)	Bio-pretreated patients (n=186)	Total (n=539)	*p*
Concomitant treatments	n=339 **195 (57.5)**	n=179 **119 (66.5)**	n=518 **314 (60.6)**	**.047**
1) DMARDs	n = 195 **123 (63.1)**	n = 119 **62 (52.1)**	n = 314 **185 (58.9)**	
	n = 123	n = 62	n = 185	
MTX (oral)	**64 (52.0)**	**36 (58.1)**	**100 (54.1)**	.437
Dosage (mg/week)	**n = 64**	**n = 36**	**n = 100**	
Mean (SD)	14.8 (4.24)	14.8 (4.49)	14.8 (4.31)	.977
Median	15.0	15.0	15.0	
Range	5.00 - 25.0	7.50 - 20.0	5.00 - 25.0	
MTX (parenteral)	**35 (28.5)**	**17 (27.4)**	**52 (28.1)**	.882
Dosage (mg/week)	**n = 35**	**n = 17**	**n = 52**	
Mean (SD)	16.9 (3.95)	15.4 (3.98)	16.4 (3.97)	.232
Median	17.5	15.0	15.0	
Range	7.50 - 25.0	10.0 - 20.0	7.50 - 25.0	
Sulfasalazine	**7 (5.69)**	**3 (4.84)**	**10 (5.41)**	1.000
Dosage (g/day)	**n = 7**	**n = 3**	**n = 10**	
Mean (SD)	2.00 (0.58)	2.33 (0.58)	2.10 (0.57)	.427
Median	2.00	2.00	2.00	
Range	1.00 - 3.00	2.00 - 3.00	1.00 - 3.00	
Leflunomide	**15 (12.2)**	**3 (4.84)**	**18 (9.73)**	.111
Dosage (mg/day)	**n = 15**	**n = 3**	**n = 18**	
Mean (SD)	20.0 (0)	20.0 (0)	20.0 (0)	NA
Median	20.0	20.0	20.0	
Range	20.0 - 20.0	20.0 - 20.0	20.0 - 20.0	
Hydroxychloroquine/ Chloroquine	**3 (2.44)**	**2 (3.23)**	**5 (2.70)**	1.000
Dosage (mg/day)	**n = 3**	**n = 2**	**n = 5**	.223
Mean (SD)	253 (129)	400 (0)	312 (121)	
Median	200	400	400	
Range	160 - 400	400 - 400	160 - 400	
Other DMARDs	**10 (8.13)**	**1 (1.61)**	**11 (5.95)**	.103
2) Corticosteroids	n = 195 **27 (13.8)**	n = 119 **20 (16.8)**	n = 314 **47 (15.0)**	
	n = 27	n = 20	n = 47	
Cortisone/hydrocortisone	**13 (48.1)**	**11 (55.0)**	**24 (51.1)**	.642
Dosage (mg/day)	**n = 13**	**n = 11**	**n = 24**	
Mean (SD)	12.3 (20.2)	6.53 (3.08)	9.64 (15.0)	.362
Median	5.00	7.50	5.50	
Range	2.00 - 75.0	0.33 - 10.0	0.33 - 75.0	
Prednisone/prednisolone/ methylprednisolone	**14 (51.9)**	**9 (45.0)**	**23 (48.9)**	.642

Total cohort	Biotherapy-naive patients (n=353)	Bio-pretreated patients (n=186)	Total (n=539)	*p*
Dosage (mg/day)	**n = 14**	**n = 9**	**n = 23**	
Mean (SD)	8.14 (6.65)	15.1 (17.5)	10.9 (12.2)	.188
Median	5.00	10.0	5.00	
Range	2.00 - 20.0	5.00 - 60.0	2.00 - 60.0	
Other corticosteroids	**2 (7.41)**	**0 (0)**	**2 (4.26)**	0.500
	n = 195	n = 119	n = 314	
3) NSAIDs/analgesics	**130 (66.7)**	**95 (79.8)**	**225 (71.7)**	
	n = 130	n = 95	n = 225	
Ibuprofen	**7 (5.38)**	**4 (4.21)**	**11 (4.89)**	.764
Dosage (mg/day)	**n = 6**	**n = 3**	**n = 9**	
Mean (SD)	183 (40.8)	733 (503)	367 (374)	**.024**
Medians	200	800	200	
Range	100 - 200	200 - 1200	100 - 1200	
Coxibs	**5 (3.85)**	**7 (7.37)**	**12 (5.33)**	.245
Dosage (mg/day)	**n = 5**	**n = 7**	**n = 12**	
Mean (SD)	79.0 (20.1)	203 (147)	151 (126)	.094
Median	75.0	200	100	
Range	60.0 - 100	60.0 - 400	60.0 - 400	
Paracetamol	**46 (35.4)**	**42 (44.2)**	**88 (39.1)**	.180
Dosage (mg/day)	**n = 42**	**n = 37**	**n = 79**	
Mean (SD)	2364 (1191)	2270 (990)	2320 (1096)	.706
Median	3000	3000	3000	
Range	1.00 - 4000	4.00 - 4000	1.00 - 4000	
Opioids	**25 (19.2)**	**22 (23.2)**	**47 (20.9)**	.474
Dosage (mg/day)	**n = 21**	**n = 17**	**n = 38**	
Mean (SD)	364 (700)	165 (250)	275 (550)	.272
Median	75.0	60.0	60.0	
Range	2.00 - 3000	2.00 - 1000	2.00 - 3000	
Other NSAIDs/analgesics	**82 (63.1)**	**55 (57.9)**	**137 (60.9)**	.431
4) Local treatment or surgery	n = 195	n = 119	n = 314	
	13 (6.67)	**10 (8.40)**	**23 (7.32)**	
	n = 13	n = 10	n = 23	
Intra-articular injections	9 (69.2)	8 (80.0)	17 (73.9)	.660
Synoviorthesis	1 (7.69)	0 (0)	1 (4.35)	1.000
Synovectomy	1 (7.69)	0 (0)	1 (4.35)	1.000
Joint replacement	3 (23.1)	2 (20.0)	5 (21.7)	1.000

- **Rheumatoid arthritis (RA)**

Concomitant treatments in the RA cohort at year 1 follow-up are given in Table 63. Year 1 co-prescription data were available for 116 RA patients. The majority were prescribed other treatments with golimumab (n=99, 85.3%), of whom 91 (91.9%) were given DMARDs, 52 (52.5%) were given NSAIDs/ analgesics, and 30 (30.3%) were given corticosteroids. A higher proportion of BT-n than BT-p patients were co-prescribed DMARDs (95.8% and 82.1%, respectively) and a greater proportion of BT-p patients received NSAIDs/analgesics (67.9%) compared to BT-n patients (46.5%).

Among patients who were co-prescribed DMARDs (n=99), 54 (59.3%) received oral MTX, 25 (27.5%) received parenteral MTX, and 9 (9.89%) were given leflunomide. Of patients who received corticosteroids (n=30), 15 (50.0%) each received prednisolone/methylprednisolone and cortisone/ hydrocortisone. Among the 52 patients co-prescribed with NSAIDs/analgesics, the majority received paracetamol (n=27, 51.9%) and other NSAIDs/analgesics (n=24, 46.2%).

Localized surgeries were performed in 11 patients (11.1%), including intra-articular injections in 8 patients (72.7%) and joint replacement in 3 patients (27.3%).

Table 63: Co-prescriptions for RA patients at year-1 visit by prior biotherapy (n=119)

Rheumatoid Arthritis (RA)	RA BT-n (n=82)	RA BT-p (n=37)	Total RA (n=119)	*p*
Concomitant treatments	n = 80 **71 (88.8)**	n = 36 **28 (77.8)**	n = 116 **99 (85.3)**	.122
1) DMARDs	n = 71 **68 (95.8)**	n = 28 **23 (82.1)**	n = 99 **91 (91.9)**	
	n = 68	**n = 23**	**n = 91**	
MTX (oral)	37 (54.4)	17 (73.9)	54 (59.3)	.100
MTX (parenteral)	22 (32.4)	3 (13.0)	25 (27.5)	.073
Sulfasalazine	1 (1.47)	0 (0)	1 (1.10)	1.000
Leflunomide	8 (11.8)	1 (4.35)	9 (9.89)	.440
Hydroxychloroquine/ Chloroquine	2 (2.94)	2 (8.70)	4 (4.40)	.264
Other DMARDs	2 (2.94)	0 (0)	2 (2.20)	1.000
2) Corticosteroids	n = 71 **20 (28.2)**	n = 28 **10 (35.7)**	n = 99 **30 (30.3)**	
	n = 20	**n = 10**	**n = 30**	
Cortisone/hydrocortisone	10 (50.0)	5 (50.0)	15 (50.0)	1.000
Prednisone/prednisolone/methylprednisolone	10 (50.0)	5 (50.0)	15 (50.0)	1.000
Other corticosteroids	1 (5.00)	0 (0)	1 (3.33)	1.000
3) NSAIDs/analgesics	n = 71 **33 (46.5)**	n = 28 **19 (67.9)**	n = 99 **52 (52.5)**	
	n = 33	**n = 19**	**n = 52**	
Ibuprofen	2 (6.06)	1 (5.26)	3 (5.77)	1.000
Paracetamol	15 (45.5)	12 (63.2)	27 (51.9)	.219
Opioids	5 (15.2)	4 (21.1)	9 (17.3)	.708
Other NSAIDs/analgesics	16 (48.5)	8 (42.1)	24 (46.2)	.657
4) Local treatment or surgery	n = 71 **5 (7.04)**	n = 28 **6 (21.4)**	n = 99 **11 (11.1)**	
	n = 5	**n = 6**	**n = 11**	
Intra-articular injections	4 (80.0)	4 (66.7)	8 (72.7)	1.000
Joint replacement	1 (20.0)	2 (33.3)	3 (27.3)	1.000

- **Psoriatic arthritis (PsA)**

Concomitant treatments in the PsA cohort at year-1 follow-up are given in Table 64; this data was available for 78 PsA patients. Most patients with PsA were prescribed other treatments with golimumab at baseline (n=58, 74.4%), of whom 44 (75.9%) received DMARDs followed by 38 (65.5%) who received NSAIDs/analgesics, and then 10 (17.2%) who received corticosteroids.

Among patients who were co-prescribed DMARDs (n=44), 22 (50.0%) received oral MTX and 13 (29.5%) received parenteral MTX. Leflunomide was co-prescribed to 7 (15.9%) patients. BT-p PsA patients were more commonly co-prescribed NSAIDs/analgesics (75.0%), compared to BT-n patients (60.5%). Of the 38 patients who received NSAIDs/analgesics, the majority received other NSAIDs/analgesics (n=22, 57.9%), followed by paracetamol (n=11, 28.9%) and opioids (n=8, 21.2%).

Of the 10 co-prescribed with corticosteroids, 6 (60.0%) had cortisone/hydrocortisone and 4 (40.0%) had prednisolone/ methylprednisolone. Local surgeries were performed in 5 BT-n PsA patients only.

Table 64: Co-prescriptions for PsA patients at year-1 visit by prior biotherapy (n=82)

Psoriatic Arthritis (PsA)	PsA BT-n (n=56)	PsA BT-p (n=26)	Total PsA (n=82)	*p*
Concomitant treatments	n = 53 **38 (71.7)**	n = 25 **20 (80.0)**	n = 78 **58 (74.4)**	.433
1) DMARDs	**n = 38** **30 (78.9)**	**n = 20** **14 (70.0)**	**n = 58** **44 (75.9)**	
	n = 30	**n = 14**	**n = 44**	
MTX (oral)	15 (50.0)	7 (50.0)	22 (50.0)	1.000
MTX (parenteral)	8 (26.7)	5 (35.7)	13 (29.5)	.724
Leflunomide	6 (20.0)	1 (7.14)	7 (15.9)	.401
Other DMARDs	2 (6.67)	0 (0)	2 (4.55)	1.000
2) Corticosteroids	**n = 38** **5 (13.2)**	**n = 20** **5 (25.0)**	**n = 58** **10 (17.2)**	
	n = 5	**n = 5**	**n = 10**	
Cortisone/hydrocortisone	2 (40.0)	4 (80.0)	6 (60.0)	.524
Prednisone/prednisolone/ methylprednisolone	3 (60.0)	1 (20.0)	4 (40.0)	.524
3) NSAIDs/analgesics	**n = 38** **23 (60.5)**	**n = 20** **15 (75.0)**	**n = 58** **38 (65.5)**	
	n = 23	**n = 15**	**n = 38**	
Ibuprofen	1 (4.35)	1 (6.67)	2 (5.26)	1.000
Coxibs	1 (4.35)	1 (6.67)	2 (5.26)	1.000
Paracetamol	5 (21.7)	6 (40.0)	11 (28.9)	.285
Opioids	6 (26.1)	2 (13.3)	8 (21.1)	.440
Other NSAIDs/analgesics	13 (56.5)	9 (60.0)	22 (57.9)	.832
4) Local treatment or surgery	n = 38 **5 (13.2)**	n = 20 **0 (0)**	n = 58 **5 (8.62)**	
	n = 5	**n = 0**	**n = 5**	
Intra-articular injections	2 (40.0)	-	2 (40.0)	NC
Synoviorthesis	1 (20.0)	-	1 (20.0)	NC
Synovectomy	1 (20.0)	-	1 (20.0)	NC
Joint replacement	2 (40.0)	-	2 (40.0)	NC

NC = Not calculated

- **Ankylosing spondylitis (AS)**

Co-treatments in the AS cohort at year-1 follow-up are given in Table 65. Year-1 co-prescription data were available for 324 AS patients. A little under half of AS patients were prescribed other treatments with golimumab at year 1 (n=157, 48.5%), which is lower than the frequency of co-prescriptions in AS patients at baseline (78.9%, Table 24). It was also lower than the proportion of RA (85.3%) and PsA patients (74.4%) who were co-prescribed a treatment at year-1.

A higher proportion of BT-p versus BT-n AS patients received co-treatments at year-1 (60.2% vs. 41.7%, *p* = .001). Among AS patients who received co-treatments (n=157), the majority got NSAIDs (n=135, 86.0%), 50 patients (31.8%) received DMARDs, and only 7 patients (4.46%) received corticosteroids.

Of the 135 patients co-prescribed with NSAIDs/analgesics, the majority received other NSAIDs/ analgesics (n=91, 67.4%), followed by paracetamol (n=50, 37.0%) and opioids (n=30, 22.2%). In patients who were co-prescribed DMARDs (n=50), 24 (48.0%) and 14 (28.0%) patients received oral and parenteral MTX, respectively. Sulfasalazine was the next frequently co-prescribed DMARD (n=7, 14.0%), along with “other” DMARDs. In patients who received corticosteroids (n=7), prednisolone/ methylprednisolone (n=4, 57.1%), and cortisone/ hydrocortisone (n=3, 42.9%) were mostly prescribed.

Local surgeries were performed in 7 (4.46%) patients, all of them being intra-articular injections.

Table 65: Co-prescriptions for AS patients at year-1 visit by prior biotherapy (n=338)

Ankylosing spondylitis (AS)	AS BT-n (n=215)	AS BT-p (n=123)	Total AS (n=338)	*p*
Concomitant treatments	n = 206 **86 (41.7)**	n = 118 **71 (60.2)**	n = 324 **157 (48.5)**	**.001**
1) DMARDs	n = 86 25 (29.1)	n = 71 25 (35.2)	n = 157 50 (31.8)	
	n = 25	**n = 25**	**n = 50**	
MTX (oral)	12 (48.0)	12 (48.0)	24 (48.0)	1.000
MTX (parenteral)	5 (20.0)	9 (36.0)	14 (28.0)	.208
Sulfasalazine	5 (20.0)	2 (8.00)	7 (14.0)	.417
Other DMARDs	6 (24.0)	1 (4.00)	7 (14.0)	.098
2) Corticosteroids	n = 86 **2 (2.33)**	n = 71 **5 (7.04)**	n = 157 **7 (4.46)**	
	n = 2	**n = 5**	**n = 7**	
Cortisone/hydrocortisone	1 (50.0)	2 (40.0)	3 (42.9)	1.000
Prednisone/prednisolone/ methylprednisolone	1 (50.0)	3 (60.0)	4 (57.1)	1.000
Other	1 (50.0)	0 (0)	1 (14.3)	.286
3) NSAIDs/analgesics	n = 86 **74 (86.0)**	n = 71 **61 (85.9)**	n = 157 **135 (86.0)**	
	n = 74	**n = 61**	**n = 135**	
Ibuprofen	4 (5.41)	2 (3.28)	6 (4.44)	.689
Coxibs	4 (5.41)	5 (8.20)	9 (6.67)	.731
Paracetamol	26 (35.1)	24 (39.3)	50 (37.0)	.614
Opioids	14 (18.9)	16 (26.2)	30 (22.2)	.309
Other NSAIDs/analgesics	53 (71.6)	38 (62.3)	91 (67.4)	.250
4) Local treatment or surgery [a]	n = 86 **3 (3.49)**	n = 71 **4 (5.63)**	n = 157 **7 (4.46)**	

[a] All local treatment or surgeries were intra-articular injections

15.4.5 Concomitant treatments at the 2-year follow-up visit

Treatments that were co-prescribed with golimumab at the year-2 follow-up visit are presented in Table 66 for the total cohort by prior biotherapy status.

Data on concomitant treatments were available for 250 BT-n patients and 119 BT-p patients. At year 2, concomitant treatments were prescribed to half the patients (n=189, 51.2%), and to a higher proportion of BT-p patients (59.7% vs 47.2% of BT-n patients, p = .025). Co-treatments were mostly DMARDs (63.0%), followed by NSAIDs/ analgesics (60.3%) and corticosteroids (15.3%). Only 7 patients (3.70%) were prescribed local or surgical treatment.

- **Disease-modifying antirheumatic drugs (DMARDs)**

At the 2-year follow-up visit, DMARDs were co-prescribed to under two-thirds of patients (n = 119, 63.0%) receiving a concomitant treatment, and more frequently to BT-n (70.3%) than BT-p patients (50.7%). The most used was oral MTX (n = 72, 60.5%), followed by parenteral MTX (n = 30, 25.2%). Leflunomide was given to 11 patients (9.24%). No significant differences were observed in the types of DMARDs prescribed, between BT-n and BT-p patients.

- **NSAIDs/analgesics**

NSAIDs/analgesics were co-prescribed to most patients (n =114, 60.3%), and more frequently to BT-p patients (80.3%) than BT-n patients (48.3%). “Other” (unspecified) NSAIDs/analgesics were most commonly prescribed (n=70, 61.4%); paracetamol was given to 36.0% of patients (n=41) and opioids to 13.2% of patients (n=15). No significant differences were observed in the types of NSAIDs/ analgesics prescribed to BT-n and BT-p patients.

- **Corticosteroids**

At the 2-year follow-up visit, corticosteroids were prescribed to only 15.3% of patients (n=29) who received a concomitant treatment, with no significant difference between BT-n and BT-p groups. Prednisolone/ methylprednisolone and cortisone/hydrocortisone were predominantly prescribed (69.0% and 27.6%, respectively).

- **Local/surgical treatment**

Local/surgical treatments were carried out in 7 patients (3.70%), of whom 6 received intra-articular injections (85.7%) and only 1 had joint replacement. Further information is presented in Table 66.

Table 66: Co-prescriptions for the total cohort at year-2 visit by prior biotherapy (n=383)

Total cohort	BT-n (n=260)	BT-p (n=123)	Total (n=383)	*p*
Concomitant treatments	n = 250	n = 119	n = 369	**.025**
	118 (47.2)	**71 (59.7)**	**189 (51.2)**	
	n = 118	n = 71	n = 189	
1) DMARDs	**83 (70.3)**	**36 (50.7)**	**119 (63.0)**	
	n = 83	n = 36	n = 119	
MTX (oral)	**48 (57.8)**	**24 (66.7)**	**72 (60.5)**	.365
Dosage (mg/week)	n =48	n = 24	n = 72	
Mean (SD)	14.0 (5.15)	14.9 (4.69)	14.3 (4.99)	.456
Median	15.0	15.0	15.0	
Range	2.50 - 25.0	7.50 - 20.0	2.50 - 25.0	
MTX (parenteral)	**22 (26.5)**	**8 (22.2)**	**30 (25.2)**	.621
Dosage (mg/week)	n = 22	n = 7	n = 29	
Mean (SD)	16.7 (4.32)	14.6 (4.66)	16.2 (4.41)	.290
Median	15.0	15.0	15.0	
Range	10.0 - 25.0	10.0 - 20.0	10.0 - 25.0	
Sulfasalazine	**3 (3.61)**	**1 (2.78)**	**4 (3.36)**	1.000
Dosage (g/day)	n = 3	n = 1	n = 4	
Mean (SD)	2.00 (0)	1.00 (.)	1.75 (0.50)	**< .001**
Median	2.00	1.00	2.00	
Range	2.00 - 2.00	1.00 - 1.00	1.00 - 2.00	
Leflunomide	**10 (12.0)**	**1 (2.78)**	**11 (9.24)**	0.170
Dosage (mg/day)	n = 10	n = 1	n = 11	
Mean (SD)	17.0 (4.83)	20.0 (0)	17.3 (4.67)	.568
Median	20.0	20.0	20.0	
Range	10.0 - 20.0	20.0 - 20.0	10.0 - 20.0	
Hydroxychloroquine/ Chloroquine	**1 (1.20)**	**2 (5.56)**	**3 (2.52)**	.217
Dosage (mg/day)	n = 1	n = 2	n = 3	1.000
Mean (SD)	400 (.)	400 (0)	400 (0)	
Median	400	400	400	
Range	400 - 400	400 - 400	400 - 400	
Other DMARDs	**2 (2.41)**	**0 (0)**	**2 (1.68)**	1.000
	n = 118	n = 71	n = 189	
2) Corticosteroids	**16 (13.6)**	**13 (18.3)**	**29 (15.3)**	
	n = 16	n = 13	n = 29	
Cortisone/hydrocortisone	**3 (18.8)**	**5 (38.5)**	**8 (27.6)**	.406
Dosage (mg/day)	n = 3	n = 5	n = 8	
Mean (SD)	3.83 (2.75)	4.50 (2.35)	4.25 (2.33)	.726
Median	2.50	5.00	4.50	
Range	2.00 - 7.00	1.00 - 7.50	1.00 - 7.50	
Prednisone/prednisolone/ methylprednisolone	**13 (81.3)**	**7 (53.8)**	**20 (69.0)**	.226
Dosage (mg/day)	n = 13	n = 7	n = 20	

Total cohort	BT-n (n=260)	BT-p (n=123)	Total (n=383)	*p*
Mean (SD)	8.88 (10.3)	6.57 (3.09)	8.08 (8.42)	.572
Median	5.00	7.00	5.00	
Range	3.00 - 40.0	2.00 - 12.0	2.00 - 40.0	
Other corticosteroids	**1 (6.25)**	**1 (7.69)**	**2 (6.90)**	1.000
	n = 118	n = 71	n = 189	
3) NSAIDs/analgesics	**57 (48.3)**	**57 (80.3)**	**114 (60.3)**	
	n = 57	n = 57	n = 114	
Ibuprofen	**4 (7.02)**	**0 (0)**	**4 (3.51)**	.118
Dosage (mg/day)	n = 4	n = 0	n = 4	
Mean (SD)	550 (443)	0 (0)	550 (443)	NA
Medians	400	0	400	
Range	200 - 1200	0	200 - 1200	
Coxibs	**3 (5.26)**	**4 (7.02)**	**7 (6.14)**	1.000
Dosage (mg/day)	n = 3	n = 4	n = 7	
Mean (SD)	247 (172)	150 (57.7)	191 (119)	.332
Median	280	150	200	
Range	60.0 - 400	100 - 200	60.0 - 400	
Paracetamol	**16 (28.1)**	**25 (43.9)**	**41 (36.0)**	.079
Dosage (mg/day)	n = 15	n = 24	n = 39	
Mean (SD)	2173 (1053)	2285 (1086)	2242 (1060)	.753
Median	2000	3000	3000	
Range	600 - 4000	200 - 4000	200 - 4000	
Opioids	**4 (7.02)**	**11 (19.3)**	**15 (13.2)**	.052
Dosage (mg/day)	n = 3	n = 11	n = 14	
Mean (SD)	370 (547)	146 (170)	194 (278)	.893
Median	100	75.0	87.5	
Range	10.0 - 1000	10.0 - 600	10.0 - 1000	
Other NSAIDs/analgesics	**39 (68.4)**	**31 (54.4)**	**70 (61.4)**	.124
	n = 118	n = 71	n = 189	
4) Local treatment or surgery	**5 (4.24)**	**2 (2.82)**	**7 (3.70)**	
	n = 5	**n = 2**	**n = 7**	
Intra-articular injections	4 (80.0)	2 (100)	6 (85.7)	
Joint replacement	1 (20.0)	0 (0)	1 (14.3)	

- **Rheumatoid arthritis (RA)**

Concomitant treatments in the RA cohort at year-2 follow-up are given in Table 67. Year-2 co-prescription data were available for 93 RA patients. The majority were prescribed other treatments with golimumab (n=77, 82.8%), of whom 71 (92.2%) were given DMARDs, 28 (36.4%) were given NSAIDs/ analgesics, and 23 (29.9%) were given corticosteroids. A higher proportion of BT-n than BT-p patients were co-prescribed DMARDs (96.4% vs. 81.8%) and a greater proportion of BT-p patients received NSAIDs/analgesics (59.1%) compared to BT-n patients (27.3%).

Among patients who were co-prescribed DMARDs (n=71), 42 (59.2%) received oral MTX, 19 (26.8%) received parenteral MTX, and 7 (9.86%) were given leflunomide – these proportions are similar to DMARD co-prescriptions reported for RA patients at year-1 of follow-up. Of patients who received corticosteroids (n=23), 17 (73.9%) received prednisolone/methylprednisolone and 6 (26.1%) received cortisone/ hydrocortisone. Among the 28 patients co-prescribed with NSAIDs/analgesics, the majority received paracetamol (n=16, 57.1%) and other NSAIDs/analgesics (n=15, 53.6%), similar to the trends observed in RA patients who were co-prescribed NSAIDs/analgesics at year-1.

Localized surgeries were performed in only 2 patients, consisting of intra-articular injections.

Table 67: Co-prescriptions for RA patients at year-2 visit by prior biotherapy (n=98)

Rheumatoid Arthritis (RA)	RA BT-n (n=66)	RA BT-p (n=31)	Total RA (n=97)	*p*
Concomitant treatments	**n = 63** 55 (87.3)	**n = 30** 22 (73.3)	**n = 93** 77 (82.8)	.095
1) DMARDs	**n = 55** 53 (96.4)	**n = 22** 18 (81.8)	**n = 77** 71 (92.2)	
	n = 53	**n = 18**	**n =71**	
MTX (oral)	30 (56.6)	12 (66.7)	42 (59.2)	.453
MTX (parenteral)	16 (30.2)	3 (16.7)	19 (26.8)	.362
Sulfasalazine	1 (1.89)	0 (0)	1 (1.41)	1.000
Leflunomide	6 (11.3)	1 (5.56)	7 (9.86)	.670
Hydroxychloroquine/ Chloroquine	1 (1.89)	2 (11.1)	3 (4.23)	.156
Other DMARDs	2 (3.77)	0 (0)	2 (2.82)	1.000
2) Corticosteroids	**n = 55** 13 (23.6)	**n = 22** 10 (45.5)	**n = 77** 23 (29.9)	
	n = 13	**n = 10**	**n = 23**	
Cortisone/hydrocortisone	2 (15.4)	4 (40.0)	6 (26.1)	.341
Prednisone/prednisolone/ methylprednisolone	11 (84.6)	6 (60.0)	17 (73.9)	.341
Other corticosteroids	1 (7.69)	0 (0)	1 (4.35)	NA
3) NSAIDs/analgesics	**n = 55** 15 (27.3)	**n = 22** 13 (59.1)	**n = 77** 28 (36.4)	
	n = 15	**n = 13**	**n = 28**	
Paracetamol	7 (46.7)	9 (69.2)	16 (57.1)	.229
Opioids	0 (0)	2 (15.4)	2 (7.14)	.206
Other NSAIDs/analgesics	10 (66.7)	5 (38.5)	15 (53.6)	.136
4) Local treatment or surgery [a]	**n = 55** 1 (1.81)	**n = 22** 1 (4.55)	**n = 77** 2 (2.60)	

[a] All local treatment or surgeries were intra-articular injections

- **Psoriatic arthritis (PsA)**

Concomitant treatments in the PsA cohort at year-2 follow-up are presented in Table 68; this data was available for 47 PsA patients. Most PsA patients were prescribed other treatments with golimumab at baseline (n=32, 68.1%), of whom 22 (68.8%) received DMARDs followed by 15 (46.9%) who received NSAIDs/analgesics, and then 5 (15.6%) who received corticosteroids.

Among patients who were co-prescribed DMARDs (n=22), 14 (63.6%) received oral MTX and 5 (22.7%) received parenteral MTX. Leflunomide was co-prescribed to 3 (13.6%) patients, and unlike the initial and year-1 visits, no other DMARDs were prescribed to PsA patients at year-2. BT-p PsA patients were more commonly co-prescribed NSAIDs/analgesics (88.9%), compared to BT-n patients (30.4%). Of the 15 patients who received NSAIDs/analgesics, two-thirds received other NSAIDs/analgesics (n=10, 66.7%), and 3 (20.0%) received paracetamol and also 3 (20.0%) received opioids.

Of the 5 co-prescribed with corticosteroids, 3 (60.0%) had prednisolone/methylprednisolone and 2 (40.0%) had cortisone/hydrocortisone. Local surgeries were performed in 2 BT-n PsA patients only, consisting of 1 intra-articular injection and 1 joint replacement.

Table 68: Co-prescriptions for PsA patients at year-2 visit by prior biotherapy (n=51)

Psoriatic Arthritis (PsA)	PsA BT-n (n=37)	PsA BT-p (n=14)	Total PsA (n=51)	*p*
Concomitant treatments	**n = 34** 23 (67.6)	**n = 13** 9 (69.2)	**n = 47** 32 (68.1)	1.000
1) DMARDs	**n = 23** 17 (73.9)	**n = 9** 5 (55.6)	**n = 32** 22 (68.8)	
	n = 17	**n = 5**	**n = 22**	
MTX (oral)	11 (64.7)	3 (60.0)	14 (63.6)	1.000
MTX (parenteral)	3 (17.6)	2 (40.0)	5 (22.7)	.548
Leflunomide	3 (17.6)	0 (0)	3 (13.6)	1.000
2) Corticosteroids	**n = 23** 3 (13.0)	**n = 9** 2 (22.2)	**n = 32** 5 (15.6)	
	n = 3	**n = 2**	**n = 5**	
Cortisone/hydrocortisone	1 (33.3)	1 (50.0)	2 (40.0)	1.000
Prednisone/prednisolone/ methylprednisolone	2 (66.7)	1 (50.0)	3 (60.0)	1.000
3) NSAIDs/analgesics	**n = 23** 7 (30.4)	**n = 9** 8 (88.9)	**n = 32** 15 (46.9)	
	n = 7	**n = 8**	**n = 15**	
Ibuprofen	1 (14.3)	0 (0)	1 (6.67)	.467
Coxibs	0 (0)	1 (12.5)	1 (6.67)	1.000
Paracetamol	0 (0)	3 (37.5)	3 (20.0)	.200
Opioids	2 (28.6)	1 (12.5)	3 (20.0)	.569
Other NSAIDs/analgesics	6 (85.7)	4 (50.0)	10 (66.7)	.282
4) Local treatment or surgery	**n = 23** 2 (8.70)	**n = 9** 0 (0)	**n = 32** 2 (6.25)	
	n = 2	**n = 0**	**n = 2**	
Intra-articular injections	1 (50.0)	-	1 (50.0)	NA
Joint replacement	1 (50.0)	-	1 (50.0)	NA

- **Ankylosing spondylitis (AS)**

Co-treatments in the AS cohort at year-2 follow-up are detailed in Table 69 below. Year-2 co-prescription data were available for 229 AS patients. About a third of AS patients were prescribed other treatments with golimumab at year 2 (n=80, 34.9%), which is a much lower proportion than AS patients who were co-prescribed treatments at year 1 (48.5%, Table 65), and at golimumab initiation (78.9%, Table 24). It was also lower than the proportion of RA (82.8%) and PsA patients (68.1%) who were co-prescribed a treatment at year-2.

Twice the proportion of BT-p versus BT-n AS patients received co-treatments at year-2 (52.6% vs. 26.1%, $p < .001$). Among those who received co-treatments (n=80), the majority got NSAIDs (n=71, 88.8%), 26 patients (32.5%) received DMARDs, and only 1 patient received corticosteroids ("other").

Of the 71 patients co-prescribed with NSAIDs/analgesics, the majority got other NSAIDs/ analgesics (n=45, 63.4%), followed by paracetamol (n=22, 31.0%) and opioids (n=10, 14.1%). In patients who were co-prescribed DMARDs (n=26), 16 (61.5%) and 6 (23.1%) patients received oral and parenteral MTX, respectively. Sulfasalazine was co-prescribed to 3 patients (11.5%).

Local surgeries were performed in only 3 (3.75%) patients, all of them being intra-articular injections.

Table 69: Co-prescriptions for AS patients at year-2 visit by prior biotherapy

Ankylosing spondylitis (AS)	AS BT-n (n=157)	AS BT-p (n=78)	Total AS (n=235)	*p*
Concomitant treatments	**n = 153** 40 (26.1)	**n = 76** 40 (52.6)	**n =229** 80 (34.9)	**< .001**
1) DMARDs	**n = 40** 13 (32.5)	**n = 40** 13 (32.5)	**n = 80** 26 (32.5)	
	n = 13	**n = 13**	**n = 26**	
MTX (oral)	7 (53.8)	9 (69.2)	16 (61.5)	.420
MTX (parenteral)	3 (23.1)	3 (23.1)	6 (23.1)	1.000
Sulfasalazine	2 (15.4)	1 (7.69)	3 (11.5)	1.000
2) Corticosteroids	**n = 40** 0 (0)	**n = 40** 1 (2.50) [a]	**n = 80** 1 (1.25) [a]	
3) NSAIDs/analgesics	**n = 40** 35 (87.5)	**n = 40** 36 (90.0)	**n = 80** 71 (88.8)	
	n = 35	**n = 36**	**n = 71**	
Ibuprofen	3 (8.57)	0 (0)	3 (4.23)	.115
Coxibs	3 (8.57)	3 (8.33)	6 (8.45)	1.000
Paracetamol	9 (25.7)	13 (36.1)	22 (31.0)	.344
Opioids	2 (5.71)	8 (22.2)	10 (14.1)	.085
Other NSAIDs/analgesics	23 (65.7)	22 (61.1)	45 (63.4)	.687
4) Local treatment or surgery [b]	**n = 40** 2 (5.00)	**n = 40** 1 (2.50)	**n = 80** 3 (3.75)	

[a] 1 'other' corticosteroid treatment
[b] All local treatment or surgeries were intra-articular injections

15.5 Administration of golimumab as reported by the patient

The administration of golimumab and satisfaction with the treatment was recorded by the patient, every month, on the injection day.

- **Rheumatoid arthritis (RA)**

Data on golimumab administration in RA patients from the 1st to the 25th injection is summarized in Table 70 and Table 71. The number of patients analyzed for each administration is shown under the injection number.

The majority of patients (96.1% at inclusion, 89.2% at 1 year and 91.3% at 2 years) declared that they had respected the planned date of golimumab injection, as per the physician's prescription. Most injections were performed with pen. The majority of first injections were performed by a professional caregiver (57.0%). After the 1st injection, the need of a professional caregiver to administer the injection gradually decreased over time to 20.7% in year-1 and down to 13.0% in year-2, towards an increase in patient autonomy: 38.4% of patients reported a self-injection at the first injection vs. 68.3% at the 13th injection and 80.4% at injection 25.

The findings regarding patient satisfaction with each injection, from the 1st to the 25th, are also shown in Table 70 and Table 71, and depicted in Figure 7. Most patients were generally satisfied with the golimumab injection.

- **Psoriatic arthritis (PsA)**

Table 72 and Table 73 show data on golimumab administration in PsA patients from the 1st to the 25th injection. The results over time follow a similar pattern to that observed for RA patients. The majority declared that they had respected the injection date assigned by their physician (95.9% at inclusion, 84.3% at 1 year and 80.8% at 2 years). Most injections were performed with a pen. Injections were mostly performed by the patient; 57.3% of administrations were autonomous at inclusion, with patient autonomy increasing and being maintained between 70.0% to 80.0% from the 2nd to the final injection. Patient satisfaction with each injection, from the 1st to the 25th, are given in Table 72 and Table 73, and schematized in Figure 8. Most patients were generally satisfied with the golimumab injection.

- **Ankylosing spondylitis (AS)**

Table 74 and Table 75 show data on golimumab administration in patients with AS, from the 1st to the 25th injection. The results are similar to those of the RA and PsA patients. The majority of patients (93.4% at inclusion, 83.4% at 1 year and 86.3% at 2 years) declared that they had respected the planned date of injection, as per the prescription. The majority of injections were performed with pen.

The injections were mostly performed by the patient (59.4% at inclusion). After the 1st injection, an increase in patient autonomy was observed: 86.0% of patients reported self-administration at the 13th injection and 85.4% at the 25th. The findings on patient satisfaction with each injection, from the 1st to the 25th, are shown in Table 74 and Table 75, and schematized in Figure 9. Most patients were generally satisfied with the golimumab injection.

Table 70 : Golimumab administration in RA patients (n=170) from the 1st to the 13th administration. Only percentages are presented for clarity.

	1st inj	2nd inj	3rd inj	4th inj	5th inj	6th inj	7th inj	8th inj	9th inj	10th inj	11th inj	12th inj	13th inj
Respect of the prescription													
n	154	144	142	128	120	118	110	101	95	95	95	91	84
Yes, %	96.1	90.9	90.1	92.9	87.4	92.3	87.2	89.0	88.4	87.2	95.7	90.0	89.2
Injecting device													
n	150	134	128	118	104	100	94	85	78	79	86	75	65
Pen, %	82.6	79.7	81.9	78.0	75.7	78.0	77.7	77.4	78.2	79.5	80.0	82.4	79.7
Syringe, %	17.4	20.3	18.1	22.0	24.3	22.0	22.3	22.6	21.8	20.5	20.0	17.6	20.3
Person giving the injection													
n	152	143	143	126	117	117	109	101	95	95	95	89	83
Patient, %	38.4	59.2	60.6	60.8	62.9	62.9	67.6	67.0	70.5	68.1	71.3	70.5	68.3
Professional caregiver, %	57.0	33.8	33.8	32.0	29.3	30.2	23.1	26.0	22.1	23.4	20.2	21.6	20.7
Other, %	4.6	7.0	5.6	7.2	7.8	6.9	9.3	7.0	7.4	8.5	8.5	7.9	11.0
Satisfaction with injection													
n	124	115	110	86	88	74	71	65	60	56	59	53	54
Extremely satisfied, %	16.3	18.4	14.7	11.8	16.1	20.5	12.9	14.1	11.7	16.4	12.1	26.9	24.5
Very Satisfied, %	35.8	25.4	23.9	35.3	35.6	26.0	30.0	35.9	40.0	36.4	41.4	32.7	32.1
Satisfied, %	43.1	50.0	50.5	48.2	42.5	45.2	51.4	35.9	41.7	43.6	39.7	32.7	39.6
Not very satisfied, %	4.9	6.2	8.3	3.5	5.8	6.9	5.7	7.8	3.3	1.8	5.2	5.8	3.8
Not at all satisfied, %	0.00	0.0	2.7	1.2	0.0	1.4	0.0	6.3	3.3	1.8	1.7	1.9	0.0

Table 71 : Golimumab administration in RA patients (n=170) from the 14st to the 25th administration. Only percentages are presented for clarity.

	14th inj	15th inj	16th inj	17th inj	18th inj	19th inj	20th inj	21st inj	22nd inj	23rd inj	24th inj	25th inj
Respect of the prescription												
n	86	85	77	74	69	69	67	66	63	57	54	47
Yes, %	88.2	92.9	96.1	89.0	83.8	92.6	93.9	84.6	88.7	96.4	92.5	91.3
Injecting device												
n	69	63	65	60	56	55	49	53	52	43	41	36
Pen, %	80.9	82.3	84.4	79.7	78.2	79.6	83.7	82.7	84.3	86.0	82.9	83.3
Syringe, %	19.1	17.7	15.6	20.3	21.8	20.4	16.3	17.3	15.7	14.0	17.1	16.7
Person giving the injection												
n	86	82	75	74	68	67	67	66	62	56	53	47
Patient, %	71.8	70.7	71.6	67.1	68.7	72.7	72.7	76.9	78.7	78.2	76.9	80.4
Professional caregiver, %	18.8	20.7	18.9	21.9	20.9	16.7	16.7	13.8	11.5	12.7	13.5	13.0
Other, %	9.4	8.5	9.5	11.0	10.4	10.6	10.6	9.2	9.8	9.1	9.6	6.5
Satisfaction with injection												
n	45	46	37	40	42	38	39	41	34	30	32	24
Extremely satisfied, %	20.5	28.9	18.9	25.6	19.5	32.4	15.8	30.0	30.3	27.6	32.3	39.1
Very Satisfied, %	47.7	44.4	40.5	35.9	36.6	37.8	47.4	32.5	36.4	37.9	41.9	39.1
Satisfied, %	27.3	24.4	37.8	30.8	34.1	27.0	34.2	37.5	33.3	31.0	25.8	17.4
Not very satisfied, %	4.5	2.2	2.7	7.7	9.8	2.7	2.6	0.0	0.0	3.5	0.0	4.4
Not at all satisfied, %	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.8	0.0	0.0

Figure 7: Histogram representing the distribution of injection satisfaction categories in RA patients from injections 1 to 25

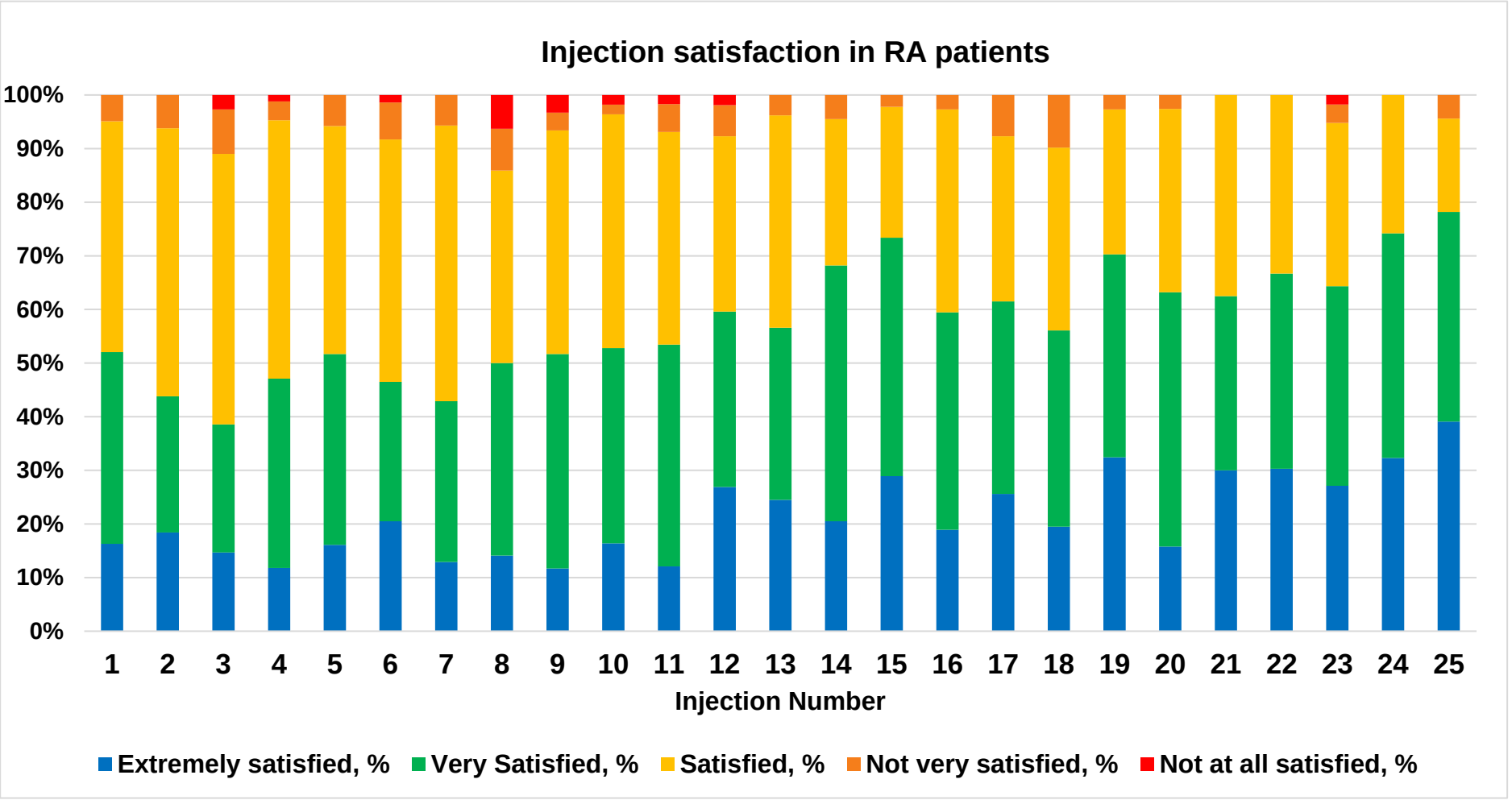


Table 72 : Golimumab administration in PsA patients (n=106) from the 1st to the 13th administration. Only percentages are presented for clarity

	1st inj	2nd inj	3rd inj	4th inj	5th inj	6th inj	7th inj	8th inj	9th inj	10th inj	11th inj	12th inj	13th inj
Respect of the prescription													
n	97	94	92	83	79	78	73	67	64	63	61	52	51
Yes, %	95.9	95.7	87.0	88.0	93.7	85.9	87.7	94.0	89.1	82.5	86.9	86.5	84.3
Injecting device													
n	95	93	87	76	75	70	62	60	56	55	55	45	44
Pen, %	77.9	78.5	80.5	77.6	78.7	78.6	77.4	80.0	76.8	78.2	76.4	80.0	84.1
Syringe, %	22.1	21.5	19.5	22.4	21.3	21.4	22.6	20.0	23.2	21.8	23.6	20.0	15.9
Person giving the injection													
n	96	94	92	82	79	76	73	65	63	61	60	51	50
Patient, %	57.3	71.3	72.8	70.7	72.2	72.4	75.3	73.8	74.6	72.1	73.3	76.5	76.0
Professional caregiver, %	34.4	19.1	18.5	18.3	17.7	15.8	15.1	15.4	14.3	16.4	16.7	13.7	12.0
Other, %	8.3	9.6	8.7	11.0	10.1	11.8	9.6	10.8	11.1	11.5	10.0	9.8	12.0
Satisfaction with injection													
n	82	79	77	60	61	61	44	39	39	37	40	35	30
Extremely satisfied, %	26.8	16.5	10.4	11.7	14.8	19.7	20.5	20.5	12.8	18.9	17.5	17.1	20.0
Very Satisfied, %	31.7	41.8	32.5	48.3	36.1	29.5	29.5	35.9	41.0	37.8	40.0	34.3	56.7
Satisfied, %	36.6	32.9	42.9	33.3	36.1	41.0	40.9	33.3	38.5	29.7	30.0	40.0	16.7
Not very satisfied, %	2.4	7.6	11.7	3.3	11.5	9.8	9.1	7.7	7.7	10.8	7.5	5.7	6.7
Not at all satisfied, %	2.4	1.3	2.6	3.3	1.6	0.0	0.00	2.6	0.0	2.7	5.0	2.9	0.0

Table 73 : Golimumab administration in PsA patients (n=106) from the 1st to the 13th administration. Only percentages are presented for clarity

	14th inj	15th inj	16th inj	17th inj	18th inj	19th inj	20th inj	21st inj	22nd inj	23rd inj	24th inj	25th inj
Respect of the prescription												
n	47	47	46	47	45	39	39	34	34	31	31	26
Yes, %	89.4	89.4	93.5	89.4	88.9	84.6	74.4	88.2	76.5	90.3	90.3	80.8
Injecting device												
n	39	40	36	39	39	33	29	30	29	23	26	22
Pen, %	74.4	80.0	80.6	82.1	74.4	75.8	82.8	76.7	75.0	87.0	80.8	90.0
Syringe, %	25.6	20.0	19.4	17.9	25.6	24.2	17.2	23.3	25.0	13.0	19.2	9.1
Person giving the injection												
n	45	45	46	47	43	39	37	34	31	30	31	25
Patient, %	77.8	77.8	78.3	76.6	72.1	79.5	75.7	76.5	74.2	76.7	74.2	76.0
Professional caregiver, %	11.1	8.9	8.7	10.6	16.3	10.3	8.1	8.8	9.7	10.0	9.7	8.0
Other, %	11.1	13.3	13.0	12.8	11.6	10.3	16.2	14.7	16.1	13.3	16.1	16.0
Satisfaction with injection												
n	32	33	26	29	28	21	25	24	18	17	15	14
Extremely satisfied, %	18.8	24.2	23.1	3.5	21.4	19.0	20.0	16.7	16.7	23.5	33.3	21.4
Very Satisfied, %	40.6	30.3	34.6	51.7	35.7	38.1	48.0	41.7	44.4	35.3	40.0	50.0
Satisfied, %	31.3	42.4	34.6	34.5	32.1	38.1	28.0	37.5	38.9	35.3	26.7	28.6
Not very satisfied, %	9.4	3.0	7.7	10.3	10.7	4.8	4.0	4.2	0.0	5.9	0.0	0.0
Not at all satisfied, %	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Figure 8: Histogram representing the distribution of injection satisfaction categories in PsA patients from injections 1 to 25

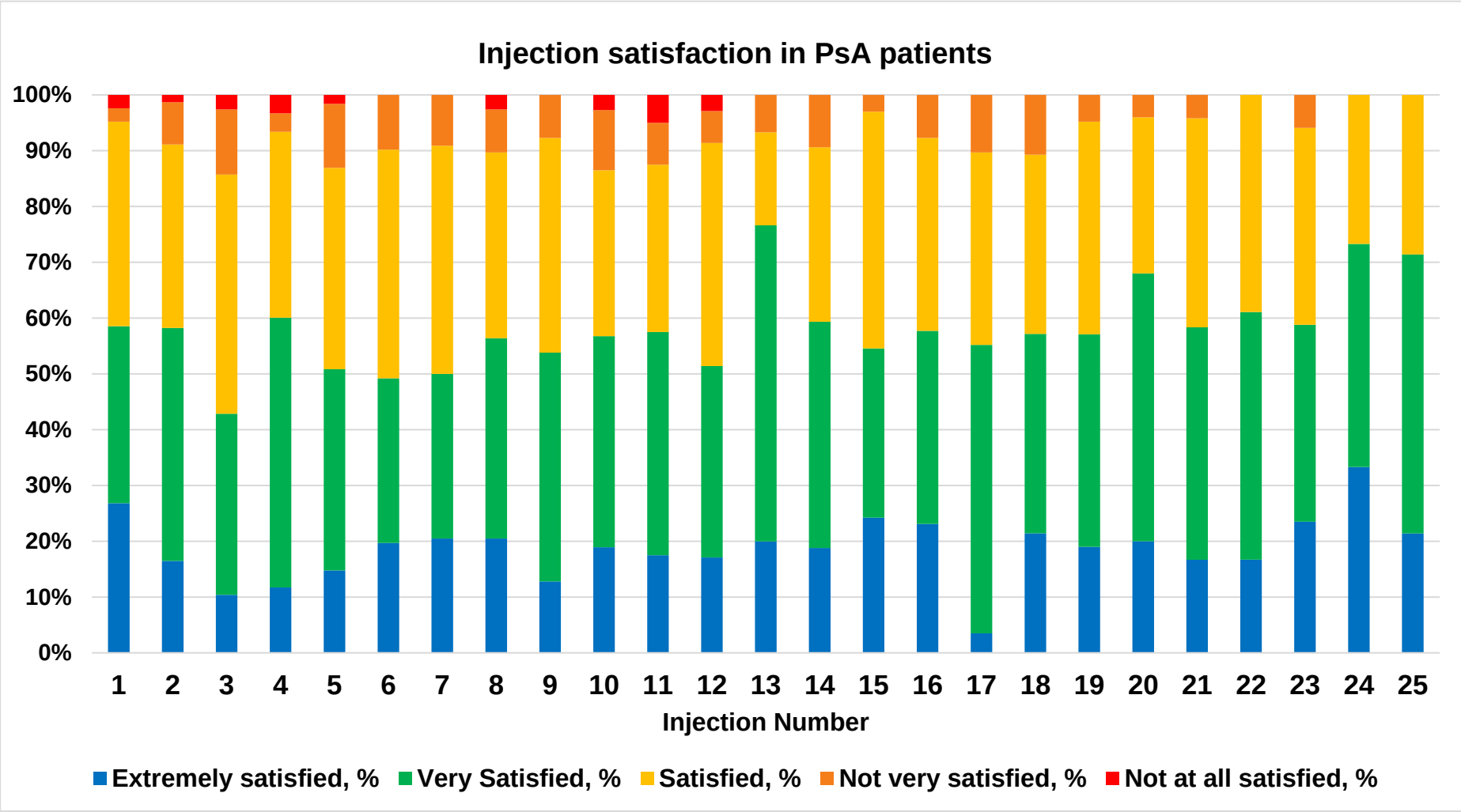


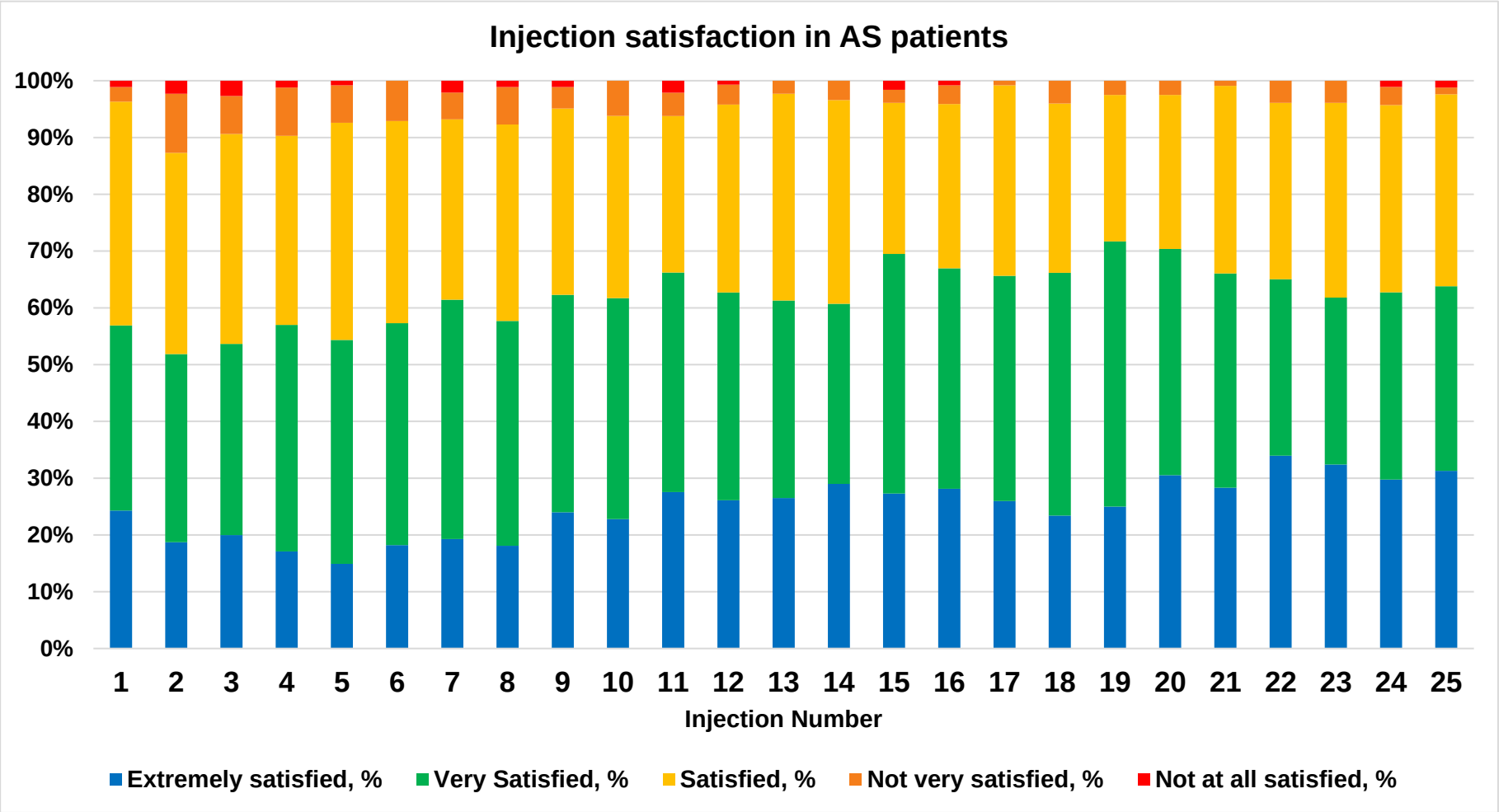
Table 74 : Golimumab administration in AS patients (n=478) from the 1st to the 13th administration. Only percentages are presented for clarity

	1st inj	2nd inj	3rd inj	4th inj	5th inj	6th inj	7th inj	8th inj	9th inj	10th inj	11th inj	12th inj	13th inj
Respect of the prescription													
n	437	427	403	382	339	310	293	274	262	247	240	225	217
Yes, %	93.4	88.8	87.8	87.4	85.3	85.8	80.2	84.7	85.5	83.8	84.2	82.7	83.4
Injecting device													
n	427	411	377	351	308	277	266	239	225	221	200	194	187
Pen, %	79.4	79.8	83.0	82.3	81.5	81.6	81.6	83.3	82.2	82.8	82.5	85.1	82.4
Syringe, %	20.6	20.2	17.0	17.7	18.5	18.4	18.4	16.7	17.8	17.2	17.5	14.9	17.6
Person giving the injection													
n	434	420	399	375	337	307	285	271	261	241	234	221	214
Patient, %	59.4	75.0	78.7	81.1	81.9	84.4	84.9	84.9	86.6	86.3	87.2	87.8	86.0
Professional caregiver, %	35.0	18.1	14.5	12.5	11.3	9.1	8.1	8.9	8.0	7.9	7.3	6.3	6.5
Other, %	5.5	6.9	6.8	6.4	6.8	6.5	7.0	6.3	5.4	5.8	5.5	5.9	7.5
Satisfaction with injection													
n	350	347	300	258	241	225	192	182	183	162	161	142	132
Extremely satisfied, %	24.3	18.7	20.0	17.1	14.9	18.2	19.3	18.1	24.0	22.8	24.8	26.1	26.5
Very Satisfied, %	32.6	33.1	33.7	39.9	39.4	39.1	42.2	39.6	38.3	38.9	34.8	36.6	34.8
Satisfied, %	39.4	35.4	37.0	33.3	38.2	35.6	31.8	34.6	32.8	32.1	24.8	33.1	36.4
Not very satisfied, %	2.6	10.4	6.7	8.5	6.6	7.1	4.7	6.6	3.8	6.2	3.7	3.5	2.3
Not at all satisfied, %	1.1	2.3	2.7	1.2	0.8	0.00	2.1	1.1	1.1	0.0	1.9	0.7	0.0

Table 75 : Golimumab administration in AS patients (n=478) from the 14st to the 25th administration. Only percentages are presented for clarity

	14th inj	15th inj	16th inj	17th inj	18th inj	19th inj	20th inj	21st inj	22nd inj	23rd inj	24th inj	25th inj
Respect of the prescription												
n	212	207	202	196	187	181	167	160	158	151	147	124
Yes, %	81.6	84.5	85.6	85.2	85.0	80.1	87.4	86.9	86.1	85.4	84.4	86.3
Injecting device												
n	175	171	176	154	154	147	136	130	138	120	115	104
Pen, %	82.9	82.5	83.5	82.5	83.8	81.0	86.0	80.8	83.3	82.5	80.0	82.7
Syringe, %	17.1	17.5	16.5	17.5	16.2	19.0	14.0	19.2	16.7	17.5	20.0	17.3
Person giving the injection												
n	213	205	201	186	181	174	160	158	154	148	142	123
Patient, %	86.4	85.4	85.1	85.5	86.7	86.8	87.5	84.2	85.7	86.5	84.5	85.4
Professional caregiver	6.6	6.8	6.0	6.4	6.1	5.7	5.0	7.6	5.8	4.7	6.3	4.9
Other, %	7.0	7.8	8.9	8.1	7.2	7.5	7.5	8.2	8.4	8.8	9.2	9.8
Satisfaction with injection												
n	145	128	121	131	124	120	118	106	103	102	94	80
Extremely satisfied, %	29.0	27.3	28.1	26.0	23.4	25.0	30.5	28.3	34.0	32.4	29.8	31.3
Very Satisfied, %	31.7	42.2	38.8	39.7	42.7	46.7	39.8	37.7	31.1	29.4	33.0	32.5
Satisfied, %	35.9	26.6	28.9	33.6	29.8	25.8	27.1	33.0	31.1	34.3	33.0	33.8
Not very satisfied, %	3.4	2.3	3.3	0.8	4.0	2.5	2.5	0.9	3.9	3.9	3.2	1.2
Not at all satisfied, %	0.0	1.6	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1	1.2

Figure 9: Histogram representing the distribution of injection satisfaction categories in PsA patients from injections 1 to 25



15.6 Disease activity as assessed by the physician

Disease activity was assessed via:

- CRP values for the three CIRDs :
- For RA and PsA: the DAS28 questionnaire and physician's global assessment of disease activity
- For AS: the ASDAS questionnaire.

The Disease Activity Index Score 28 (DAS28) is a validated instrument [23, 24] and is used in routine rheumatology. It combines the evaluation of tender joints (28 joints), swollen joints (28 joints), CRP or ESR, and patient's global assessment of disease activity, to obtain a score ranging from 0 to 10. Disease activity can be interpreted as low (DAS28 ≤3.2), moderate (3.2< DAS28 ≤ 5.1), or high (DAS28 > 5.1).

The Ankylosing spondylitis Disease Activity Score (ASDAS) measures disease activity using an algorithm that assesses back pain, morning stiffness duration, joint pain/swelling, patient global disease activity assessment, and CRP [26]. The global score ranges from 0 to 10; a score of <1.3 is the threshold for an inactive disease state, between 1.3 and 2.1: moderate disease activity, between 2.1 and 3.5: high disease activity and a score >3.5 signifies very high disease activity [27].

For the analyses of disease activity evolutions, the CRP based scores will be prioritized in this report.

Physician GA is the physician global assessment of disease activity on a 100-mm visual analogic scale (VAS) ranging from 0 to 100, where 0 = non-active disease and 100 = extremely active disease.

15.6.1 Disease activity at baseline

- **Rheumatoid arthritis (RA) disease activity at baseline:**

At baseline, no significant differences in disease activity severity between BT-n and BT-p patients with RA were observed. Baseline disease activity (based on CRP) was available for 160 of 170 RA patients. It was moderate for the majority of RA patients (n=102, 63.8%), high for 35 patients (21.9%) and low for 23 patients (14.4%). For the overall RA cohort, the mean DAS28-CRP score was 4.34, and the mean physician's global assessment (GA) of disease activity was 52.2. These results are detailed in Table 76 below.

Table 76: Baseline disease activity in rheumatoid arthritis (RA) patients by prior biotherapy

Rheumatoid arthritis (RA)	BT-n patients (n=110)	BT-p patients (n=59)	Total (n=169)	*p*
Physician's GA of RA activity				.865
n	106	58	164	
Mean (SD)	52.5 (16.7)	51.7 (16.8)	52.2 (16.7)	
Median	52.0	55.0	53.0	
Range	0 - 90.0	10.0 - 86.0	0 - 90.0	
DAS 28 (ESR)				.351
n	98	53	151	
Mean (SD)	4.46 (1.35)	4.68 (1.05)	4.54 (1.25)	
Median	4.55	4.68	4.61	
Range	0.68 - 7.16	1.88 - 6.82	0.68 - 7.16	
RA activity level (DAS28 ESR)				**.028**
n	98	53	151	
Low (DAS28<=3.2)	19 (19.4)	2 (3.77)	21 (13.9)	
Moderate (3.2<DAS28<=5.1)	52 (53.1)	35 (66.0)	87 (57.6)	
High (DAS28>5.1)	27 (27.6)	16 (30.2)	43 (28.5)	

Rheumatoid arthritis (RA)	BT-n patients (n=110)	BT-p patients (n=59)	Total (n=169)	*p*
DAS 28 (CRP)				.669
n	105	55	160	
Mean (SD)	4.33 (1.14)	4.38 (1.06)	4.34 (1.11)	
Median	4.33	4.33	4.33	
Range	1.72 - 7.18	1.41 - 6.74	1.41 - 7.18	
RA activity level (DAS28 CRP)				.651
n	105	55	160	
Low (DAS28<=3.2)	17 (16.2)	6 (10.9)	23 (14.4)	
Moderate (3.2<DAS28<=5.1)	66 (62.9)	36 (65.5)	102 (63.8)	
High (DAS28>5.1)	22 (21.0)	13 (23.6)	35 (21.9)	

- **Psoriatic arthritis (PsA):**

At baseline (Table 77), no significant differences were noted between BT-n and BT-p patients in mean DAS28 scores and patient distribution as per disease activity severity. Baseline disease activity (based on CRP) was available for 97 of 106 PsA patients. The mean DAS28-CRP was 3.89, and the mean physician's GA of disease activity was 54.0. Disease activity was moderate for almost two-thirds of PsA patients (n=64, 66.0%), low for 22 patients (22.7%), and high for 11 patients (11.3%).

Table 77 : Baseline disease activity in patients with psoriatic arthritis (PsA) by prior biotherapy

Psoriatic arthritis (PsA)	BT-n patients (n=70)	BT-p patients (n=36)	Total (n=106)	*p*
Physician's global assessment of PsA activity				.308
n	68	35	103	
Mean (SD)	53.1 (15.8)	55.9 (18.3)	54.0 (16.7)	
Median	52.0	60.0	54.0	
Range	6.00 - 87.0	19.0 - 81.0	6.00 - 87.0	
DAS 28 (ESR)				.159
n	65	26	91	
Mean (SD)	3.89 (1.16)	4.19 (1.34)	3.98 (1.22)	
Median	4.01	4.47	4.05	
Range	0.53 - 6.43	1.22 - 6.23	0.53 - 6.43	
PsA activity level (DAS28 ESR)				.056
n	65	26	91	
Low (DAS28<=3.2)	14 (21.5)	6 (23.1)	20 (22.0)	
Moderate (3.2<DAS28<=5.1)	44 (67.7)	12 (46.2)	56 (61.5)	
High (DAS28>5.1)	7 (10.8)	8 (30.8)	15 (16.5)	
DAS 28 (CRP)				.113
n	67	30	97	
Mean (SD)	3.79 (0.92)	4.12 (1.15)	3.89 (1.00)	
Median	3.93	4.25	4.01	
Range	1.11 - 5.71	1.11 - 5.80	1.11 - 5.80	
PsA activity level (DAS28 CRP)				.061
n	67	30	97	

Psoriatic arthritis (PsA)	BT-n patients (n=70)	BT-p patients (n=36)	Total (n=106)	*p*
Low (DAS28<=3.2)	16 (23.9)	6 (20.0)	22 (22.7)	
Moderate (3.2<DAS28<=5.1)	47 (70.1)	17 (56.7)	64 (66.0)	
High (DAS28>5.1)	4 (5.97)	7 (23.3)	11 (11.3)	

- **Ankylosing spondylitis (AS)**

Baseline ASDAS (based on CRP) was available for 447 of 478 AS patients. No significant differences were observed between BT-n and BT-p patients at baseline in all aspects (Table 78). The average ASDAS-CRP score for the AS cohort was 3.16. Disease activity was reported as high for over 266 patients (59.5%), very high for 145 patients (32.4%) and moderate for only 35 patients (7.83%). Compared to RA and PsA groups, baseline disease activity seemed more severe in AS patients.

Table 78 : Baseline disease activity in ankylosing spondylitis (AS) patients by prior biotherapy

Ankylosing spondylitis (AS)	BT-n patients (n=291)	BT-p patients (n=187)	Total (n=478)	*p*
ASDAS (ESR)				**.025**
n	249	160	409	
Mean (SD)	2.87 (0.79)	3.03 (0.73)	2.93 (0.77)	
Median	2.83	3.01	2.91	
Range	0.96 - 5.16	1.05 - 5.25	0.96 - 5.25	
AS activity level (ASDAS ESR)				.463
n	249	160	409	
Inactive (ASDAS<1.3)	3 (1.20)	1 (0.63)	4 (0.98)	
Moderate (1.3<=ASDAS<2.1)	36 (14.5)	15 (9.38)	51 (12.5)	
High (ASDAS>=2.1)	160 (64.3)	110 (68.8)	270 (66.0)	
Very high (ASDAS ≥3.5)	50 (20.1)	34 (21.3)	84 (20.5)	
ASDAS (CRP)				.337
n	274	173	447	
Mean (SD)	3.18 (0.79)	3.12 (0.78)	3.16 (0.79)	
Median	3.16	3.08	3.14	
Range	1.35 - 5.39	1.17 - 5.76	1.17 - 5.76	
AS activity level (ASDAS CRP)				.690
n	274	173	447	
Inactive (ASDAS<1.3)	0 (0)	1 (0.58)	1 (0.22)	
Moderate (1.3<=ASDAS<2.1)	22 (8.03)	13 (7.51)	35 (7.83)	
High (ASDAS>=2.1)	161 (58.8)	105 (60.7)	266 (59.5)	
Very high (ASDAS ≥3.5)	91 (33.2)	54 (31.2)	145 (32.4)	

15.6.2 Disease activity at year-1 of follow-up

Disease activity scores were calculated based on the CRP levels of patients for whom the data was available.

- **Rheumatoid arthritis (RA) disease activity at year 1 visit**

One-year follow-up data was available for 123 RA patients out of the 170 at baseline (72.5%), biotherapy history was missing for 1 of these patients. Average physician's GA of disease activity was 21.3 for the RA group, and mean DAS28-CRP (available for 96 patients) was 2.50, with no significant difference between BT-n and BT-p patients. Overall disease activity, according to DAS28-CRP scores, was low in 79.2% of patients, moderate in 19.8%, and high in only 1.04% of patients. Significant clinical improvement, equal to a DAS28-CRP score decrease of ≥ 1.2 points, occurred in 68.1% of RA patients who completed follow-up at year 1 (Table 79).

Table 79 : Disease activity at year-1 of follow-up in patients with rheumatoid arthritis (RA) by prior biotherapy, n = 122

Rheumatoid arthritis (RA)	BT-n patients (n=84)	BT-p patients (n=38)	Total (n=122 [a])	*p*
Physician's GA of RA activity				.390
n	71	31	102	
Mean (SD)	20.5 (18.5)	23.3 (18.9)	21.3 (18.6)	
Median	14.0	19.0	15.0	
Range	0 - 74.0	0 - 74.0	0 - 74.0	
DAS 28 (ESR)				.257
n	63	25	88	
Mean (SD)	2.53 (1.07)	2.87 (1.21)	2.63 (1.11)	
Median	2.56	2.86	2.60	
Range	0.58 - 5.29	0.77 - 5.56	0.58 - 5.56	
RA activity level (DAS28 ESR)				.252
n	63	25	88	
Low (DAS28<=3.2)	48 (76.2)	16 (64.0)	64 (72.7)	
Moderate (3.2<DAS28<=5.1)	14 (22.2)	7 (28.0)	21 (23.9)	
High (DAS28>5.1)	1 (1.59)	2 (8.00)	3 (3.41)	
Significant clinical improvement (Score change ≥ 1.2)				.375
n	57	25	83	
No	15 (26.3)	9 (36.0)	24 (29.3)	
Yes	42 (73.7)	16 (64.0)	58 (70.7)	
DAS 28 (CRP)				.174
n	66	30	96	
Mean (SD)	2.40 (0.89)	2.71 (1.03)	2.50 (0.94)	
Median	2.30	2.64	2.43	
Range	0.96 - 4.54	1.24 - 5.50	0.96 - 5.50	
RA activity level (DAS28 CRP)				.427
n	66	30	96	
Low (DAS28<=3.2)	53 (80.3)	23 (76.7)	76 (79.2)	
Moderate (3.2<DAS28<=5.1)	13 (19.7)	6 (20.0)	19 (19.8)	

Rheumatoid arthritis (RA)	BT-n patients (n=84)	BT-p patients (n=38)	Total (n=122 [a])	*p*
High (DAS28>5.1)	0 (0)	1 (3.33)	1 (1.04)	
Significant clinical improvement (Score change ≥ 1.2)				.104
n	64	30	95	
No	17 (26.6)	13 (43.3)	30 (31.9)	
Yes	47 (73.4)	17 (56.7)	64 (68.1)	

[a] Prior biotherapy status was missing for 1 patient

- **Psoriatic arthritis (PsA) disease activity at year 1 visit**

Data from the follow-up visit at 1 year was available for 84 PsA patients, of 106 at baseline (79.2%). Overall disease activity, as per DAS28-CRP, was low for 70.7% of patients, moderate for 25.9%, and high for only 2 patients (3.45%). Average physician's GA of disease activity was 28.5, and average DAS28-CRP score was 2.64, with no significant differences between BT-n and BT-p patients. Significant clinical improvement occurred in 54.5% of PsA participants who attended the follow-up visit at 1 year. Details on PsA activity at 1-year follow-up are provided in Table 80.

Table 80 : Disease activity at year-1 of follow-up in patients with psoriatic arthritis (PsA) by prior biotherapy, n = 84

Psoriatic arthritis (PsA)	BT-n patients (n=56)	BT-p patients (n=28)	Total (n=84)	*p*
Physician's GA of PsA activity				**.004**
n	46	21	67	
Mean (SD)	23.3 (21.5)	40.0 (22.7)	28.5 (23.1)	
Median	14.5	42.0	23.0	
Range	0 - 94.0	5.00 - 79.0	0 - 94.0	
DAS 28 (ESR)				**.018**
n	37	17	54	
Mean (SD)	2.34 (1.22)	3.24 (1.37)	2.63 (1.33)	
Median	2.51	3.48	2.74	
Range	0.49 - 5.99	0.84 - 5.56	0.49 - 5.99	
PsA activity level (DAS28 ESR)				**.035**
n	37	17	54	
Low (DAS28<=3.2)	28 (75.7)	7 (41.2)	35 (64.8)	
Moderate (3.2<DAS28<=5.1)	8 (21.6)	8 (47.1)	16 (29.6)	
High (DAS28>5.1)	1 (2.70)	2 (11.8)	3 (5.56)	
Significant clinical improvement (Score change ≥ 1.2)				.435
n	34	13	47	
No	14 (41.2)	7 (53.8)	21 (44.7)	
Yes	20 (58.8)	6 (46.2)	26 (55.3)	
DAS 28 (CRP)				.059
n	41	17	58	
Mean (SD)	2.41 (0.94)	3.18 (1.36)	2.64 (1.13)	
Median	2.45	3.10	2.54	
Range	1.08 - 5.18	1.31 - 5.76	1.08 - 5.76	

Psoriatic arthritis (PsA)	BT-n patients (n=56)	BT-p patients (n=28)	Total (n=84)	*p*
PsA activity level (DAS28 CRP)				.146
n	41	17	58	
Low (DAS28<=3.2)	32 (78.0)	9 (52.9)	41 (70.7)	
Moderate (3.2<DAS28<=5.1)	8 (19.5)	7 (41.2)	15 (25.9)	
High (DAS28>5.1)	1 (2.44)	1 (5.88)	2 (3.45)	
Significant clinical improvement (Score change ≥ 1.2)				.912
n	40	15	55	
No	18 (45.0)	7 (46.7)	25 (45.5)	
Yes	22 (55.0)	8 (53.3)	30 (54.5)	

- **Ankylosing spondylitis (AS) disease activity at year 1 visit**

Year-1 follow-up data was available for 350 AS patients out of the 478 at baseline (73.2%). At 1-year, AS activity appeared to be significantly lower and much improved in BT-n over BT-p patients (Table 81).

ASDAS-CRP assessments were available for 255 AS patients, and the mean score was 1.71 in BT-n compared to 2.09 in BT-p patients (p = .001). The proportion of patients with high and very high disease activity in the BT-p group was almost twice more than in the BT-n group (44.9% vs. 27.1%, p = .015). Furthermore, almost twice the proportion of BT-n than BT-p patients attained an ASDAS-CRP score indicating remission (38.6% vs. 22.5%, p = .015).

Significant clinical improvement (change in ASDAS CRP ≥1.1), occurred in 64.8% of BT-n and 44.0% of BT-p patients (p = .002). Major improvement (change in ASDAS CRP ≥ 2), was noted in 28.9% of BT-n and 15.5% of BT-p AS patients (p = .020). These data are presented in Table 81 below.

Table 81 : Disease activity at year-1 of follow-up in patients with ankylosing spondylitis (AS) by prior biotherapy, n = 350

Ankylosing spondylitis (AS)	BT-n patients (n=224)	BT-p patients (n=126)	Total (n=350)	*p*
ASDAS (ESR)				**< .001**
n	152	82	234	
Mean (SD)	1.70 (0.86)	2.18 (0.91)	1.87 (0.91)	
Median	1.59	2.08	1.71	
Range	0.29 - 4.72	0.68 - 5.59	0.29 - 5.59	
AS activity level (ASDAS ESR)				**.002**
n	152	82	234	
Inactive (ASDAS<1.3)	58 (38.2)	15 (18.3)	73 (31.2)	
Moderate (1.3<=ASDAS<2.1)	54 (35.5)	27 (32.9)	81 (34.6)	
High (ASDAS>=2.1)	34 (22.4)	35 (42.7)	69 (29.5)	
Very high (ASDAS ≥3.5)	6 (3.95)	5 (6.10)	11 (4.70)	
Significant clinical improvement (Score change ≥ 1.1)				**<.001**
n	133	76	209	
No	56 (42.1)	53 (69.7)	109 (52.2)	
Yes	77 (57.9)	23 (30.3)	100 (47.8)	

Ankylosing spondylitis (AS)	BT-n patients (n=224)	BT-p patients (n=126)	Total (n=350)	*p*
Major improvement (Change in ASDAS ESR ≥2)				**.013**
n	133	76	209	
No	105 (78.9)	70 (92.1)	175 (83.7)	
Yes	28 (21.1)	6 (7.89)	34 (16.3)	
ASDAS (CRP)				**.001**
n	166	89	255	
Mean (SD)	1.71 (0.93)	2.09 (0.90)	1.84 (0.93)	
Median	1.54	2.00	1.71	
Range	0.17 - 4.92	0.46 - 4.56	0.17 - 4.92	
AS activity level (ASDAS CRP)				**.015**
n	166	89	255	
Inactive (ASDAS<1.3)	64 (38.6)	20 (22.5)	84 (32.9)	
Moderate (1.3<=ASDAS<2.1)	57 (34.3)	29 (32.6)	86 (33.7)	
High (ASDAS>=2.1)	37 (22.3)	34 (38.2)	71 (27.8)	
Very high (ASDAS ≥3.5)	8 (4.82)	6 (6.74)	14 (5.49)	
Significant clinical improvement (Score change ≥ 1.1)				**.002**
n	159	84	243	
No	56 (35.2)	47 (56.0)	103 (42.4)	
Yes	103 (64.8)	37 (44.0)	140 (57.6)	
Major improvement (Change in ASDAS CRP ≥2)				**.020**
n	159	84	243	
No	113 (71.1)	71 (84.5)	184 (75.7)	
Yes	46 (28.9)	13 (15.5)	59 (24.3)	

15.6.3 Disease activity at year-2 of follow-up

- **Rheumatoid arthritis (RA) disease activity at year 2 visit**

Two years follow up was available for 98 RA patients of 170 at baseline (57.6%). Compared to the results at year 1, disease activity demonstrated significant improvements in RA patients, and more so in BT-n than in BT-p patients (Table 82). Average physician's GA of disease activity was 17.9 (14.7 for BT-n and 24.2 for BT-p patients, *p*= .012). Mean DAS28-CRP (2.28) was available for 72 RA patients at 2 years, and for BT-n and BT-p patients was 2.11 and 2.65, respectively (*p*= .020). The majority of RA patients (86.1%) had weak disease activity at 2 years, and the remaining 13.9% had moderate disease activity; 71.8% of RA patients demonstrated clinically significant improvements from baseline (79.2% of BT-n vs. 56.5% of BT-p patients, *p* = .047).

Table 82 : Disease activity at year-2 of follow-up in patients with RA by prior biotherapy, n = 98

Rheumatoid arthritis (RA)	BT-n patients (n=66)	BT-p patients (n=31)	Total (n=97 [a])	*p*
Physician's GA of RA activity				**.012**
n	54	28	82	
Mean (SD)	14.7 (14.2)	24.2 (17.6)	17.9 (16.0)	
Median	10.0	22.5	13.5	
Range	0 - 69.0	0 - 67.0	0 - 69.0	
DAS 28 (ESR)				.249
n	47	22	69	
Mean (SD)	2.27 (0.96)	2.79 (1.39)	2.44 (1.13)	
Median	2.40	2.64	2.42	
Range	0.28 - 4.28	0.77 - 5.41	0.28 - 5.41	
RA activity level (DAS28 ESR)				**.039**
n	47	22	69	
Low (DAS28<=3.2)	39 (83.0)	15 (68.2)	54 (78.3)	
Moderate (3.2<DAS28<=5.1)	8 (17.0)	4 (18.2)	12 (17.4)	
High (DAS28>5.1)	0 (0)	3 (13.6)	3 (4.35)	
Significant clinical improvement (Score change ≥ 1.2)				0.129
n	42	22	64	
No	8 (19.0)	8 (36.4)	16 (25.0)	
Yes	34 (81.0)	14 (63.6)	48 (75.0)	
DAS 28 (CRP)				**.020**
n	49	23	72	
Mean (SD)	2.11 (0.67)	2.65 (0.94)	2.28 (0.80)	
Median	2.03	2.47	2.14	
Range	0.96 - 3.49	1.46 - 5.07	0.96 - 5.07	
RA activity level (DAS28 CRP)				.065
n	49	23	72	
Low (DAS28<=3.2)	45 (91.8)	17 (73.9)	62 (86.1)	
Moderate (3.2<DAS28<=5.1)	4 (8.16)	6 (26.1)	10 (13.9)	
Significant clinical improvement (Score change ≥ 1.2)				**.047**
n	48	23	71	
No	10 (20.8)	10 (43.5)	20 (28.2)	
Yes	38 (79.2)	13 (56.5)	51 (71.8)	

[a] Prior biotherapy status was missing for 1 patient

- **Psoriatic arthritis (PsA) disease activity at year 2 visit**

Data at 2 years follow-up was available for 52 PsA patients from 106 at inclusion (49.1%). Unlike the results observed in the RA cohort at year 2, no significant differences in disease activity improvement were noted between BT-n and BT-p groups at year 2. Average physician's GA of disease activity for the overall PsA cohort was 20.2 and the mean DAS28-CRP (available for 35 PsA patients) was 2.00. A majority (91.4%) had low disease activity and 72.7% showed significant clinical improvement at year 2, from baseline. These results are detailed in Table 83.

Table 83 : Disease activity at year-2 of follow-up in patients with PsA by prior biotherapy, n = 52

Psoriatic arthritis (PsA)	BT-n patients (n=38)	BT-p patients (n=14)	Total (n=52)	*p*
Physician's GA of PsA activity				.508
n	29	10	39	
Mean (SD)	20.3 (21.8)	20.1 (15.6)	20.2 (20.2)	
Median	11.0	15.5	13.0	
Range	0 - 72.0	2.00 - 47.0	0 - 72.0	
DAS 28 (ESR)				.845
n	25	9	34	
Mean (SD)	2.06 (1.09)	2.03 (0.74)	2.05 (1.00)	
Median	2.01	1.88	1.98	
Range	0.51 - 4.69	1.13 - 3.83	0.51 - 4.69	
PsA activity level (DAS28 ESR)				1.000
n	25	9	34	
Low (DAS28<=3.2)	22 (88.0)	8 (88.9)	30 (88.2)	
Moderate (3.2<DAS28<=5.1)	3 (12.0)	1 (11.1)	4 (11.8)	
Significant clinical improvement (Score change ≥ 1.2)				1.000
n	23	8	31	
No	8 (34.8)	2 (25.0)	10 (32.3)	
Yes	15 (65.2)	6 (75.0)	21 (67.7)	
DAS 28 (CRP)				.770
n	25	10	35	
Mean (SD)	2.01 (0.85)	1.96 (0.66)	2.00 (0.79)	
Median	1.88	1.77	1.80	
Range	1.03 - 4.45	1.47 - 3.73	1.03 - 4.45	
PsA activity level (DAS28 CRP)				1.000
n	25	10	35	
Low (DAS28<=3.2)	23 (92.0)	9 (90.0)	32 (91.4)	
Moderate (3.2<DAS28<=5.1)	2 (8.00)	1 (10.0)	3 (8.57)	
Significant clinical improvement (Score change ≥ 1.2)				1.000
n	24	9	33	
No	7 (29.2)	2 (22.2)	9 (27.3)	
Yes	17 (70.8)	7 (77.8)	24 (72.7)	

- **Ankylosing spondylitis (AS) disease activity at year 2 visit**

Disease activity data at 2 years was available for 241 AS patients of 478 at baseline (50.4%). As with the year 1 results, disease activity demonstrated further improvements in BT-n over BT-p AS patients at year 2 (Table 84). ASDAS-CRP was available for 194 AS patients, and the mean score was 1.70 (1.54 in BT-n vs. 1.99 in BT-p patients, *p* = .002).

Disease activity, was high and very high for 27.8% of AS patients (BT-p 39.1% vs. BT-n 21.6%, *p* = .036). Remission was observed in 38.1% of patients (BT-n 44.0% vs. BT-p 27.5%, *p* = .036).

Significant clinical improvement, (decrease in ASDAS CRP ≥1.1 from baseline), occurred in 59.8% of patients (67.2% of BT-n versus 46.2% of BT-p patients, *p* = .005). Major improvement (decrease in ASDAS CRP ≥2 from baseline), was noted in 31.0% of AS patients, with no significant difference between BT-n and BT-p groups. Details on AS activity at 2 years of follow-up are provided in Table 84.

Table 84 : Disease activity at year-2 of follow-up in patients with AS by prior biotherapy, n = 241

Ankylosing spondylitis (AS)	BT-n patients (n=161)	BT-p patients (n=80)	Total (n=241)	*p*
ASDAS (ESR)				**< .001**
n	114	61	175	
Mean (SD)	1.51 (0.83)	1.96 (0.83)	1.67 (0.85)	
Median	1.39	1.76	1.49	
Range	0.41 - 4.14	0.45 - 3.93	0.41 - 4.14	
AS activity level (ASDAS ESR)				**.009**
n	114	61	175	
Inactive (ASDAS<1.3)	51 (44.7)	13 (21.3)	64 (36.6)	
Moderate (1.3<=ASDAS<2.1)	40 (35.1)	26 (42.6)	66 (37.7)	
High (ASDAS>=2.1)	20 (17.5)	18 (29.5)	38 (21.7)	
Very high (ASDAS ≥3.5)	3 (2.63)	4 (6.56)	7 (4.00)	
Significant clinical improvement (Score change ≥ 1.1)				.074
n	99	52	151	
No	42 (42.4)	30 (57.7)	72 (47.7)	
Yes	57 (57.6)	22 (42.3)	79 (52.3)	
Major improvement (Change in ASDAS ESR ≥2)				.206
n	99	52	151	
No	75 (75.8)	44 (84.6)	119 (78.8)	
Yes	24 (24.2)	8 (15.4)	32 (21.2)	
ASDAS (CRP)				**.002**
n	125	69	194	
Mean (SD)	1.54 (0.91)	1.99 (0.96)	1.70 (0.95)	
Median	1.37	1.84	1.55	
Range	0.12 - 4.05	0.14 - 4.46	0.12 - 4.46	
AS activity level (ASDAS CRP)				**.036**
n	125	69	194	
Inactive (ASDAS<1.3)	55 (44.0)	19 (27.5)	74 (38.1)	
Moderate (1.3<=ASDAS<2.1)	43 (34.4)	23 (33.3)	66 (34.0)	
High (ASDAS>=2.1)	22 (17.6)	20 (29.0)	42 (21.6)	
Very high (ASDAS ≥3.5)	5 (4.00)	7 (10.1)	12 (6.19)	
Significant clinical improvement (Score change ≥ 1.1)				**.005**
n	119	65	184	
No	39 (32.8)	35 (53.8)	74 (40.2)	
Yes	80 (67.2)	30 (46.2)	110 (59.8)	
Major improvement (Change in ASDAS CRP ≥2)				.476
n	119	65	184	
No	80 (67.2)	47 (72.3)	127 (69.0)	
Yes	39 (32.8)	18 (27.7)	57 (31.0)	

15.6.4 Disease activity evolution from inclusion to 2 years.

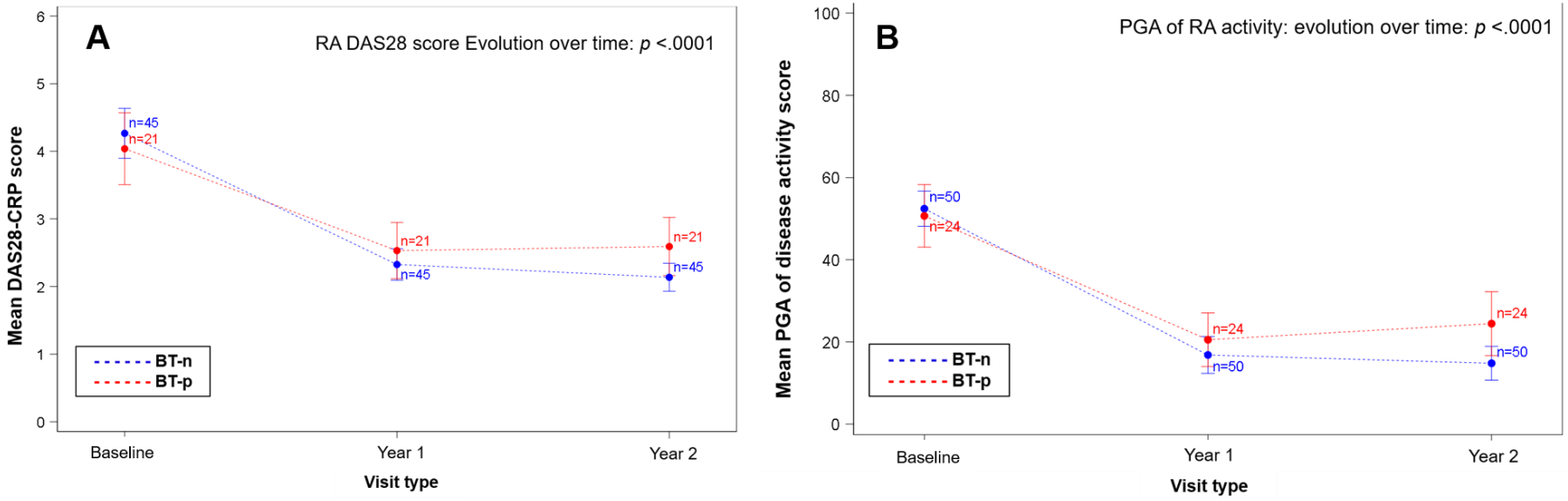
A repeated-measures analysis (2 factor ANOVA) was conducted on the influence of two independent variables (time and prior biotherapy status) on disease activity score changes (DAS28 or ASDAS). Prior biotherapy status consisted of two levels (BT-n and BT-p). The Student's t-test was performed to compare disease activity scores at baseline and year 2.

- **Disease activity evolution for RA patients**

As discussed in section 15.6.3, an improvement in disease activity (as assessed by the DAS28-CRP tool and by the physician) was observed for both, BT-n and BT-p RA patients at 2 years, since inclusion. Figure 10 below depicts the evolution of mean DAS28-CRP scores (A) and PGA of disease activity (B) from baseline to study-end, for patients for whom these data were available at baseline, year-1 and year-2.

Comparing DAS28-CRP and PGA score evolution for BT-n versus BT-p patients from inclusion to 2 years revealed that the improvements in disease activity over time are significant ($p < .0001$ for DAS28-CRP and PGA), but the differences in improvements are not significant between BT-n and BT-p subgroups ($p= .052$ for DAS28-CRP and p= .1273 for PGA). The difference in DAS28 means of RA patients at baseline and 2 years were found to be significant (t-test, p< .0001, n=66). The physician's GA of disease activity also improved significantly for RA patients at 2 years from baseline (t-test, n=74, p< .0001).

Figure 10: Evolution of mean DAS28-CRP (A) and physicians' GA of disease activity (B) from inclusion to 2 years for RA patients, by biotherapy

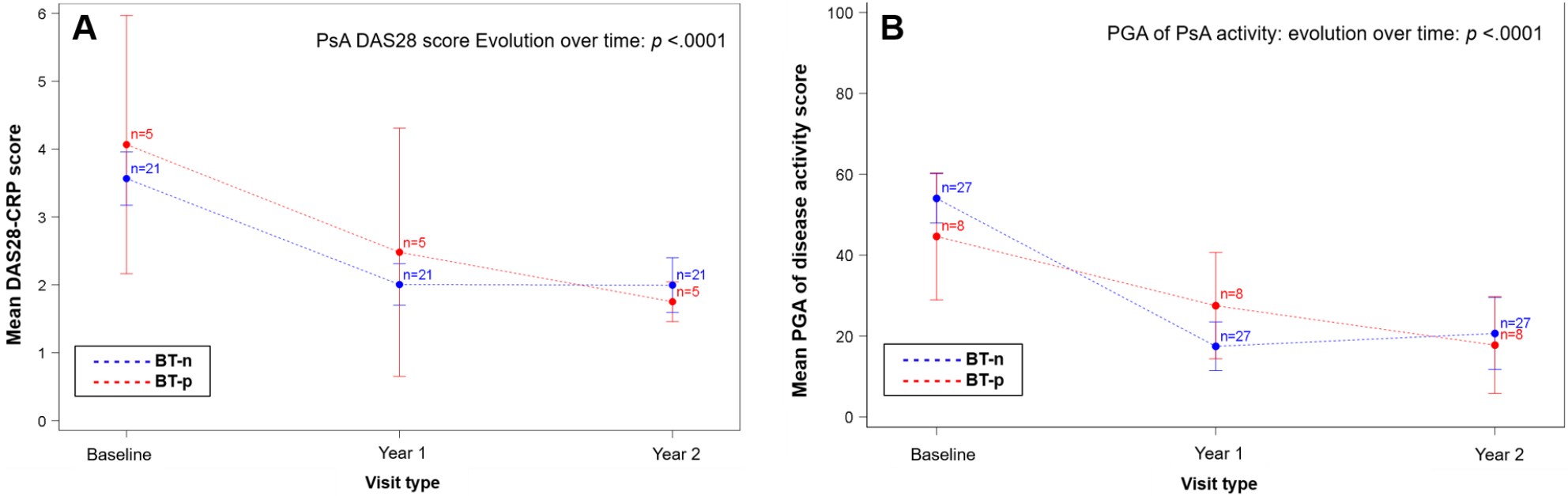


- **Disease activity evolution for PsA patients**

Figure 11 below schematizes the evolution of the mean DAS28-CRP score (A) and PGA of disease activity (B) from inclusion to 2 years, for PsA patients for whom these data were available at inclusion, year-1 and year-2. A significant improvement compared to baseline was reported for the DAS28-CRP score at 2 years (p< .0001, n=26). The physician's GA of disease activity also improved significantly for PsA patients at 2 years (n=35, p< .0001).

A repeated-measures analysis (ANOVA, 2 factors) comparing the evolution of mean DAS28-CRP and PGA scores, over time and by biotherapy history revealed that the decrease in disease activity from baseline to 2 years is significant for PsA patients in both (p< .001 for DAS28-CRP and PGA), and also that the difference in improvements between BT-n versus BT-p patients are significant (p= .0139 for DAS28-CRP and p= .0259 for PGA), with improvements being greater for BT-n patients.

Figure 11: Evolution of mean DAS28-CRP (A) and physicians' GA of disease activity (B) from inclusion to 2 years for PsA patients, by biotherapy

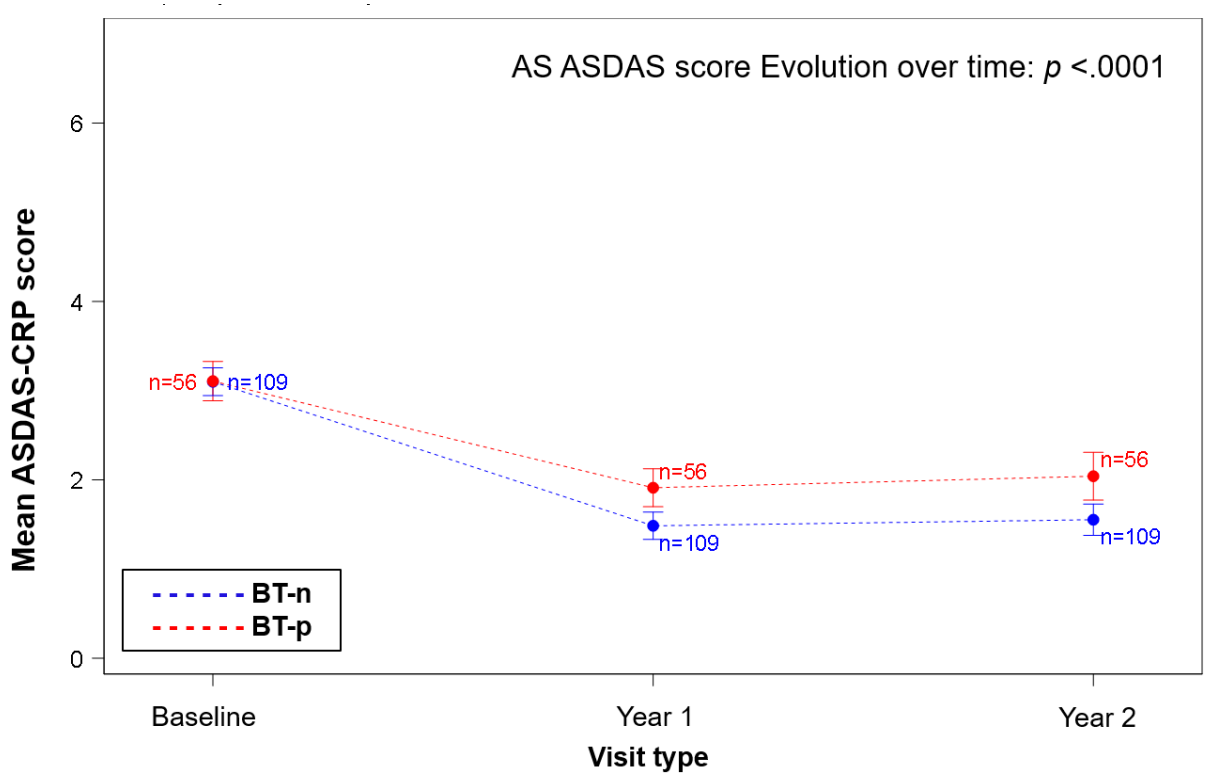


- **Disease activity evolution for AS patients**

A significant reduction in the mean ASDAS score was observed for both BT-n and BT-p PsA patients at 2 years, from inclusion. Figure 12 portrays this evolution from inclusion to follow-up, for AS patients for whom data were available at inclusion, year-1 and year-2, and confirms that the difference in disease activity mean scores at baseline and 2 years are significant (p< .0001, n=165).

A 2-factor ANOVA analysis showed that improvements in disease activity from baseline to 2 years are significant for BT-n and BT-p AS patients (p < .0001), and also that differences in ASDAS improvements between BT-n and BT-p subgroups are significant (p= .0051), with improvements being better for BT-n patients.

Figure 12: Evolution of mean ASDAS-CRP from inclusion to 2 years for AS patients, by biotherapy



15.6.5 Disease activity at golimumab discontinuation

The following section presents disease activity assessments (DAS28 and ASDAS) for patients who discontinued golimumab permanently at any time during the study. Generally, the mean disease activity scores (derived from CRP) at discontinuation were similar to the mean scores at baseline (section 15.6.1), implying no significant improvements in disease activity. Moreover, the distribution of patients as per disease severity is also similar to baseline.

- **Rheumatoid arthritis (RA)**

Golimumab was permanently discontinued in 72 RA patients and disease activity data were available for 57 patients. No significant differences were noted between BT-n and BT-p groups. Overall disease activity, as per the DAS28 CRP, was moderate in 47.5%, low in 32.5% and high in 20.0% of RA patients who discontinued golimumab. Average physician's GA of RA activity was 50.4. Further details are provided in Table 85.

Table 85 : Disease activity at golimumab discontinuation in RA patients by prior biotherapy

Rheumatoid arthritis (RA)	BT-n patients (n=34)	BT-p patients (n=23)	Total (n=57)	*p*
Physician's global assessment of RA activity				.373
n	28	16	44	
Mean (SD)	52.1 (22.5)	47.4 (21.3)	50.4 (21.9)	
Median	56.5	49.0	54.0	
Range	0 - 82.0	18.0 - 81.0	0 - 82.0	
DAS 28 (ESR)				.156
n	25	14	39	
Mean (SD)	3.93 (1.21)	4.80 (1.69)	4.25 (1.44)	
Median	3.93	4.90	4.10	
Range	1.43 - 5.73	2.46 - 7.45	1.43 - 7.45	
RA activity level (DAS28 ESR)				.344
n	25	14	39	
Low (DAS28<=3.2)	9 (36.0)	4 (28.6)	13 (33.3)	
Moderate (3.2<DAS28<=5.1)	11 (44.0)	4 (28.6)	15 (38.5)	
High (DAS28>5.1)	5 (20.0)	6 (42.9)	11 (28.2)	
DAS 28 (CRP)				.094
n	26	14	40	
Mean (SD)	3.80 (0.98)	4.62 (1.44)	4.09 (1.21)	
Median	3.73	4.54	3.93	
Range	1.60 - 5.66	2.67 - 7.07	1.60 - 7.07	
RA activity level (DAS28 CRP)				.240
n	26	14	40	
Low (DAS28<=3.2)	9 (34.6)	4 (28.6)	13 (32.5)	
Moderate (3.2<DAS28<=5.1)	14 (53.8)	5 (35.7)	19 (47.5)	
High (DAS28>5.1)	3 (11.5)	5 (35.7)	8 (20.0)	

- **Psoriatic arthritis (PsA)**

Golimumab was permanently discontinued in 54 PsA patients, and disease activity data was available for 39 patients. There was no significant difference between BT-n and BT-p patients for any item of PsA activity at golimumab discontinuation. Overall disease activity, as per DAS28-CRP, was moderate in 66.7%, low in 23.8% and high in 9.52% of patients. Average physician's GA of PsA activity was 60.4. Details on PsA activity at golimumab discontinuation are provided in Table 86.

Table 86: Disease activity at golimumab discontinuation in PsA patients by prior biotherapy

Psoriatic arthritis (PsA)	BT-n patients (n=21)	BT-p patients (n=18)	Total (n=39)	*p*
Physician's global assessment of PsA activity				.581
n	14	14	28	
Mean (SD)	61.9 (17.1)	58.9 (16.1)	60.4 (16.4)	
Median	65.0	57.0	60.0	
Range	21.0 - 87.0	29.0 - 84.0	21.0 - 87.0	
DAS 28 (ESR)				.414
n	9	12	21	
Mean (SD)	4.05 (1.06)	3.56 (1.26)	3.77 (1.17)	
Median	4.44	3.81	3.86	
Range	2.33 - 5.87	1.00 - 5.71	1.00 - 5.87	
PsA activity level (DAS28 ESR)				1.000
n	9	12	21	
Low (DAS28<=3.2)	2 (22.2)	3 (25.0)	5 (23.8)	
Moderate (3.2<DAS28<=5.1)	6 (66.7)	8 (66.7)	14 (66.7)	
High (DAS28>5.1)	1 (11.1)	1 (8.33)	2 (9.52)	
DAS 28 (CRP)				0.418
n	10	11	21	
Mean (SD)	4.02 (0.82)	3.56 (1.24)	3.78 (1.06)	
Median	3.98	3.52	3.88	
Range	2.63 - 5.42	1.63 - 5.60	1.63 - 5.60	
PsA activity level (DAS28 CRP)				1.000
n	10	11	21	
Low (DAS28<=3.2)	2 (20.0)	3 (27.3)	5 (23.8)	
Moderate (3.2<DAS28<=5.1)	7 (70.0)	7 (63.6)	14 (66.7)	
High (DAS28>5.1)	1 (10.0)	1 (9.09)	2 (9.52)	

- **Ankylosing spondylitis (AS)**

Golimumab was discontinued in 214 AS patients; disease activity data was available for 160 patients. There was no significant difference between BT-n and BT-p patients for any item of AS activity at golimumab discontinuation. Mean ASDAS-CRP at discontinuation was 2.96. AS activity was very high for a quarter of the patients, high for 61.7% of patients, and inactive for only 6 patients. Further details are given in Table 87.

Table 87 : Disease activity at golimumab discontinuation in AS patients by prior biotherapy

Ankylosing spondylitis (AS)	BT-n patients (n=85)	BT-p patients (n=75)	Total (n=160)	*p*
ASDAS (ESR)				0.169
n	54	40	94	
Mean (SD)	2.82 (0.87)	2.98 (0.70)	2.89 (0.80)	
Median	2.83	2.93	2.89	
Range	0.89 - 5.33	0.94 - 4.34	0.89 - 5.33	
AS activity level (ASDAS ESR)				0.273
n	54	40	94	
Inactive (ASDAS<1.3)	2 (3.70)	2 (5.00)	4 (4.26)	
Moderate (1.3<=ASDAS<2.1)	7 (13.0)	1 (2.50)	8 (8.51)	
High (ASDAS>=2.1)	35 (64.8)	26 (65.0)	61 (64.9)	
Very high (ASDAS ≥3.5)	10 (18.5)	11 (27.5)	21 (22.3)	
ASDAS (CRP)				0.724
n	62	45	107	
Mean (SD)	2.96 (0.95)	2.95 (0.77)	2.96 (0.88)	
Median	2.97	2.96	2.96	
Range	0.63 - 5.50	0.55 - 4.35	0.55 - 5.50	
AS activity level (ASDAS CRP)				0.371
n	62	45	107	
Inactive (ASDAS < 1.3)	3 (4.84)	3 (6.67)	6 (5.61)	
Moderate (1.3<=ASDAS<2.1)	7 (11.3)	1 (2.22)	8 (7.48)	
High (ASDAS>=2.1)	37 (59.7)	29 (64.4)	66 (61.7)	
Very high (ASDAS ≥3.5)	15 (24.2)	12 (26.7)	27 (25.2)	

15.7 Specific disease characteristics at year-1 and year-2 of follow-up

The following data were recorded by the rheumatologist during the annual visits:

- For RA: new extra-articular manifestations since the previous visit
- For PsA and AS: new localizations and extra-articular manifestations since the previous visit.

- **Rheumatoid arthritis (RA):** Among 114 assessable patients at year-1, 1 patient developed a new extraarticular problem, and among 93 patients at year-2, there were 4. Details are given in Table 88.

Table 88 : New extra-articular manifestations at year-1 and year-2 of follow-up in RA patients

	Year 1 (n=123)	Year 2 (n=98)
New extra-articular manifestation		
n	114	93
No	113 (99.1)	89 (95.7)
Yes	1 (0.88) [a]	4 (4.30) [b]

[a] 1 pleuro-pulmonary complication

[b] of which 1 pleuro-pulmonary complication, 1 cardiac attack, and 2 others.

- **Psoriatic arthritis (PsA):** Among 75 assessable patients at year 1, there were 3 new extra-articular manifestations, and at year 2, there was only 1 new extra-articular manifestation among 46 assessable patients. New localizations developed among 11 of 75 patients at year 1 (14.7%), of which 7 had affected peripheral joints, 5 patients with enthesis complications, 3 patients with affected axial skeleton and 2 with affected sacroiliac joints.
  New localizations were found in 3 of 46 patients at year 2 (6.52%), all with affected peripheral joints Details are given in Table 89.

Table 89 : New localizations and extra-articular manifestations at year-1 and year-2 (PsA)

	Year 1 (n=84)	Year 2 (n=52)
New extra-articular manifestations		
n	75	46
No	72 (96.0)	45 (97.8)
Yes	3 (4.00)	1 (2.17)
Type of extra-articular manifestation		
n	3	1
• *Cardiac attack*	1 (33.3)	0 (0)
• *Other*	2 (66.7)	1 (100.0)
New clinical forms or localizations		
n	75	46
No	64 (85.3)	43 (93.5)
Yes	11 (14.7)	3 (6.52)
Type of clinical form	**n = 11**	**n = 3**
Peripheral manifestation: joints	7 (63.6)	3 (100.0)
Peripheral manifestation: entheses	5 (45.5)	0 (0)
Axial manifestation: sacroiliac joints	2 (18.2)	0 (0)
Axial manifestation: axial skeleton	3 (27.3)	0 (0)

• **Ankylosing spondylitis (AS):** At year 1, a minority of AS patients had new localizations (n=52, 16.5%) and new extra-articular manifestations (n=13, 4.10%). New localizations were mainly in the sacroiliac joints (n=36, 69.2%) and axial skeleton (n=29, 55.8%). At year 2, only 8 of 227 patients (3.52%) had new extra-articular manifestations and 32 of 229 patients (14.0%) had developed new localizations, mostly in the axial skeleton (n=20, 62.5%) and sacroiliac joints (n=18, 56.3%). The results are elaborated in Table 90.

Table 90 : New localizations and extraarticular manifestations at year-1 and year-2 in AS patients

	Year 1 (n=350)	Year 2 (n=241)
New extra-articular manifestations		
n	317	227
No	304 (95.9)	219 96.5)
Yes	13 (4.10)	8 (3.52)
Type of extra-articular manifestation		
n	13	8
• *Acute anterior uveitis*	7 (53.8)	4 (50.0)
• *Cardiac complications*	2 (15.4)	1 (12.5)
• *Other extra-articular manifestations*	4 (30.8)	3 (37.5)
New clinical forms or localizations		
n	315	229
No	263 (83.5)	197 (86.0)
Yes	52 (16.5)	32 (14.0)
Type of clinical form	**n = 52**	**n = 32**
Peripheral manifestation: entheses	15 (28.8)	7 (21.9)
Peripheral manifestation: joints	12 (23.1)	13 (40.6)
Axial manifestation: sacroiliac joints	36 (69.2)	18 (56.3)
Axial manifestation: Axial skeleton	29 (55.8)	20 (62.5)

15.8 Disease activity as assessed by the patients

Disease activity was assessed by the patient every 3 injections.

- For RA and PsA: using the RAPID3 questionnaire
- For AS: using the BASDAI questionnaire

The Routine Assessment of Patient Index Data 3 (RAPID3) questionnaire is a validated self-report instrument [35] comprising one score assessing functional capacity and two VAS (ranging from 0 to 10) assessing pain and patient global estimate of status, respectively. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questionnaire is a validated instrument [36], also as a French version [37], and is used in routine rheumatology. It includes 6 items pertaining to the 5 major symptoms of AS: fatigue, spinal pain, joint pain/swelling, areas of localized tenderness, and morning stiffness. To give each symptom equal weighting, the mean of the two scores relating to morning stiffness is taken. The resulting 0 to 50 score is divided by 5 to give a final BASDAI score ranging from 0 to 10.

A repeated-measures analysis (2 factor ANOVA) was conducted on the influence of two independent variables (time and prior biotherapy status) on disease activity score changes (RAPID3 or BASDAI). Prior biotherapy status consisted of two levels (BT-n and BT-p).

- **Rheumatoid arthritis (RA)**

At inclusion, the RAPID3 score was reported for 125 of 170 patients with RA. Overall, the mean RAPID3 score at inclusion was 4.49, and scores were comparable for BT-n and BT-p patients. As shown in Table 91, the RAPID3 score decreased over time in patients treated with golimumab. A significant improvement was observed over the 2-year period (p <.0001), as depicted in Figure 13; a significant difference was also observed in RAPID3 score change between BT-n and BT-p RA patients (ANOVA, p <.0001), with RAPID3 showing greater improvement for BT-n than for BT-p patients. For patients still on golimumab treatment at year 2, a significant improvement RAPID3 at 2 years was reported compared to baseline (n=31, p < .0001, paired t-test).

For patients who discontinued golimumab, the mean RAPID3 score seems to be higher than at inclusion, although the significance of this observation could not be confirmed using statistical tests due to the limited number of data at withdrawal.

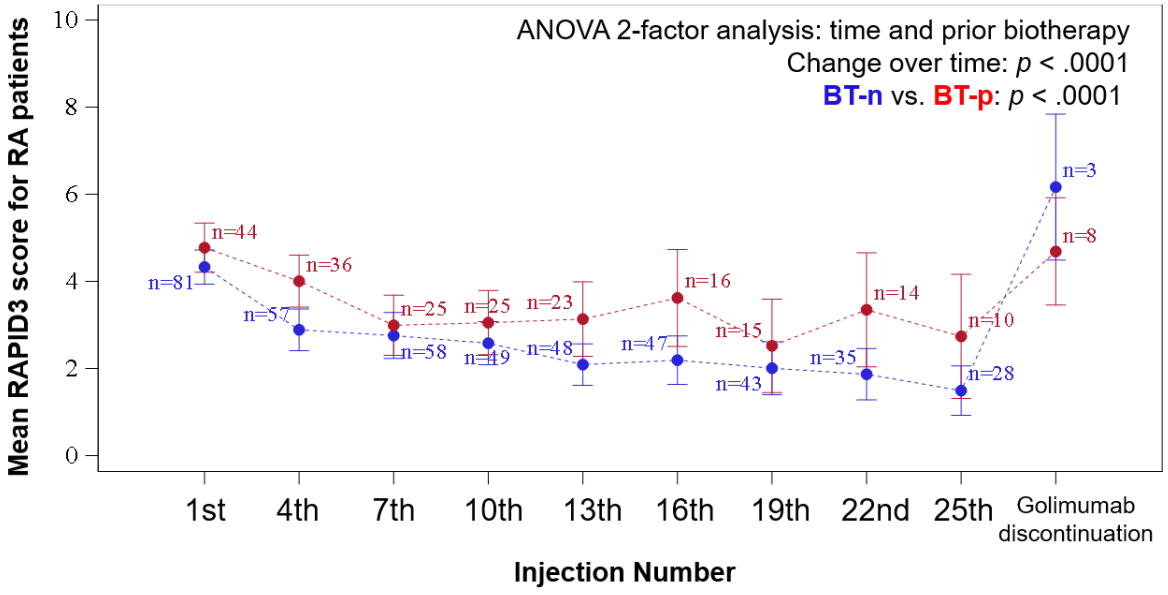
Table 91 : RAPID3 scores of patients with Rheumatoid arthritis (RA) by prior biotherapy

	BT-n (n=110)	BT-p (n=59)	Total (n=169 [a])	*p*
Inclusion and 1st injection				0.190
n	81	44	125	
Mean (SD)	4.33 (1.77)	4.78 (1.85)	4.49 (1.81)	
Median	4.67	4.75	4.67	
Range	0.61 - 7.78	1.39 - 8.44	0.61 - 8.44	
At 4th injection				**.004**
n	57	36	93	
Mean (SD)	2.89 (1.80)	4.01 (1.76)	3.32 (1.86)	
Median	3.22	4.28	3.56	
Range	0 - 6.61	0.22 - 7.72	0 - 7.72	
At 7th injection				.608
n	58	25	83	
Mean (SD)	2.76 (2.00)	2.99 (1.67)	2.83 (1.90)	
Median	2.44	3.00	2.72	
Range	0 - 8.00	0.17 - 6.83	0 - 8.00	
At 10th injection				.276
n	49	25	74	
Mean (SD)	2.58 (1.73)	3.05 (1.78)	2.74 (1.75)	
Median	2.67	3.17	2.67	
Range	0 - 6.56	0.33 - 7.33	0 - 7.33	
At 13th injection				**.022**
n	48	23	71	
Mean (SD)	2.09 (1.64)	3.14 (1.97)	2.43 (1.81)	
Median	1.56	2.78	2.00	
Range	0 - 5.44	0.33 - 6.78	0 - 6.78	
At 16th injection				**.013**
N	47	16	63	
Mean (SD)	2.19 (1.89)	3.62 (2.09)	2.56 (2.02)	
Median	1.44	3.78	2.00	

	BT-n (n=110)	BT-p (n=59)	Total (n=169 [a])	*p*
Range	0 - 7.00	0 - 7.56	0 - 7.56	
At 19th injection				.386
N	43	15	58	
Mean (SD)	2.01 (1.97)	2.52 (1.94)	2.14 (1.96)	
Median	1.11	1.89	1.42	
Range	0 - 7.44	0.17 - 6.00	0 - 7.44	
At 22nd injection				**.017**
N	35	14	49	
Mean (SD)	1.87 (1.72)	3.35 (2.26)	2.29 (1.98)	
Median	1.22	3.39	1.50	
Range	0 - 7.11	0 - 6.61	0 - 7.11	
At 25th injection				**.043**
n	28	10	38	
Mean (SD)	1.49 (1.47)	2.74 (1.99)	1.82 (1.69)	
Median	0.94	2.17	1.28	
Range	0.11 - 4.50	0 - 5.33	0 - 5.33	
At golimumab discontinuation				.137
n	3	8	11	
Mean (SD)	6.17 (0.67)	4.69 (1.47)	5.09 (1.44)	
Median	6.56	5.00	5.39	
Range	5.39 - 6.56	2.22 - 7.00	2.22 - 7.00	

[a] Prior biotherapy data missing for 1 RA patient

Figure 13: Evolution of RAPID3 from baseline to 2 years in RA patients, by prior biotherapy



- **Psoriatic arthritis (PsA)**

At inclusion, the RAPID3 score was reported in 74 of 106 patients with PsA. Overall, the mean RAPID3 score at inclusion was 5.31, and was significantly better for BT-n patients than for BT-p patients (Table 92). As seen in Table 92, the RAPID3 score decreased over the 2-year period in patients treated with golimumab. There was a significant difference in RAPID3 score over time from inclusion to the 25th injection (ANOVA, *p* <.0001), as shown in

Figure 14. There was also a significant difference in RAPID3 score improvement between BT-n and BT-p PsA patients (ANOVA, *p* <.0001), with disease activity showing greater improvement for BT-n than for BT-p patients. For patients still on golimumab treatment at year 2, a significant improvement RAPID3 at 2 years was reported compared to baseline (n=15, p= .0163, paired t-test).

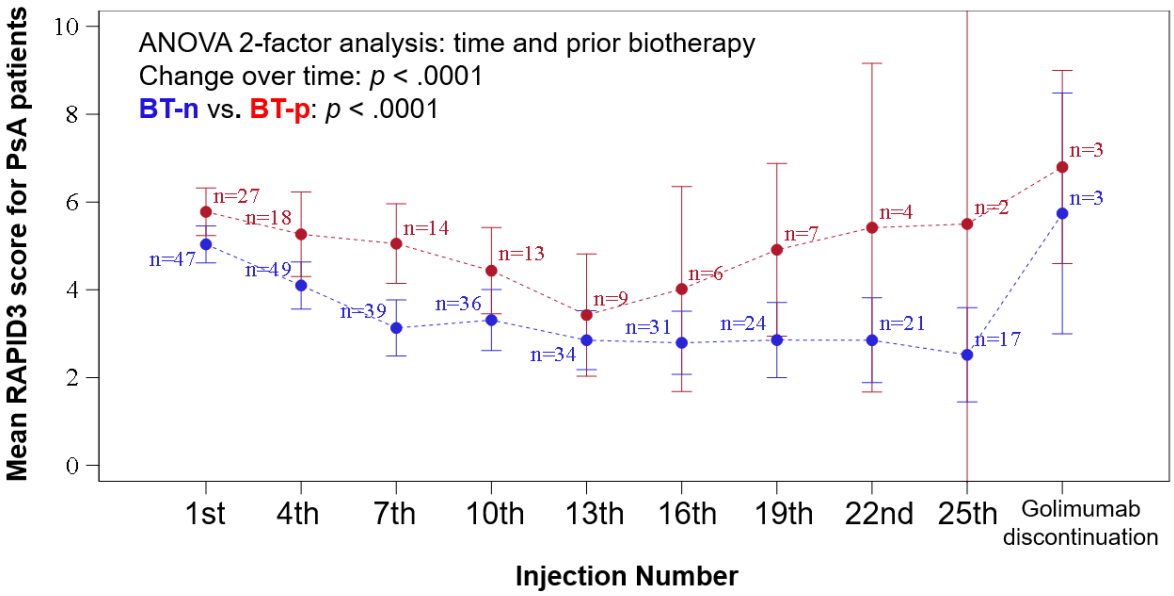
For patients who discontinued golimumab, the mean RAPID3 score seems to be higher than inclusion; although this could not be confirmed using statistical tests due to the limited number of data at withdrawal.

Table 92 : RAPID3 scores of patients with psoriatic arthritis (PsA) by prior biotherapy

	BT-n (n=70)	BT-p (n=36)	Total (n=106)	*p*
Inclusion and 1st injection				**.033**
n	47	27	74	
Mean (SD)	5.04 (1.44)	5.78 (1.37)	5.31 (1.45)	
Median	5.00	5.78	5.22	
Range	0.67 - 7.50	3.78 - 8.17	0.67 - 8.17	
At 4th injection				**.028**
n	49	18	67	
Mean (SD)	4.10 (1.87)	5.27 (1.94)	4.41 (1.94)	
Median	4.67	5.61	4.72	
Range	0.33 - 7.28	1.89 - 7.89	0.33 - 7.89	
At 7th injection				**.002**
n	39	14	53	
Mean (SD)	3.13 (1.97)	5.05 (1.57)	3.64 (2.04)	
Median	3.33	4.58	3.61	
Range	0 - 7.33	3.11 - 7.94	0 - 7.94	
At 10th injection				.082
n	36	13	49	
Mean (SD)	3.31 (2.05)	4.44 (1.63)	3.61 (2.00)	
Median	2.86	4.17	3.39	
Range	0 - 7.44	2.22 - 7.28	0 - 7.44	
At 13th injection				.427
n	34	9	43	
Mean (SD)	2.85 (1.92)	3.43 (1.81)	2.97 (1.90)	
Median	2.28	3.33	2.56	
Range	0.28 - 6.22	1.22 - 6.56	0.28 - 6.56	
At 16th injection				.179
N	31	6	37	
Mean (SD)	2.79 (1.96)	4.02 (2.22)	2.99 (2.02)	

	BT-n (n=70)	BT-p (n=36)	Total (n=106)	*p*
Median	2.33	4.50	2.61	
Range	0 - 6.39	1.00 - 6.44	0 - 6.44	
At 19th injection				**.027**
N	24	7	31	
Mean (SD)	2.86 (2.03)	4.91 (2.13)	3.32 (2.20)	
Median	2.89	4.72	3.33	
Range	0 - 6.78	1.67 - 8.22	0 - 8.22	
At 22nd injection				**.039**
N	21	4	25	
Mean (SD)	2.85 (2.12)	5.42 (2.35)	3.26 (2.32)	
Median	2.00	6.56	3.00	
Range	0 - 6.78	1.89 - 6.67	0 - 6.78	
At 25th injection				.068
n	17	2	19	
Mean (SD)	2.52 (2.09)	5.50 (1.34)	2.83 (2.20)	
Median	2.11	5.50	2.39	
Range	0 - 7.17	4.56 - 6.44	0 - 7.17	
At golimumab discontinuation				.266
n	3	3	6	
Mean (SD)	5.74 (1.10)	6.80 (0.89)	6.27 (1.07)	
Median	6.11	6.56	6.33	
Range	4.50 - 6.61	6.06 - 7.78	4.50 - 7.78	

Figure 14 : Evolution of RAPID3 from baseline to 2 years in PsA patients, by prior biotherapy



- **Ankylosing spondylitis (AS)**

The BASDAI score was reported in 430 of 478 AS patients at inclusion. Overall, the mean BASDAI score at inclusion was 5.48. This baseline score was significantly better for BT-n than for BT-p patients, and this significance was found through all injections (Table 93).

BASDAI scores showed improvements from inclusion up to 2 years for patients treated with golimumab, (ANOVA, $p < .0001$), as shown in Figure 15. Repeated measures analysis also demonstrated a significant difference in BASDAI score change between BT-n and BT-p AS patients (ANOVA, $p < .0001$), with BASDAI showing greater improvement for BT-n than for BT-p patients. For patients still on golimumab treatment at year 2, a significant improvement BASDAI at 2 years was reported compared to baseline (n=106, p <.0001, paired t-test).

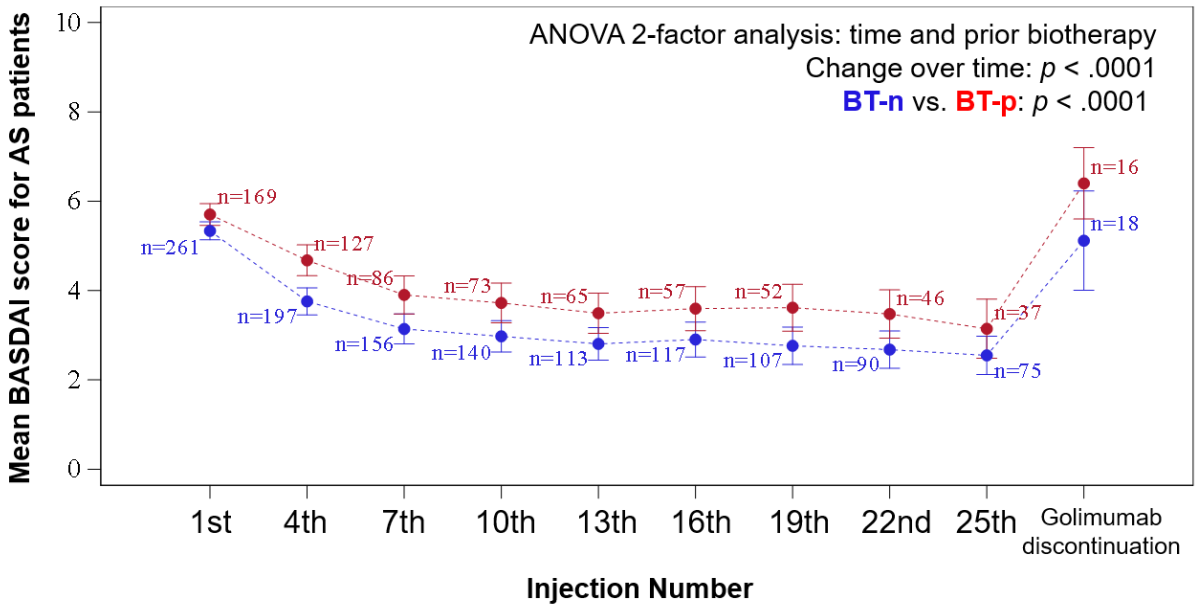
For patients who discontinued golimumab, the mean RAPID3 score seems to be higher than at inclusion; although this could not be confirmed using statistical tests due to the limited number of data at withdrawal.

Table 93 : BASDAI scores of patients with ankylosing spondylitis (AS) by prior biotherapy

	BT-n (n=291)	BT-p (n=187)	Total (n=478)	*p*
Inclusion and 1st injection				.023
n	261	169	430	
Mean (SD)	5.34 (1.65)	5.70 (1.60)	5.48 (1.64)	
Median	5.40	5.73	5.60	
Range	0.63 - 9.60	0.020 - 8.99	0.020 - 9.60	
At 4th injection				0.000
n	197	127	324	
Mean (SD)	3.76 (2.16)	4.68 (1.97)	4.12 (2.13)	
Median	3.35	4.65	4.05	
Range	0 - 9.05	0.40 - 8.90	0 - 9.05	
At 7th injection				.007
n	156	86	242	
Mean (SD)	3.14 (2.13)	3.90 (1.99)	3.41 (2.11)	
Median	2.65	3.75	3.19	
Range	0 - 7.95	0.20 - 9.40	0 - 9.40	
At 10th injection				.011
n	140	73	213	
Mean (SD)	2.97 (2.09)	3.72 (1.91)	3.23 (2.05)	
Median	2.47	3.55	2.95	
Range	0 - 8.30	0.22 - 8.20	0 - 8.30	
At 13th injection				.022
n	113	65	178	
Mean (SD)	2.81 (1.97)	3.49 (1.81)	3.06 (1.94)	
Median	2.34	3.40	2.59	
Range	0 - 7.57	0.54 - 7.54	0 - 7.57	
At 16th injection				.038
N	117	57	174	
Mean (SD)	2.90 (2.13)	3.60 (1.86)	3.13 (2.07)	

	BT-n (n=291)	BT-p (n=187)	Total (n=478)	*p*
Median	2.21	3.19	2.54	
Range	0 - 7.85	0.23 - 7.68	0 - 7.85	
At 19th injection				.017
N	107	52	159	
Mean (SD)	2.76 (2.19)	3.62 (1.88)	3.04 (2.13)	
Median	1.94	3.69	2.57	
Range	0 - 9.00	0.40 - 8.80	0 - 9.00	
At 22nd injection				.025
N	90	46	136	
Mean (SD)	2.68 (1.99)	3.47 (1.82)	2.95 (1.97)	
Median	2.24	3.73	2.57	
Range	0 - 7.06	0.020 - 7.86	0 - 7.86	
At 25th injection				.123
n	75	37	112	
Mean (SD)	2.55 (1.87)	3.14 (1.99)	2.75 (1.92)	
Median	2.07	2.47	2.24	
Range	0 - 7.52	0 - 8.33	0 - 8.33	
At golimumab discontinuation				.061
n	18	16	34	
Mean (SD)	5.12 (2.24)	6.40 (1.50)	5.72 (2.00)	
Median	5.60	5.99	5.83	
Range	1.17 - 7.77	4.32 - 8.90	1.17 - 8.90	

Figure 15: Evolution of BASDAI from baseline to 2 years in AS patients, by prior biotherapy



15.9 Patient global impression of change (PGIC)

The Patient global impression of change (PGIC) scale estimates the degree of change, since the beginning of treatment, in activity limitations, symptoms, emotions, and overall quality of life related to a painful condition [32]. It uses a 7-point numerical scale ranging from 1 = no change to 7 = a great deal better. A favorable improvement is noticed when the score is ≥ 5.

PGIC data was recorded by the patient at every injection, starting from the second injection, and also upon golimumab discontinuation. Data only from the 2nd, 13th and 25th injections and upon golimumab discontinuation will be presented in the upcoming tables for brevity. Corresponding figures, conversely, will present the mean PGIC scores from all injections and at discontinuation.

A repeated-measures analysis (2 factor ANOVA) was conducted on the influence of two independent variables (time and prior biotherapy status) on PGIC evolution from baseline to 2 years. Prior biotherapy status consisted of two levels (BT-n and BT-p).

- **Rheumatoid arthritis (RA)**

The PGIC scale was reported by 137 patients at the 2nd injection, 78 patients at the 13th and 46 patients at the 25th injection from 170 RA patients. There was no significant difference in PGIC scores between BT-n and BT-p patients at each injection. Overall, the average PGIC was 3.31 at the 2nd injection vs. 6.07 at the 25th injection.

As shown in Table 94, the PGIC score increased gradually over time in patients treated with golimumab, reflecting the improvement in disease activity, which was discussed earlier. The percentage of patients with improvement also appeared to increase over time, for those still on golimumab: 30.7% who felt a favorable change after the 2nd injection, 78.2% after the 13th and 89.1% at the 25th. PGIC improvement over time was significant (p <.0001), and more so for BT-n than BT-p patients (p < .0001).

The average PGIC score upon golimumab discontinuation was lower than at 2nd injection, at 1.92 points, with only 1 patient out of 12 reporting a favorable change. This implies that patients who discontinued golimumab had lower global improvement.

Table 94 : PGIC scale in patients with RA at 2nd, 13th and 25th injection and at g

Rheumatoid arthritis (RA)	BT-n (n=110)	BT-p (n=59)	Total (n=169)	*p*
At 2nd injection				.511
n	90	47	137	
Mean (SD)	3.39 (1.87)	3.17 (1.79)	3.31 (1.84)	
Median	3.00	3.00	3.00	
Range	1.00 - 7.00	1.00 - 7.00	1.00 - 7.00	
Favorable change due to injection				.582
n	90	47	137	
No	61 (67.8)	34 (72.3)	95 (69.3)	
Yes	29 (32.2)	13 (27.7)	42 (30.7)	
At 13th injection				.087
n	55	23	78	
Mean (SD)	5.64 (1.24)	5.04 (1.66)	5.46 (1.39)	
Median	6.00	5.00	6.00	
Range	2.00 - 7.00	2.00 - 7.00	2.00 - 7.00	

Rheumatoid arthritis (RA)	BT-n (n=110)	BT-p (n=59)	Total (n=169)	*p*
Favorable change due to injection				.072
n	55	23	78	
No	9 (16.4)	8 (34.8)	17 (21.8)	
Yes	46 (83.6)	15 (65.2)	61 (78.2)	
At 25th injection				.221
n	35	11	46	
Mean (SD)	6.17 (0.95)	5.73 (1.27)	6.07 (1.04)	
Median	6.00	6.00	6.00	
Range	3.00 - 7.00	4.00 - 7.00	3.00 - 7.00	
Favorable change due to injection				.080
n	35	11	46	
No	2 (5.71)	3 (27.3)	5 (10.9)	
Yes	33 (94.3)	8 (72.7)	41 (89.1)	
At golimumab discontinuation				.783
n	4	8	12	
Mean (SD)	1.75 (1.50)	2.00 (1.41)	1.92 (1.38)	
Median	1.00	1.50	1.00	
Range	1.00 - 4.00	1.00 - 5.00	1.00 - 5.00	
Favorable change at discontinuation				1.000
n	4	8	12	
No	4 (100)	7 (87.5)	11 (91.7)	
Yes	0 (0)	1 (12.5)	1 (8.33)	

- **Psoriatic arthritis (PsA)**

The PGIC scale was reported for 94 patients at the 2nd injection, 49 at the 13th and 26 for the final injection, over 106 PsA patients. Mean PGIC scale for all patients was 3.65 at the 2nd injection vs. 5.92 at the 25th injection. As shown in Table 95, the PGIC score increased gradually over time in patients treated with golimumab, reflecting the improvement in the overall patient's health status (*p* <.0001). Moreover, PGIC was significantly better for BT-n than in BT-p patients from the 2nd to the final injection, (*p* <.0001) meaning that BT-n patients responded better to the injection. The percentage of patients with improvement also appears to increase over time, for those still on golimumab. The mean PGIC score reported for 8 PsA patients at golimumab discontinuation was 2.75, with equal number of BT-n and BT-p patients.

Table 95 : PGIC scale in PsA patients at 2nd, 13th and 25th injection and at golimumab discontinuation, by prior biotherapy

Psoriatic arthritis (RA)	BT-n (n=70)	BT-p (n=36)	Total (n=106)	*p*
At 2nd injection				.054
n	64	30	94	
Mean (SD)	3.92 (2.10)	3.07 (1.68)	3.65 (2.01)	
Median	5.00	3.00	3.00	

Psoriatic arthritis (RA)	BT-n (n=70)	BT-p (n=36)	Total (n=106)	*p*
Range	1.00 - 7.00	1.00 - 6.00	1.00 - 7.00	
Favorable change due to injection				.010
n	64	30	94	
No	31 (48.4)	23 (76.7)	54 (57.4)	
Yes	33 (51.6)	7 (23.3)	40 (42.6)	
At 13th injection				.140
n	38	11	49	
Mean (SD)	5.68 (1.47)	4.91 (1.64)	5.51 (1.53)	
Median	6.00	5.00	6.00	
Range	2.00 - 7.00	2.00 - 7.00	2.00 - 7.00	
Favorable change due to injection				1.000
n	38	11	49	
No	9 (23.7)	3 (27.3)	12 (24.5)	
Yes	29 (76.3)	8 (72.7)	37 (75.5)	
At 25th injection				.176
n	22	4	26	
Mean (SD)	6.09 (1.38)	5.00 (1.83)	5.92 (1.47)	
Median	7.00	5.00	6.50	
Range	2.00 - 7.00	3.00 - 7.00	2.00 - 7.00	
Favorable change due to injection				.099
n	22	4	26	
No	2 (9.09)	2 (50.0)	4 (15.4)	
Yes	20 (90.9)	2 (50.0)	22 (84.6)	
At golimumab discontinuation				.080
n	4	4	8	
Mean (SD)	4.00 (2.16)	1.50 (1.00)	2.75 (2.05)	
Median	4.50	1.00	2.00	
Range	1.00 - 6.00	1.00 - 3.00	1.00 - 6.00	
Favorable change at discontinuation				.429
n	4	4	8	
No	2 (50.0)	4 (100)	6 (75.0)	
Yes	2 (50.0)	0 (0)	2 (25.0)	

- **Ankylosing spondylitis (AS)**

The PGIC score was reported for 413 patients at the 2nd injection, 211 patients at the 13th injection and 123 patients at the 25th injection, from the 478 patients with AS. Overall, PGIC scores seemed to improve for all AS patients over time (p <.0001). The percentage of patients with improvement also appeared to increase over time, for those still on golimumab.

The improvement in PGIC among BT-n patients was shown to be significantly greater compared to the BT-p group (p < .0001). Apart from the final injection, and at golimumab discontinuation, the average PGIC score is shown to be significantly enhanced in BT-n than in BT-p patients (Table 96), meaning that the BT-n patients responded better to the injection than BT-p patients.

PGIC scale at golimumab discontinuation was reported for 39 AS patients, and was low: 2.62, meaning that patients who discontinued golimumab treatment declared having less global improvement.

Table 96 : PGIC scale in patients with AS at 2nd, 13th and 25th injection and at golimumab discontinuation, by prior biotherapy

Ankylosing spondylitis (AS)	BT-n (n=291)	BT-p (n=187)	Total (n=478)	*p*
At 2nd injection				.000
n	256	157	413	
Mean (SD)	3.87 (2.07)	3.14 (1.83)	3.59 (2.01)	
Median	4.00	3.00	3.00	
Range	1.00 - 7.00	1.00 - 7.00	1.00 - 7.00	
Favorable change due to injection				**.006**
n	256	157	413	
No	148 (57.8)	112 (71.3)	260 (63.0)	
Yes	108 (42.2)	45 (28.7)	153 (37.0)	
At 13th injection				.**004**
n	141	70	211	
Mean (SD)	5.61 (1.39)	4.99 (1.58)	5.40 (1.48)	
Median	6.00	6.00	6.00	
Range	1.00 - 7.00	2.00 - 7.00	1.00 - 7.00	
Favorable change due to injection				**.009**
n	141	70	211	
No	24 (17.0)	23 (32.9)	47 (22.3)	
Yes	117 (83.0)	47 (67.1)	164 (77.7)	
At 25th injection				.203
n	87	36	123	
Mean (SD)	5.72 (1.44)	5.36 (1.40)	5.62 (1.43)	
Median	6.00	6.00	6.00	
Range	2.00 - 7.00	2.00 - 7.00	2.00 - 7.00	
Favorable change due to injection				.772
n	87	36	123	
No	15 (17.2)	7 (19.4)	22 (17.9)	
Yes	72 (82.8)	29 (80.6)	101 (82.1)	
At golimumab discontinuation				**.036**
n	19	20	39	
Mean (SD)	3.21 (1.69)	2.05 (1.64)	2.62 (1.74)	
Median	3.00	1.00	2.00	
Range	1.00 - 6.00	1.00 - 7.00	1.00 - 7.00	
Favorable change at discontinuation				.235
n	19	20	39	
No	14 (73.7)	18 (90.0)	32 (82.1)	
Yes	5 (26.3)	2 (10.0)	7 (17.9)	

15.10 Pain Related to Rheumatic Disease

Pain severity was reported by the patient for every injection, at the morning of the injection date and at golimumab discontinuation, using a visual analog scale (VAS). The VAS ranges from 0 (best) to 100 (worse score).

Data only at the 1st, 13th and 25th injections and upon golimumab discontinuation will be presented in the upcoming tables for brevity. A repeated-measures analysis (2 factor ANOVA) was conducted on the influence of two independent variables (time and prior biotherapy status) on pain severity change from baseline to 2 years. Prior biotherapy status consisted of two levels (BT-n and BT-p).

- **Rheumatoid arthritis (RA)**

Of the 170 RA patients, pain severity was reported for 151 patients at baseline 81 at the 13th injection and 45 at the final injection; the mean scores were 50.1/100, 26.6/100 and 20.8/100, respectively, showing that pain severity reduced by 30 points on the VAS for pain from baseline to 2 years. A repeated-measures analysis of the influence of 2 factors on pain severity changes: time and prior biotherapy status of patient showed that pain improvement over-time is significantly for the RA cohort from 1st to 25th injection (ANOVA, $p < .0001$) and also for BT-n compared to BT-p patients (ANOVA, $p < .0001$). For patients still on golimumab treatment at year 2, a significant improvement in pain severity at 2 years was reported compared to baseline (n=45, p <.0001, paired t-test).

Pain severity at golimumab discontinuation was reported by 12 RA patients (4 BT-n vs. 8 BT-p patients) and was higher than at baseline (57.6). The scores are presented in Table 97.

Table 97 : Pain measured using a VAS in RA patients at 1st, 13th and 25th injection, and upon golimumab discontinuation by prior biotherapy

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=169*)	p
At inclusion/1st injection				.070
n	98	53	151	
Mean (SD)	47.6 (23.4)	54.6 (24.5)	50.1 (24.0)	
Median	51.5	60.0	54.0	
Range	0 - 91.0	9.00 - 100	0 - 100	
At 13th injection				.605
n	57	24	81	
Mean (SD)	25.3 (20.8)	29.5 (23.3)	26.6 (21.5)	
Median	18.0	29.5	20.0	
Range	2.00 - 75.0	2.00 - 70.0	2.00 - 75.0	
At 25th injection				**.043**
n	34	11	45	
Mean (SD)	18.0 (20.3)	29.5 (18.8)	20.8 (20.3)	
Median	11.0	38.0	13.0	
Range	2.00 - 88.0	4.00 - 52.0	2.00 - 88.0	
At golimumab discontinuation				.495
n	4	8	12	
Mean (SD)	64.5 (13.7)	54.1 (26.3)	57.6 (22.7)	
Median	62.5	60.5	61.0	
Range	53.0 - 80.0	20.0 - 89.0	20.0 - 89.0	

** Prior biotherapy status not available for 1 patient*

- **Psoriatic arthritis (PsA)**

Pain severity was reported for 97 patients at baseline 49 patients at injection 13 and 26 patients at injection 25, from 106 PsA patients. Overall, pain decreased over time from the 1st to the 13th to the 25th injection (means 63.9/100, 30.4/100 and 26.3/100, respectively), reflecting the improvement of pain severity related to PsA, for patients persisting on golimumab.

Pain severity improvement over time was statistically significant (ANOVA, $p < .0001$). Improvement was also significantly better for BT-n than BT-p patients (ANOVA, $p < .0001$). For patients still on golimumab treatment at year 2, a significant improvement in pain severity at 2 years was reported compared to baseline (n=26, p =.0004, paired t-test).

Pain severity at golimumab permanent discontinuation was reported for 8 PsA patients (4 each BT-n and BT-p) and was higher than at baseline (78.0 vs. 63.9), meaning that patients who discontinued golimumab showed a worsening in pain severity. The scores are presented in Table 98.

Table 98 : Pain measured using a VAS in patients with PsA at 1st, 13th and 25th injection, and upon golimumab discontinuation by prior biotherapy

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
At inclusion/1st injection				.242
n	64	33	97	
Mean (SD)	62.3 (20.4)	67.0 (20.8)	63.9 (20.5)	
Median	64.5	69.0	66.0	
Range	11.0 - 97.0	3.00 - 100	3.00 - 100	
At 13th injection				.601
n	37	12	49	
Mean (SD)	29.0 (23.7)	34.6 (24.7)	30.4 (23.8)	
Median	22.0	38.0	25.0	
Range	3.00 - 77.0	0 - 66.0	0 - 77.0	
At 25th injection				.943
n	22	4	26	
Mean (SD)	25.8 (26.9)	29.0 (28.8)	26.3 (26.6)	
Median	16.0	27.5	16.0	
Range	0 - 84.0	0 - 61.0	0 - 84.0	
At golimumab discontinuation				0.175
n	4	4	8	
Mean (SD)	67.0 (27.9)	89.0 (6.68)	78.0 (22.1)	
Median	77.0	90.5	86.0	
Range	27.0 - 87.0	80.0 - 95.0	27.0 - 95.0	

- **Ankylosing spondylitis (AS)**

Out of 478 AS patients, pain severity was reported for 436 patients at baseline, 214 patients at the 13th injection and 125 patients at the final injection.

Overall, an improvement in pain severity related to AS was reported from baseline to year-1 to year-2 (means 64.6/100, 31.5/100 and 28.5/100, respectively). The improvement of pain severity over time, from inclusion to injection 25, was statistically significant for those continuing treatment (ANOVA, $p < .0001$). The changes were also significantly better for BT-n over BT-p patients (ANOVA, $p < .0001$).

For patients still on golimumab treatment at year 2, a significant improvement in pain severity at 2 years was reported compared to baseline (n=117, p <.0001, paired t-test).

Pain severity at golimumab discontinuation was reported for 39 AS patients and was comparable to that at baseline, meaning that patients who discontinued the golimumab treatment showed no improvement in pain severity.

Table 99 : Pain measured using a VAS in patients with AS at 1st, 13th and 25th injection, and upon golimumab discontinuation by prior biotherapy

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
At inclusion/1st injection				.054
n	264	172	436	
Mean (SD)	63.2 (22.5)	66.9 (22.3)	64.6 (22.5)	
Median	68.0	73.5	69.5	
Range	0 - 100	0 - 100	0 - 100	
At 13th injection				**.001**
n	145	69	214	
Mean (SD)	28.1 (23.9)	38.7 (24.5)	31.5 (24.5)	
Median	20.0	32.0	24.0	
Range	0 - 92.0	1.00 - 80.0	0 - 92.0	
At 25th injection				.235
n	87	38	125	
Mean (SD)	26.6 (22.6)	32.8 (25.8)	28.5 (23.7)	
Median	19.0	26.0	21.0	
Range	0 - 77.0	0 - 98.0	0 - 98.0	
At golimumab withdrawal				.305
n	19	20	39	
Mean (SD)	60.3 (29.5)	71.5 (24.6)	66.0 (27.3)	
Median	74.0	78.5	77.0	
Range	5.00 - 99.0	5.00 - 99.0	5.00 - 99.0	

15.11 Health status

The EQ-5D questionnaire was completed by the patient at baseline, every 3 injections, and upon golimumab discontinuation. The European Quality of Life-5 Dimensions (EQ-5D) measurement tool is validated [29] and widely used in economic studies and assessments by health services. The EQ-5D-5L was chosen for this study as it is more precise than the -3L version. A French version is provided by the EuroQol Group (http://www.euroqol.org/). The questionnaire includes 5 questions assessing 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). The EQ-5D score ranges from 0 (death) to 1 (perfect health). Since some health status, characterized by incapacity and severe pain, are considered to be worse than death, these are attributed negative values (up to -0.53).

A repeated-measures analysis (2 factor ANOVA) was conducted on the influence of two independent variables (time and prior biotherapy status) on EQ-5D score change from baseline to 2 years. Prior biotherapy status consisted of two levels (BT-n and BT-p).

- **Rheumatoid arthritis (RA)**

The health status assessed with EQ-5D was reported for 127 patients at baseline vs. 76 patients at the 13th injection and 42 patients at the 25th injection over the 170 patients with RA (Table 100).

Overall, this score increased from the 1st to the 25th injection in the global population (0.43 vs. 0.73) as well as within the BT-n patients (0.48 vs 0.75) and the BT-p patients (0.35 vs 0.63), reflecting the improvement of health status of RA patients over treatment time. Moreover, the difference in mean EQ-5D index at baseline and 2 years for patients continuing treatment was found to be significant (paired t-test, n=36, $p < .0001$)

The 2-factor ANOVA analysis implied that treatment duration as well as prior biotherapy status had a significant impact on the patients' health status ($p < .0001$), with the impact being enhanced for BT-n patients over BT-p patients ($p < .0001$). This change in EQ-5D index is schematized in Figure 16.

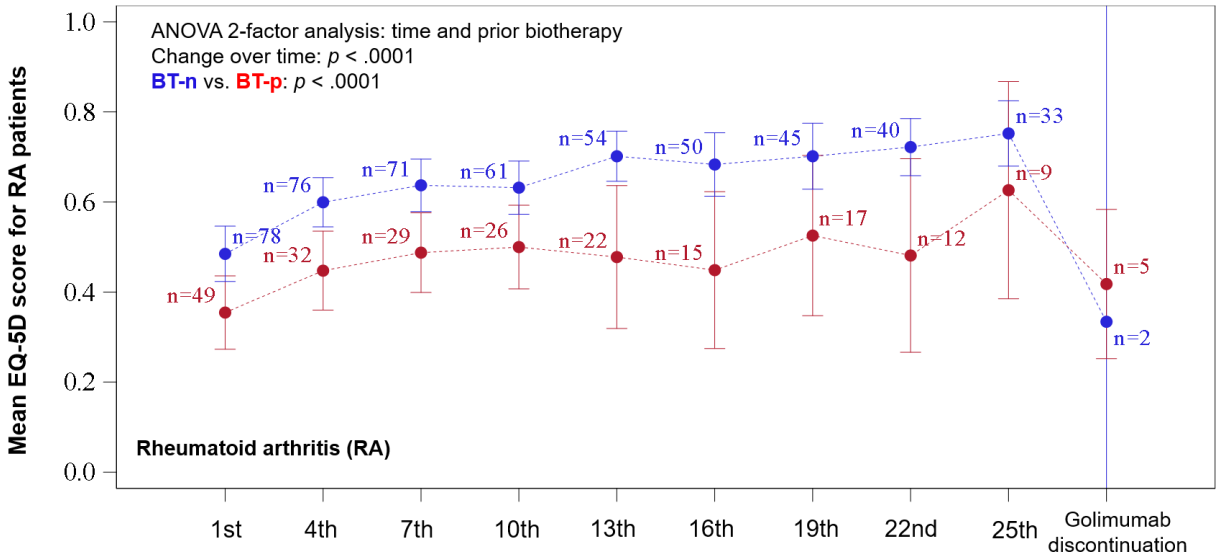
The mean EQ-5D index at golimumab permanent discontinuation was reported for no more than 7 RA patients (2 BT-n and 5 BT-p) and was lower than for patients having continued golimumab treatment during the entire study (0.39 vs. 0.43).

Table 100 : EQ-5D in patients with RA, from inclusion to 2 years, by prior biotherapy

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=170)	p
Inclusion				0.011
n	78	49	127	
Mean (SD)	0.48 (0.27)	0.35 (0.28)	0.43 (0.28)	
Median	0.50	0.36	0.41	
Range	-0.07 - 1.00	-0.39 - 0.91	-0.39 - 1.00	
4th injection				0.003
n	76	32	108	
Mean (SD)	0.60 (0.24)	0.45 (0.24)	0.55 (0.25)	
Median	0.62	0.44	0.54	
Range	-0.00 - 1.00	-0.19 - 0.84	-0.19 - 1.00	
7th injection				0.006
n	71	29	100	
Mean (SD)	0.64 (0.25)	0.49 (0.23)	0.59 (0.25)	
Median	0.64	0.53	0.60	
Range	-0.09 - 1.00	0.005 - 0.84	-0.09 - 1.00	
10th injection				0.017
n	61	26	87	
Mean (SD)	0.63 (0.23)	0.50 (0.23)	0.59 (0.24)	
Median	0.66	0.46	0.61	
Range	0.16 - 1.00	-0.04 - 0.84	-0.04 - 1.00	
13th injection				0.001
n	54	22	76	
Mean (SD)	0.70 (0.20)	0.48 (0.36)	0.64 (0.28)	
Median	0.71	0.48	0.69	
Range	0.19 - 1.00	-0.36 - 0.91	-0.36 - 1.00	
16th injection				0.004
n	50	15	65	
Mean (SD)	0.68 (0.25)	0.45 (0.31)	0.63 (0.28)	
Median	0.76	0.51	0.71	

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=170)	p
Range	0.099 - 1.00	-0.09 - 0.91	-0.09 - 1.00	
19th injection				0.028
n	45	17	62	
Mean (SD)	0.70 (0.24)	0.53 (0.35)	0.65 (0.28)	
Median	0.73	0.58	0.71	
Range	0.094 - 1.00	-0.10 - 0.93	-0.10 - 1.00	
22nd injection				0.003
n	40	12	52	
Mean (SD)	0.72 (0.20)	0.48 (0.34)	0.67 (0.26)	
Median	0.78	0.49	0.71	
Range	0.13 - 1.00	-0.11 - 0.93	-0.11 - 1.00	
25th injection				0.154
n	33	9	42	
Mean (SD)	0.75 (0.20)	0.63 (0.31)	0.73 (0.23)	
Median	0.79	0.69	0.78	
Range	0.23 - 1.00	0.14 - 1.00	0.14 - 1.00	
At golimumab withdrawal				0.561
n	2	5	7	
Mean (SD)	0.33 (0.24)	0.42 (0.13)	0.39 (0.15)	
Median	0.33	0.38	0.38	
Range	0.16 - 0.51	0.24 - 0.59	0.16 - 0.59	

Figure 16 : Change in health status in RA patients throughout the study assessed using the EQ-5D index



- **Psoriatic arthritis (PsA)**

The health status assessment using EQ-5D was reported for 86 patients at baseline vs. 47 patients at the 13th injection and 23 patients at the 25th injection over 106 patients with PsA (Table 101).

The score increased from the 1st to the 25th injection in the global population (0.36 vs. 0.67) as well as within the BT-n patients (0.41 vs 0.67) and the BT-p patients (0.24 vs 0.66), reflecting the improvement of health status of RsA patients over treatment time. Nevertheless, the difference in mean EQ-5D index at baseline and 2 years for patients continuing treatment was not found to be significant, as per the paired t-test (n=17, p = .0636).

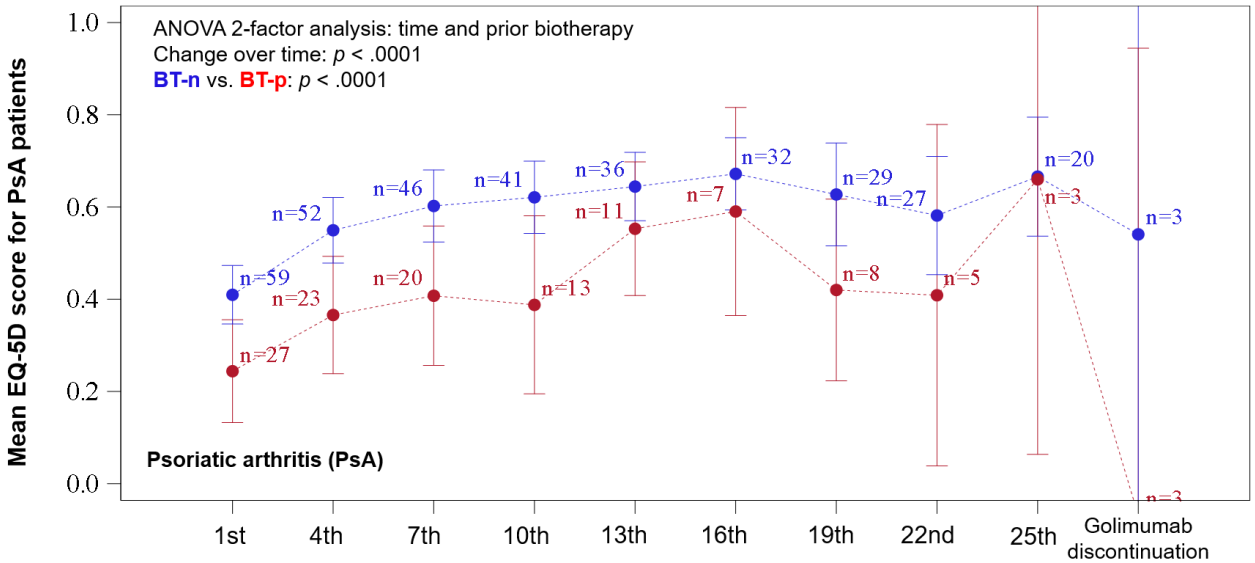
However, the 2-factor ANOVA analysis implied that treatment duration as well as biotherapy had a significant impact of the patients' health status (p <.0001), with the impact being greater for BT-n patients over BT-p patients (p <.0001). This change in EQ-5D index is schematized in Figure 17. The mean EQ-5D index at golimumab discontinuation was reported for only 6 PsA patients (3 BT-n and 3 BT-p) and was lower than for patients having continued golimumab treatment during the entire study (0.24 vs. 0.36).

Table 101 : EQ-5D in PsA patients, from baseline to 2 years, by prior biotherapy

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
Inclusion				0.007
n	59	27	86	
Mean (SD)	0.41 (0.24)	0.24 (0.28)	0.36 (0.27)	
Median	0.38	0.28	0.37	
Range	-0.13 - 0.91	-0.12 - 0.82	-0.13 - 0.91	
4th injection				0.008
n	52	23	75	
Mean (SD)	0.55 (0.26)	0.37 (0.29)	0.49 (0.28)	
Median	0.60	0.34	0.49	
Range	0.099 - 1.00	-0.13 - 1.00	-0.13 - 1.00	
7th injection				0.012
n	46	20	66	
Mean (SD)	0.60 (0.26)	0.41 (0.32)	0.54 (0.29)	
Median	0.66	0.37	0.58	
Range	0.14 - 1.00	-0.19 - 1.00	-0.19 - 1.00	
10th injection				0.008
n	41	13	54	
Mean (SD)	0.62 (0.25)	0.39 (0.32)	0.56 (0.28)	
Median	0.67	0.37	0.65	
Range	-0.02 - 1.00	-0.16 - 1.00	-0.16 - 1.00	
13th injection				0.231
n	36	11	47	
Mean (SD)	0.64 (0.22)	0.55 (0.22)	0.62 (0.22)	
Median	0.70	0.59	0.66	
Range	0.089 - 1.00	0.25 - 0.84	0.089 - 1.00	
16th injection				0.384
n	32	7	39	
Mean (SD)	0.67 (0.22)	0.59 (0.24)	0.66 (0.22)	
Median	0.70	0.58	0.69	

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
Range	0.11 - 1.00	0.27 - 0.93	0.11 - 1.00	
19th injection				0.075
n	29	8	37	
Mean (SD)	0.63 (0.29)	0.42 (0.24)	0.58 (0.29)	
Median	0.63	0.44	0.56	
Range	0.002 - 1.00	0.082 - 0.84	0.002 - 1.00	
22nd injection				0.277
n	27	5	32	
Mean (SD)	0.58 (0.32)	0.41 (0.30)	0.55 (0.32)	
Median	0.67	0.31	0.56	
Range	-0.17 - 1.00	0.18 - 0.93	-0.17 - 1.00	
25th injection				0.972
n	20	3	23	
Mean (SD)	0.67 (0.28)	0.66 (0.24)	0.67 (0.27)	
Median	0.71	0.75	0.73	
Range	0.078 - 1.00	0.39 - 0.84	0.078 - 1.00	
At golimumab withdrawal				0.111
n	3	3	6	
Mean (SD)	0.54 (0.32)	-0.07 (0.41)	0.24 (0.47)	
Median	0.36	-0.28	0.36	
Range	0.36 - 0.91	-0.33 - 0.40	-0.33 - 0.91	

Figure 17 : Change in health status in PsA patients throughout the study assessed with the EQ-5D index



- **Ankylosing spondylitis (AS)**

The health status assessed with EQ-5D was reported for 422 patients at baseline vs. 204 patients at the 13th injection and 123 patients at the 25th injection over 478 patients with AS (Table 102).

Overall, this score increased from the 1st to the 25th injection in the global population (0.38 vs. 0.64) as well as within BT-n patients (0.39 vs 0.67) and BT-p patients (0.36 vs 0.58), reflecting the improvement in health status of AS patients over treatment time. Moreover, the difference in mean EQ-5D index at baseline and 2 years for those continuing golimumab was found to be significant (paired t-test, n=113, $p < .0001$).

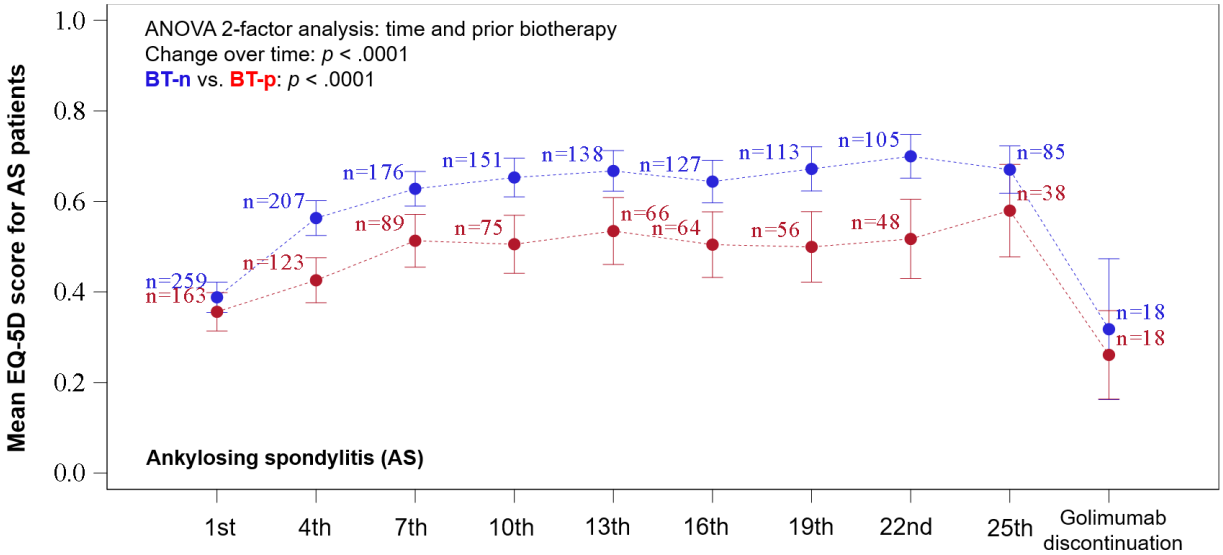
The 2-factor ANOVA analysis implied that treatment duration as well as biotherapy had a significant impact of the patients' health status ($p <.0001$), with the impact being greater for BT-n patients over BT-p patients ($p <.0001$). This change in EQ-5D index is schematized in Figure 18. The mean EQ-5D index at golimumab permanent discontinuation was reported for only 36 AS patients (18 in both groups) and was lower than at inclusion (0.32 vs. 0.26), indicating a worsening of health status.

Table 102 : EQ-5D in patients with AS, from inclusion to 2 years, by prior biotherapy

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
Inclusion				0.241
n	259	163	422	
Mean (SD)	0.39 (0.27)	0.36 (0.27)	0.38 (0.27)	
Median	0.38	0.36	0.36	
Range	-0.33 - 1.00	-0.24 - 0.91	-0.33 - 1.00	
4th injection				0.000
n	207	123	330	
Mean (SD)	0.56 (0.28)	0.43 (0.28)	0.51 (0.29)	
Median	0.59	0.42	0.55	
Range	-0.29 - 1.00	-0.45 - 0.93	-0.45 - 1.00	
7th injection				0.001
n	176	89	265	
Mean (SD)	0.63 (0.26)	0.51 (0.28)	0.59 (0.27)	
Median	0.66	0.53	0.60	
Range	-0.08 - 1.00	-0.32 - 1.00	-0.32 - 1.00	
10th injection				0.000
n	151	75	226	
Mean (SD)	0.65 (0.27)	0.51 (0.28)	0.60 (0.28)	
Median	0.69	0.55	0.61	
Range	-0.33 - 1.00	-0.35 - 1.00	-0.35 - 1.00	
13th injection				0.002
n	138	66	204	
Mean (SD)	0.67 (0.27)	0.53 (0.30)	0.62 (0.28)	
Median	0.77	0.56	0.67	
Range	-0.13 - 1.00	-0.28 - 1.00	-0.28 - 1.00	
16th injection				0.001
n	127	64	191	
Mean (SD)	0.64 (0.27)	0.50 (0.29)	0.60 (0.28)	
Median	0.70	0.54	0.63	
Range	-0.13 - 1.00	-0.34 - 1.00	-0.34 - 1.00	

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
19th injection				0.000
n	113	56	169	
Mean (SD)	0.67 (0.26)	0.50 (0.29)	0.61 (0.28)	
Median	0.69	0.52	0.64	
Range	-0.44 - 1.00	-0.34 - 1.00	-0.44 - 1.00	
22nd injection				0.000
n	105	48	153	
Mean (SD)	0.70 (0.25)	0.52 (0.30)	0.64 (0.28)	
Median	0.76	0.57	0.69	
Range	0.044 - 1.00	-0.33 - 1.00	-0.33 - 1.00	
25th injection				0.083
n	85	38	123	
Mean (SD)	0.67 (0.24)	0.58 (0.31)	0.64 (0.27)	
Median	0.69	0.67	0.69	
Range	0.13 - 1.00	-0.34 - 1.00	-0.34 - 1.00	
At golimumab withdrawal				0.518
n	18	18	36	
Mean (SD)	0.32 (0.31)	0.26 (0.20)	0.29 (0.26)	
Median	0.30	0.20	0.23	
Range	-0.36 - 0.89	-0.06 - 0.76	-0.36 - 0.89	

Figure 18 : Change in health status in AS patients throughout the study assessed using the EQ-5D index



15.12 Functional ability

Functional ability was evaluated using the Health Assessment Questionnaire (HAQ) index by the patient at baseline, every 3 injections, and at golimumab discontinuation.

The HAQ disability index is a 20-question instrument assessing the degree of difficulty the subject had in accomplishing tasks in 8 functional areas over the previous week (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) [30]. Responses in each functional area are scored from 0 (no difficulty) to 3 (inability to perform a task in that functional area). The HAQ score is calculated as the sum of the category scores divided by the number of categories scored, giving a possible range of scores from 0 to 3.

A repeated-measures analysis (2 factor ANOVA) was conducted on the influence of two independent variables (time and prior biotherapy status) on HAQ score change from baseline to 2 years. Prior biotherapy status consisted of two levels (BT-n and BT-p).

- **Rheumatoid arthritis (RA)**

From the 170 RA patients enrolled, functional ability was reported for 115 patients at baseline, 75 at year-1 and 44 at year-2. There was no significant difference in HAQ scores between BT-n and BT-p patients at inclusion, but for each injection thereafter, the enhancement in functional ability was significantly better for BT-n than BT-p RA patients (see Table 103), with the HAQ index decreasing more steeply for BT-n patients from injections 1 to 25.

The evolution of the HAQ score is schematized in Figure 19. The improvement in functional ability was statistically significant from baseline to year 2, and was more improved for BT-n than BT-p patients, as shown by the 2-factor ANOVA with repeated measures ($p < .0001$). For patients still on golimumab treatment at year 2, a significant improvement in functional ability score at 2 years was reported compared to baseline (n=34, p= .0008, paired t-test).

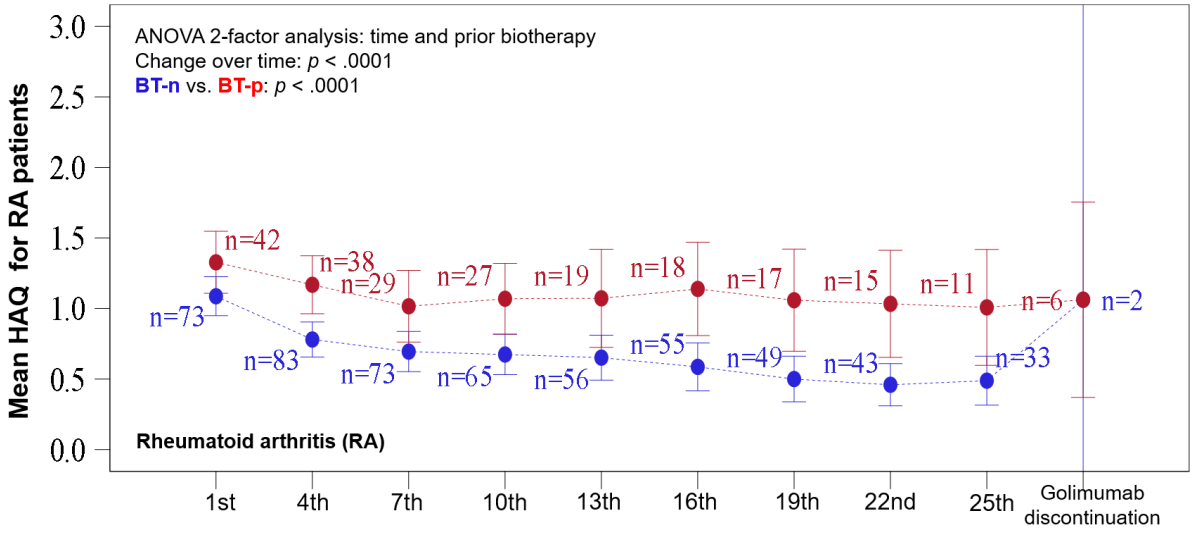
HAQ at golimumab discontinuation was provided for 8 RA patients (2 BT-n and 6 BT-p patients), and was similar to the score at baseline, denoting no improvement in functional ability upon discontinuation.

Table 103 : Functional ability measured with the HAQ in patients with RA through 2 years of treatment and at golimumab discontinuation, by prior biotherapy

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=170)	p
Inclusion				0.110
n	73	42	115	
Mean (SD)	1.09 (0.59)	1.33 (0.70)	1.18 (0.64)	
Median	1.13	1.20	1.13	
Range	0 - 2.50	0.25 - 2.63	0 - 2.63	
4th injection				**0.002**
n	83	38	121	
Mean (SD)	0.78 (0.57)	1.17 (0.63)	0.90 (0.61)	
Median	0.75	1.13	0.88	
Range	0 - 2.25	0 - 2.50	0 - 2.50	
7th injection				**0.027**
n	73	29	102	
Mean (SD)	0.69 (0.61)	1.02 (0.67)	0.79 (0.64)	
Median	0.50	0.88	0.69	
Range	0 - 2.38	0 - 2.25	0 - 2.38	
10th injection				**0.003**

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=170)	p
n	65	27	92	
Mean (SD)	0.67 (0.58)	1.07 (0.63)	0.79 (0.62)	
Median	0.63	1.13	0.75	
Range	0 - 2.43	0 - 2.50	0 - 2.50	
13th injection				**0.023**
n	56	19	75	
Mean (SD)	0.65 (0.59)	1.07 (0.72)	0.76 (0.65)	
Median	0.50	1.00	0.63	
Range	0 - 2.25	0 - 2.38	0 - 2.38	
16th injection				**0.002**
n	55	18	73	
Mean (SD)	0.59 (0.63)	1.14 (0.67)	0.72 (0.68)	
Median	0.38	1.25	0.50	
Range	0 - 2.38	0.13 - 2.38	0 - 2.38	
19th injection				**0.004**
n	49	17	66	
Mean (SD)	0.50 (0.56)	1.06 (0.70)	0.64 (0.65)	
Median	0.25	1.13	0.44	
Range	0 - 2.38	0 - 2.00	0 - 2.38	
22nd injection				**0.004**
n	43	15	58	
Mean (SD)	0.46 (0.49)	1.03 (0.69)	0.61 (0.60)	
Median	0.25	1.00	0.38	
Range	0 - 1.63	0 - 2.38	0 - 2.38	
25th injection				**0.018**
n	33	11	44	
Mean (SD)	0.49 (0.49)	1.01 (0.61)	0.62 (0.56)	
Median	0.38	1.00	0.50	
Range	0 - 1.38	0 - 1.71	0 - 1.71	
At golimumab discontinuation				1.000
n	2	6	8	
Mean (SD)	1.06 (0.97)	1.06 (0.66)	1.06 (0.67)	
Median	1.06	1.00	1.00	
Range	0.38 - 1.75	0.13 - 2.00	0.13 - 2.00	

Figure 19 : Change in functional ability in patients with RA through 24 months, assessed using the HAQ index



- **Psoriatic arthritis (PsA)**

The functional ability was reported for 80 patients at baseline 49 patients at the 13th injection and 24 patients for the final injection, from 106 PsA patients. As shown in Table 104, the HAQ index decreased gradually from the 1st to the 25th injection, reflecting a major improvement of functional ability over treatment time for all PsA patients; indeed, for patients still on golimumab treatment at year 2, a significant improvement in functional ability was reported vs. baseline (1.14 vs. 0.59, n=20, *p*= .0152, paired t-test).

ANOVA analyses with 2-factors additionally revealed that HAQ score ameliorations for BT-n patients were significantly better than for BT-p patients (*p* <.0001), and that score improvement over time was also significant (*p* <.0001). This change in HAQ index is portrayed in Figure 20.

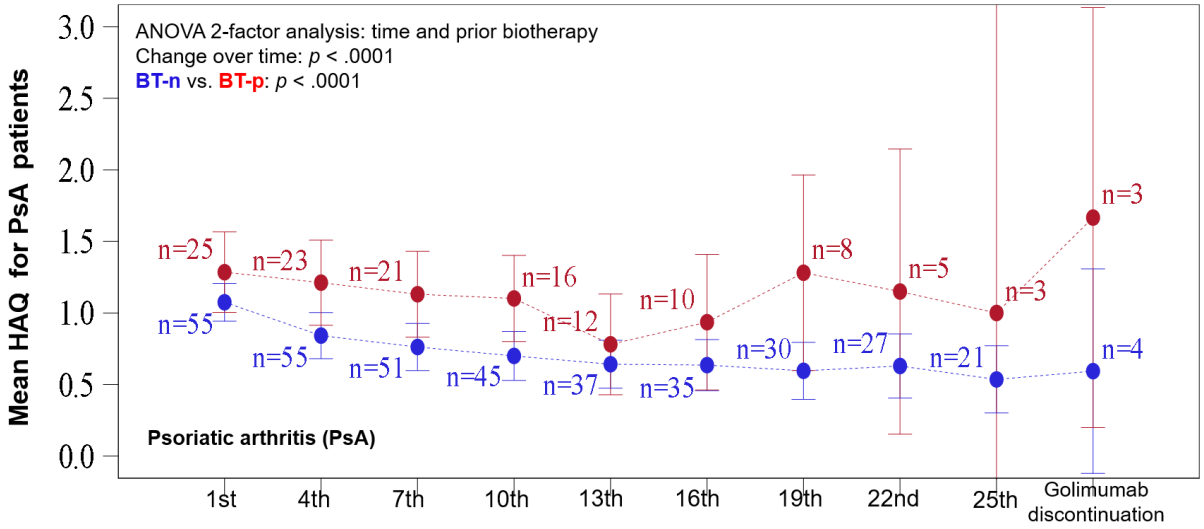
Functional ability at golimumab discontinuation was provided for no more than 7 PsA patients (4 BT-n and 3 BT-p patients) and similar to baseline, signifying no particular improvement upon golimumab discontinuation.

Table 104 : Functional ability measured with the HAQ in patients with PsA through 2 years of treatment and at golimumab discontinuation, by prior biotherapy

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
Inclusion				0.219
n	55	25	80	
Mean (SD)	1.08 (0.49)	1.29 (0.68)	1.14 (0.56)	
Median	1.13	1.13	1.13	
Range	0 - 2.13	0.13 - 2.50	0 - 2.50	
4th injection				0.023
n	55	23	78	
Mean (SD)	0.84 (0.59)	1.21 (0.69)	0.95 (0.64)	
Median	0.75	1.13	0.88	
Range	0 - 3.00	0 - 2.63	0 - 3.00	

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
7th injection				0.020
n	51	21	72	
Mean (SD)	0.76 (0.59)	1.13 (0.66)	0.87 (0.63)	
Median	0.75	1.00	0.88	
Range	0 - 2.00	0 - 2.63	0 - 2.63	
10th injection				0.019
n	45	16	61	
Mean (SD)	0.70 (0.57)	1.10 (0.56)	0.81 (0.59)	
Median	0.63	1.13	0.75	
Range	0 - 2.00	0 - 1.88	0 - 2.00	
13th injection				0.362
n	37	12	49	
Mean (SD)	0.64 (0.50)	0.78 (0.55)	0.68 (0.51)	
Median	0.63	0.75	0.63	
Range	0 - 2.00	0 - 2.00	0 - 2.00	
16th injection				0.254
n	35	10	45	
Mean (SD)	0.64 (0.52)	0.94 (0.66)	0.70 (0.56)	
Median	0.63	0.87	0.75	
Range	0 - 1.75	0 - 2.00	0 - 2.00	
19th injection				0.035
n	30	8	38	
Mean (SD)	0.60 (0.53)	1.28 (0.82)	0.74 (0.66)	
Median	0.50	1.00	0.56	
Range	0 - 1.88	0 - 2.63	0 - 2.63	
22nd injection				0.191
n	27	5	32	
Mean (SD)	0.63 (0.57)	1.15 (0.80)	0.71 (0.62)	
Median	0.50	1.13	0.56	
Range	0 - 1.75	0 - 2.13	0 - 2.13	
25th injection				0.627
n	21	3	24	
Mean (SD)	0.54 (0.52)	1.00 (1.15)	0.59 (0.61)	
Median	0.38	0.75	0.38	
Range	0 - 1.75	0 - 2.25	0 - 2.25	
At golimumab discontinuation				0.074
n	4	3	7	
Mean (SD)	0.59 (0.45)	1.67 (0.59)	1.05 (0.74)	
Median	0.69	1.88	1.00	
Range	0 - 1.00	1.00 - 2.13	0 - 2.13	

Figure 20 : Change in functional ability in patients with PsA through 24 months, assessed using the HAQ index



- **Ankylosing spondylitis (AS)**

Functional ability was reported for 446 patients at baseline, 210 patients at year-1 and 123 patients at year-2, out of 478 patients with AS. HAQ score was significantly better in BT-n patients than in BT-p AS patients at all injections, except the final (however, this could be attributed to a possibly diminished statistical power due to lower patient numbers at year-2).

The improvement in functional ability over-time was statistically significant, and more so for BT-n than BT-p patients, (2-factor ANOVA, $p < .0001$). This change in HAQ index is schematized in Figure 21.

For patients still on golimumab treatment at year-2, a significant improvement in functional ability was reported compared to baseline (0.97 vs. 0.50, n=120, p = < .0001, paired t-test).

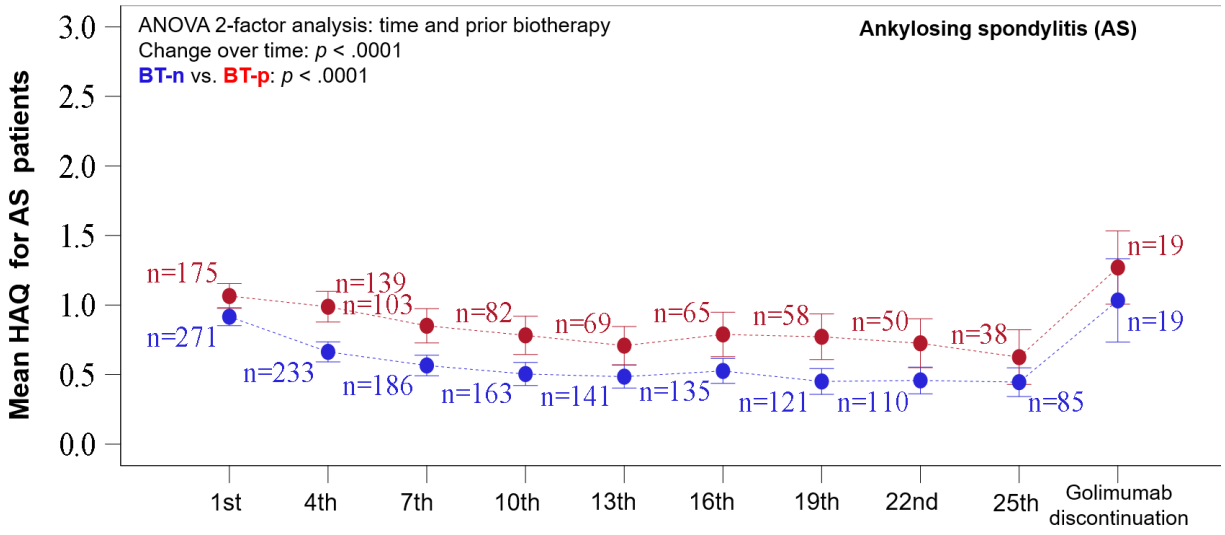
Functional disability at golimumab discontinuation was provided for 38 AS patients (19 each in BT-n and BT-p groups) and was slightly higher than at baseline, showing that patients who stopped the treatment had a worsening of functional ability.

Table 105 : Functional ability measured with the HAQ in patients with AS through 2 years of treatment and at golimumab discontinuation, by prior biotherapy

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
Inclusion				0.013
n	271	175	446	
Mean (SD)	0.92 (0.53)	1.06 (0.59)	0.97 (0.56)	
Median	0.88	1.00	0.88	
Range	0 - 2.25	0 - 2.63	0 - 2.63	
4th injection				<0.001
n	233	139	372	
Mean (SD)	0.66 (0.55)	0.99 (0.65)	0.78 (0.61)	
Median	0.63	0.88	0.75	
Range	0 - 2.13	0 - 2.50	0 - 2.50	
7th injection				<0.001
n	186	103	289	

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
Mean (SD)	0.57 (0.51)	0.85 (0.63)	0.67 (0.57)	
Median	0.50	0.75	0.63	
Range	0 - 2.00	0 - 2.25	0 - 2.25	
10th injection				<0.001
n	163	82	245	
Mean (SD)	0.50 (0.53)	0.78 (0.62)	0.60 (0.58)	
Median	0.38	0.75	0.50	
Range	0 - 2.25	0 - 2.00	0 - 2.25	
13th injection				0.004
n	141	69	210	
Mean (SD)	0.49 (0.50)	0.71 (0.57)	0.56 (0.53)	
Median	0.38	0.63	0.50	
Range	0 - 2.13	0 - 2.38	0 - 2.38	
16th injection				0.006
n	135	65	200	
Mean (SD)	0.53 (0.53)	0.79 (0.64)	0.61 (0.58)	
Median	0.38	0.75	0.50	
Range	0 - 2.13	0 - 2.25	0 - 2.25	
19th injection				0.001
n	121	58	179	
Mean (SD)	0.45 (0.51)	0.77 (0.62)	0.55 (0.57)	
Median	0.25	0.63	0.50	
Range	0 - 2.38	0 - 2.38	0 - 2.38	
22nd injection				0.007
n	110	50	160	
Mean (SD)	0.46 (0.51)	0.73 (0.62)	0.54 (0.56)	
Median	0.31	0.63	0.50	
Range	0 - 2.25	0 - 2.38	0 - 2.38	
25th injection				0.111
n	85	38	123	
Mean (SD)	0.45 (0.48)	0.63 (0.60)	0.50 (0.52)	
Median	0.38	0.50	0.38	
Range	0 - 2.00	0 - 2.13	0 - 2.13	
At golimumab discontinuation				0.420
n	19	19	38	
Mean (SD)	1.03 (0.62)	1.27 (0.55)	1.15 (0.59)	
Median	1.25	1.25	1.25	
Range	0 - 2.00	0.25 - 2.75	0 - 2.75	

Figure 21 : Change in functional ability in patients with AS through 24 months, assessed using the HAQ index



15.13 Quality of life (QoL)

QoL was assessed using the SF-12 questionnaire was reported by the patient at inclusion, at 1 year and at golimumab discontinuation.

The SF12 provides two scores: the physical component summary (PCS) score and the mental component summary (MCS) score. Both scores were constructed in a way that the average of the general population is 50. The score of MCS may range between 5.89058 and 71.96825. The PCS score may range between 9.94738 and 70.02246.

- **Rheumatoid arthritis (RA)**

QoL was reported for 119 patients at baseline, 72 at 1 year and 36 at 2 years, from 170 patients with RA. The mean PSC score at inclusion was significantly better for BT-n RA patients than for BT-p RA patients (37.4 vs. 32.9, p < .010) as seen in Table 106. As shown in Table 106, average PCS and MCS scores improved from the 1st to the 13th injection and more so up to the final injection (PCS: 35.8 vs 43.1 vs. 47.0, respectively; MCS: 41.1 vs. 45.8 vs. 47.5, respectively), reflecting the improvement of quality of life related to RA disease over treatment time. PCS score at inclusion versus year-2 is significantly better for those who continued treatment (35.8 vs. 47.0, n = 36, p < .0001, t-test). Difference in score at baseline and year-2 is not significant for the MCS component (41.1 vs. 47.5, n=36, p= .0513, t-test).

QoL at golimumab discontinuation was provided for 7 RA patients (2 BT-n and 5 BT-p). The average PCS and MCS scores at golimumab discontinuation were lower than at baseline (Table 106).

Table 106 : Quality of life assessed with the SF-12 questionnaire for patients with RA at

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=170)	p
PSC at inclusion and 1st injection				0.010
n	77	42	119	
Mean (SD)	37.4 (8.37)	32.9 (9.78)	35.8 (9.11)	

	Biotherapy-naive patients (n=110)	Bio-pretreated patients (n=59)	Total (n=170)	p
Median	36.9	34.0	36.0	
Range	20.0 - 57.2	4.75 - 54.8	4.75 - 57.2	
PSC at 13th injection				0.447
n	53	19	72	
Mean (SD)	43.6 (8.28)	41.8 (8.87)	43.1 (8.41)	
Median	44.0	42.4	43.5	
Range	22.4 - 56.0	29.0 - 57.5	22.4 - 57.5	
PSC at 25th injection				0.253
n	28	8	36	
Mean (SD)	47.9 (8.24)	43.9 (9.54)	47.0 (8.57)	
Median	47.2	45.0	46.9	
Range	27.3 - 64.8	30.4 - 55.7	27.3 - 64.8	
PSC at golimumab discontinuation				0.174
n	2	5	7	
Mean (SD)	27.2 (13.6)	37.5 (5.45)	34.5 (8.71)	
Median	27.2	35.6	35.6	
Range	17.6 - 36.8	33.9 - 47.1	17.6 - 47.1	
MSC at inclusion and 1st injection				0.628
n	77	42	119	
Mean (SD)	41.5 (9.46)	40.5 (12.9)	41.1 (10.8)	
Median	41.6	39.9	41.1	
Range	17.6 - 62.2	15.6 - 77.1	15.6 - 77.1	
MSC at 13th injection				**.030**
n	53	19	72	
Mean (SD)	47.4 (9.57)	41.4 (11.5)	45.8 (10.4)	
Median	48.4	40.6	46.3	
Range	22.4 - 63.4	25.1 - 62.4	22.4 - 63.4	
MSC at 25th injection				0.702
n	28	8	36	
Mean (SD)	47.9 (8.43)	46.3 (14.1)	47.5 (9.76)	
Median	50.0	46.4	50.0	
Range	29.0 - 60.0	29.3 - 63.0	29.0 - 63.0	
MSC at golimumab discontinuation				.096
n	2	5	7	
Mean (SD)	49.1 (2.01)	37.5 (7.50)	40.8 (8.37)	
Median	49.1	40.1	43.1	
Range	47.7 - 50.5	27.9 - 45.1	27.9 - 50.5	

- **Psoriatic arthritis (PsA)**

QoL was reported for 88 patients at baseline 48 at one year, and 25 at year-2, from a total of 106 patients with PsA.

PCS score at baseline versus year-2 is significantly better for those who continued treatment (34.7 vs. 44.4, n = 25, p= .0009, t-test). Difference in score at baseline and year-2 is not significant for the MCS component (40.0 vs. 48.8, n=25, p= .0815, t-test).

QoL at golimumab discontinuation was provided only 5 PsA patients (3 biotherapy naïve patient and 2 biotherapy pretreated patients). Average PCS scores were comparable, and the MCS score at discontinuation was slightly better than at inclusion.

Table 107 : Quality of life assessed with the SF-12 questionnaire for patients with PsA at baseline, at 1 year, 2 years and at golimumab withdrawal, by prior biotherapy

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
PSC at inclusion and 1st injection				0.187
n	58	30	88	
Mean (SD)	35.5 (8.01)	33.2 (6.95)	34.7 (7.70)	
Median	34.8	34.7	34.7	
Range	21.9 - 56.1	17.2 - 44.9	17.2 - 56.1	
PSC at 13th injection				0.022
n	37	11	48	
Mean (SD)	44.7 (7.22)	38.6 (8.22)	43.3 (7.81)	
Median	45.9	41.7	44.7	
Range	30.1 - 59.9	24.5 - 47.8	24.5 - 59.9	
PSC at 25th injection				0.479
n	21	4	25	
Mean (SD)	45.0 (8.42)	41.4 (14.0)	44.4 (9.24)	
Median	45.1	44.2	45.0	
Range	30.5 - 59.0	21.9 - 55.1	21.9 - 59.0	
PSC at golimumab discontinuation				0.089
n	3	2	5	
Mean (SD)	39.8 (7.67)	25.6 (0.29)	34.1 (9.48)	
Median	40.7	25.6	31.7	
Range	31.7 - 47.0	25.4 - 25.8	25.4 - 47.0	
MSC at inclusion and 1st injection				0.031
n	58	30	88	
Mean (SD)	41.8 (10.1)	36.6 (11.0)	40.0 (10.6)	
Median	40.5	38.0	39.5	
Range	17.9 - 67.5	17.9 - 56.7	17.9 - 67.5	
MSC at 13th injection				0.703
n	37	11	48	
Mean (SD)	45.3 (9.84)	44.1 (5.65)	45.0 (9.01)	
Median	47.0	43.2	45.1	
Range	19.1 - 62.1	36.1 - 55.1	19.1 - 62.1	
MSC at 25th injection				0.681
n	21	4	25	

	Biotherapy-naive patients (n=70)	Bio-pretreated patients (n=36)	Total (n=106)	p
Mean (SD)	49.2 (10.9)	46.8 (8.84)	48.8 (10.5)	
Median	51.4	50.2	50.8	
Range	20.3 - 64.3	33.7 - 53.0	20.3 - 64.3	
MSC at golimumab discontinuation				0.884
n	3	2	5	
Mean (SD)	42.9 (13.8)	41.0 (10.7)	42.1 (11.1)	
Median	46.6	41.0	46.6	
Range	27.6 - 54.4	33.4 - 48.6	27.6 - 54.4	

- **Ankylosing spondylitis (AS)**

Quality of life was reported for 412 patients at baseline 194 at year-1 and 117 at year-2, from 478 patients with AS. There were significant differences in average PCS scores between BT-n and BT-p patients at all timepoints, with PCS scores being better for BT-n patients. As shown in Table 108, average PCS and MCS scores increased from the 1st to the 25th injection, reflecting the enhancement of quality of life related to RA disease over treatment time.

PCS score at inclusion versus year-2 is significantly better for those who continued treatment (34.4 vs. 44.5, n=117, p< .0001, t-test). Difference in score at baseline and year-2 is also significant for the MCS component (40.5 vs. 46.4, n=117, p= .0017, t-test). Quality of life at golimumab discontinuation was provided for 37 AS patients (18 BT-n and 19 BT-p patients). Both average PCS and MCS scores were slightly worse at golimumab withdrawal than at baseline, reflecting that patients who stopped the treatment had a quality of life worsened.

Table 108 : Quality of life assessed with the SF-12 questionnaire for patients with AS at baseline, at 1 year, 2 years and at golimumab withdrawal, by prior biotherapy

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
PSC at inclusion and 1st injection				0.035
n	260	152	412	
Mean (SD)	35.2 (9.48)	33.2 (8.32)	34.4 (9.11)	
Median	35.4	32.3	34.0	
Range	12.9 - 58.3	14.8 - 64.6	12.9 - 64.6	
PSC at 13th injection				0.003
n	130	64	194	
Mean (SD)	45.1 (9.05)	41.0 (8.58)	43.7 (9.08)	
Median	45.5	41.1	44.0	
Range	19.2 - 69.0	15.8 - 59.9	15.8 - 69.0	
PSC at 25th injection				0.026
n	81	36	117	
Mean (SD)	45.7 (7.68)	41.9 (9.66)	44.5 (8.48)	
Median	45.3	42.4	44.3	
Range	29.8 - 58.9	21.8 - 59.6	21.8 - 59.6	
PSC at golimumab discontinuation				0.328
n	18	19	37	

	Biotherapy-naive patients (n=291)	Bio-pretreated patients (n=187)	Total (n=478)	p
Mean (SD)	34.6 (11.0)	31.6 (7.63)	33.1 (9.44)	
Median	35.5	31.5	32.7	
Range	14.5 - 55.5	16.8 - 44.2	14.5 - 55.5	
MSC at inclusion and 1st injection				0.627
n	260	152	412	
Mean (SD)	40.3 (10.1)	40.8 (9.96)	40.5 (10.0)	
Median	40.0	41.3	40.5	
Range	14.7 - 65.9	15.9 - 67.4	14.7 - 67.4	
MSC at 13th injection				0.797
n	130	64	194	
Mean (SD)	45.0 (10.5)	44.5 (10.5)	44.8 (10.5)	
Median	44.4	44.3	44.3	
Range	17.4 - 63.4	20.6 - 65.6	17.4 - 65.6	
MSC at 25th injection				0.031
n	81	36	117	
Mean (SD)	47.6 (8.38)	43.5 (11.2)	46.4 (9.49)	
Median	47.7	43.0	46.5	
Range	27.8 - 62.5	20.2 - 63.4	20.2 - 63.4	
MSC at golimumab discontinuation				0.783
n	18	19	37	
Mean (SD)	37.7 (12.2)	38.8 (10.3)	38.3 (11.1)	
Median	38.8	41.1	39.3	
Range	12.0 - 62.0	17.6 - 57.5	12.0 - 62.0	

15.14 Consumption of Healthcare and Health Services Related to the Studied Disease

15.14.1 Consumption of Healthcare and Health Services

Consumption of healthcare and health services was reported at every injection by the patient including, hospitalizations (≥24h and <24h), physician office visits, laboratory tests, imaging (X-ray/MRI/CT-scan), physical therapy and sick leaves (number of days)

- **Rheumatoid arthritis (RA)**

Table 109 describes the consumption of healthcare resources prior to golimumab initiation and during treatment with golimumab, which was reported for 168 patients at baseline, 83 patients at one year and 45 patients at year 2. Healthcare resource consumption data at golimumab discontinuation was provided for 10 patients.

The number of patients having hospitalizations (≥24h and <24h) for medical reasons or surgery decreased over time, compared to before golimumab initiation: 23 and 44 respectively prior to initiation (n=168) as to 2 and 1 at one year (n=83) and 1 and 1 at 2 years (n=45). The same result was observed over time for the number of nursing visits.
Regarding the missed work days, a decrease was observed within the first year of treatment when the number dropped from 8.21 days at baseline (n=168) to 4.20 days after 12 months (n=83). However, in 12-15 and 15-18 months of treatment the count of missed work days increased to 17.2 (n=74) and 17.4 (n=64), respectively. Following this period, the number fell drastically: 1.62 days between 18-21 months (n=61) and 0.33 days between 21-24 months (n=45). Number of GP, rheumatologist and radiologist visits tended to decrease over time while the number of visits at the dermatologist was rather stable.

- **Psoriatic arthritis (PsA)**

Table 110 describes the consumption of healthcare and health services prior to golimumab initiation and during treatment for PsA patients, reported for 106 patients at baseline, 51 patients at one year and 26 patients at year 2. Consumption of healthcare and health services at golimumab permanent discontinuation was provided for no more than 7 patients. The number of patients having hospitalizations (≥24h and <24h) for medical reasons or surgery decreased over time, compared to before golimumab initiation, 9 and 22 respectively (n=106) to 2 and 4 at one year (n=51) and 0 at two years (n=45).
The number of nursing visits increased during the first half of the year from 1.03 at baseline (n=106) to 7.43 at 6 months (n=72). Following this period, the number dropped to 1.11 and 0.51 days between 6-9 and 9-12 months, respectively and was rather stable till the end of the study period. The number of work days missed decreased over the course of the study.

- **Ankylosing spondylitis (AS)**

Table 111 describes the consumption of healthcare and health services prior to golimumab initiation and during treatment, reported for 477 AS patients at baseline vs. 209 at one year and 118 at 2 years. Consumption of healthcare and health services at golimumab permanent discontinuation was provided for 38 patients.
Gradually over time, from baseline to 2 years of treatment, the number of patients having hospitalizations ≥24h and <24h decreased: 121 and 58, respectively 3 months before golimumab initiation (n=477) to 7 to 5 at year 1 (n=206) and to 0 hospitalizations at year 2 (n=118). Nursing visits, GP, rheumatologist and radiologist office visits, blood tests, X-Ray exams and use of physical therapy sessions also decreased slightly. Dermatologists' visits remained stable whereas other physician's office visits increased slightly. Missed work days decreased progressively from 11.3 days before golimumab initiation to 1.73 days in the three months before the 25th injection.

Table 109 : Healthcare Resource utilization prior to golimumab initiation and during golimumab treatment in patients with RA, n = 170

Results*	For 3 months prior to treatment initiation (n=168)	For 3 months after treatment initiation (n=125)	Between month 3-6 of treatment (n=107)	Between month 6 -9 of treatment (n=90)	Between month 9 -12 of treatment (n=83)	Between month 12 -15 of treatment (n=74)	Between month 15 -18 of treatment (n=64)	Between month 18 -21 of treatment (n=61)	Between month 21 -24 of treatment (n=45)	1 month before golimumab discontinuation (n=10)
Hospitalizations >24h, n (%)										
Medical, surgery	23 (13.7)	4 (3.20)	0 (0)	3 (3.33)	0 (0)	2 (2.70)	2 (3.13)	1 (1.64)	1 (2.22)	0 (0)
Mean duration (SD) [days]	*3.78 (1.78)*	*6.75 (6.24)*	*.*	*11.3 (16.2)*	*.*	*47.5 (60.1)*	*2.00 (1.41)*	*3.00 (0)*	*1.00 (0)*	-
Psychiatry	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aftercare / Rehabilitation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hospitalizations <24h, n (%)										
Medical, surgery	44 (26.2)	5 (4.00)	5 (4.67)	1 (1.11)	4 (4.82)	1 (1.35)	0 (0)	1 (1.64)	1 (2.22)	0 (0)
Mean number (SD)	*1.30 (0.67)*	*1.00 (0)*	*1.00 (0)*	*1.00 (0)*	*1.00 (0)*	*1.00 (0)*	-	*1.00 (0)*	*1.00 (0)*	-
Psychiatry	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aftercare / Rehabilitation	0 (0)	2 (1.60)	2 (1.87)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean number (SD)	-	*4.00 (4.24*	*1.50 (0.71)*	-	-	-	-	-	-	-
Nursing visits*	2.18 (7.73)	1.82 (3.41)	1.81 (3.82)	1.73 (3.70)	2.22 (5.82)	1.32 (3.32)	0.64 (1.95)	0.54 (1.39)	0.33 (0.88)	0.20 (0.63)
Physician office visits*										
GP	1.24 (1.29)	1.33 (1.46)	1.07 (1.34)	1.17 (1.47)	1.10 (1.45)	1.04 (1.93)	0.78 (1.35)	1.08 (1.68)	0.76 (1.07)	0.70 (0.82)
Dermatologist	0.14 (0.44)	0.18 (0.57)	0.15 (0.56)	0.17 (0.74)	0.11 (0.35)	0.27 (1.32)	0.094 (0.34)	0.18 (0.53)	0.24 (0.96)	0.10 (0.32)
Rheumatologist	1.66 (1.04)	1.05 (1.22)	1.14 (1.79)	0.88 (0.92)	1.10 (1.19)	0.92 (0.98)	0.83 (0.88)	0.70 (0.84)	0.80 (0.81)	0.90 (0.74)
Radiologist	0.61 (0.76)	0.32 (0.85)	0.33 (1.02)	0.21 (0.55)	0.24 (0.53)	0.30 (0.92)	0.22 (0.52)	0.30 (0.67)	0.20 (0.46)	0.30 (0.48)
Other	0.25 (0.61)	0.48 (1.45)	0.49 (1.97)	0.26 (0.74)	0.43 (1.51)	0.23 (0.63)	0.34 (1.21)	0.13 (0.43)	0.20 (0.63)	0 (0)
Blood tests*	2.05 (1.41)	2.27 (1.79)	2.13 (1.49)	2.03 (1.52)	2.07 (2.31)	1.96 (3.84)	1.80 (1.03)	1.67 (1.48)	1.58 (1.14)	0.80 (0.63)
X-ray exams*	0.96 (0.93)	0.43 (1.03)	0.41 (1.05)	0.44 (1.06)	0.49 (0.92)	0.41 (0.99)	0.30 (0.68)	0.33 (0.75)	0.29 (0.63)	0.70 (1.06)
Physical therapy*	0.93 (4.44)	1.56 (4.22)	2.59 (6.19)	2.14 (5.60)	2.27 (8.94)	5.01 (21.7)	5.95 (30.5)	1.75 (5.16)	1.24 (4.09)	0 (0)
Work days missed*	8.21 (23.8)	4.74 (17.6)	1.29 (9.19)	6.40 (51.0)	4.20 (31.3)	17.2 (13.3)	17.4 (127)	1.62 (11.5)	0.33 (2.24)	1.50 (3.37)

* Data are expressed as mean (SD); mean number of each type of visit or examination

Table 110 : Healthcare Resource utilization prior to golimumab initiation and during golimumab treatment in patients with PsA, n = 106

Results*	For 3 months prior to treatment initiation (n=106)	For 3 months after treatment initiation (n=82)	Between month 3-6 of treatment (n=72)	Between month 6 -9 of treatment (n=62)	Between month 9 -12 of treatment (n=51)	Between month 12 -15 of treatment (n=46)	Between month 15 -18 of treatment (n=39)	Between month 18 -21 of treatment (n=33)	Between month 21 -24 of treatment (n=26)	1 month before golimumab discontinuation (n=7)
Hospitalizations >24h, n (%)										
Medical, surgery	9 (8.49)	7 (8.54)	1 (1.39)	1 (1.61)	2 (3.92)	1 (2.17)	1 (2.56)	2 (6.06)	0 (0)	0 (0)
Mean Duration (SD) [days]	*9.00 (19.2)*	*8.14 (8.32)*	*90.0 (0)*	*7.00 (0)*	*5.50 (0.71)*	*8.00 (0)*	*14.0 (0)*	*5.00 (2.83)*	-	-
Psychiatry	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aftercare / Rehabilitation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hospitalizations <24h, n (%)										
Medical, surgery	22 (20.8)	6 (7.32)	1 (1.39)	3 (4.84)	4 (7.84)	3 (6.52)	2 (5.13)	1 (3.03)	0 (0)	0 (0)
Mean number (SD)	*1.18 (0.50)*	*1.00 (0)*	*3.00 (0)*	*1.00 (0)*	*1.00 (0)*	*2.00 (0)*	*1.00 (0)*	*1.00 (0)*	-	
Psychiatry	0 (0)	1 (1.22)	1 (1.39)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean number (SD)	-	*1.00 (0)*	*2.00 (0)*	-	-	-	-	-	-	
Aftercare / Rehabilitation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.56)	1 (3.03)	0 (0)	0 (0)
Mean number (SD)	-	-	-	-	-	-	*13.0 (0)*	*19.0 (0)*	-	
Nursing visits*	1.03 (2.81)	1.37 (3.85)	7.43 (53.0)	1.11 (2.84)	0.51 (1.54)	0.33 (0.76)	0.41 (1.25)	0.55 (1.09)	0.38 (1.24)	0.57 (0.98)
Physician office visits*										
GP	1.62 (1.65)	2.09 (2.14)	1.96 (2.84)	1.74 (2.37)	1.88 (2.25)	1.61 (1.68)	1.21 (1.45)	1.70 (2.26)	1.38 (1.58)	0.71 (1.11)
Dermatologist	0.31 (0.50)	0.29 (0.69)	0.069 (0.31)	0.34 (0.83)	0.35 (0.74)	0.28 (0.62)	0.23 (0.63)	0.24 (0.50)	0.038 (0.20)	0.14 (0.38)
Rheumatologist	1.75 (1.14)	0.96 (0.85)	0.92 (0.95)	1.00 (1.33)	1.00 (1.06)	0.61 (0.68)	0.72 (0.79)	0.42 (0.61)	0.42 (0.50)	0.86 (0.69)
Radiologist	0.67 (0.71)	0.15 (0.42)	0.43 (1.06)	0.37 (1.16)	0.41 (1.00)	0.28 (0.86)	0.26 (0.68)	0.18 (0.58)	0.077 (0.27)	0 (0)
Other	0.21 (0.60)	0.65 (1.75)	0.56 (1.56)	0.42 (1.27)	0.43 (1.28)	0.41 (1.29)	0.38 (1.35)	0.33 (0.96)	0.038 (0.20)	0.43 (0.79)
Blood tests*	2.25 (2.26)	2.45 (1.68)	2.63 (2.31)	2.37 (2.31)	2.08 (2.27)	2.07 (1.94)	1.95 (1.86)	2.76 (4.52)	1.62 (1.33)	1.43 (1.27)
X-ray exams*	1.08 (1.28)	0.30 (0.71)	0.50 (1.17)	0.66 (1.60)	0.51 (1.22)	0.41 (0.96)	0.38 (0.91)	0.42 (0.94)	0.15 (0.37)	0.29 (0.76)
Physical therapy*	3.14 (10.6)	2.90 (8.76)	4.24 (15.0)	2.76 (7.35)	3.90 (11.5)	2.72 (6.93)	5.44 (15.2)	3.03 (8.06)	6.27 (13.0)	0.86 (2.27)
Work days missed*	10.1 (26.5)	7.51 (21.6)	6.26 (17.0)	3.42 (13.6)	5.43 (21.8)	3.35 (14.8)	3.26 (15.0)	1.12 (4.01)	0.27 (1.37)	4.43 (11.7)

* Data are expressed as mean (SD); mean number of each type of visit or examination

Table 111 : Healthcare Resource utilization prior to golimumab initiation and during golimumab treatment in patients with AS, n = 478

Results	For 3 months prior to treatment initiation (n=477)	For 3 months after treatment initiation (n=374)	Between month 3-6 of treatment (n=286)	Between month 6 -9 of treatment (n=244)	Between month 9 -12 of treatment (n=209)	Between month 12 -15 of treatment (n=195)	Between month 15 -18 of treatment (n=177)	Between month 18 -21 of treatment (n=151)	Between month 21 -24 of treatment (n=118)	1 month before golimumab discontinuation (n=38)
Hospitalizations >24h, n (%)										
Medical, surgery	58 (12.2)	12 (3.21)	9 (3.15)	6 (2.46)	5 (2.39)	5 (2.56)	3 (1.69)	4 (2.65)	0 (0)	3 (7.89)
Mean Duration (SD) [days]	*4.55 (3.34)*	*4.42 (2.11)*	*3.89 (4.40)*	*6.83 (3.82)*	*3.20 (1.64)*	*2.60 (1.82)*	*3.33 (2.08)*	*4.50 (0.58)*	-	*6.67 (1.53)*
Psychiatry	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aftercare / Rehabilitation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hospitalizations <24h, n (%)										
Medical, surgery	121 (25.4)	25 (6.68)	7 (2.45)	7 (2.87)	9 (4.31)	7 (3.59)	5 (2.82)	5 (3.31)	1 (0.85)	2 (5.26)
Mean number (SD)	*1.33 (0.96)*	*2.80 (5.77)*	*1.29 (0.76)*	*1.00 (0)*	*1.56 (1.33)*	*1.29 (0.76)*	*1.00 (0)*	*1.60 (0.89)*	*1.00 (0)*	*1.50 (0.71)*
Psychiatry	0 (0)	2 (0.53)	2 (0.70)	1 (0.41)	1 (0.48)	1 (0.51)	2 (1.13)	0 (0)	0 (0)	0 (0)
Mean number (SD)	-	*1.00 (0)*	*2.00 (1.41)*	*1.00 (0)*	*1.00 (0)*	*1.00 (0)*	*1.50 (0.71)*	-	-	-
Aftercare / Rehabilitation	0 (0)	3 (0.80)	2 (0.70)	1 (0.41)	1 (0.48)	0 (0)	0 (0)	1 (0.66)	0 (0)	0 (0)
Mean number (SD)	-	*1.67 (0.58)*	*1.00 (0)*	*1.00 (0)*	*1.00 (0)*	-	-	*1.00 (0)*	-	-
Nursing visits*	0.72 (3.16)	0.77 (2.25)	0.52 (1.72)	0.61 (2.11)	0.36 (1.24)	0.39 (1.48)	0.40 (1.31)	0.47 (1.35)	0.29 (0.80)	0.21 (0.62)
Physician office visits*										
GP	1.87 (1.86)	1.79 (2.03)	1.45 (1.91)	1.30 (2.34)	1.31 (1.81)	1.13 (1.68)	1.07 (1.51)	1.13 (1.66)	1.07 (1.56)	1.13 (1.26)
Dermatologist	0.16 (0.39)	0.14 (0.42)	0.17 (0.57)	0.11 (0.37)	0.17 (0.60)	0.11 (0.42)	0.090 (0.34)	0.19 (0.63)	0.13 (0.42)	0.13 (0.41)
Rheumatologist	1.44 (1.05)	0.68 (0.99)	0.85 (0.98)	0.66 (0.84)	0.73 (0.91)	0.55 (0.77)	0.46 (0.64)	0.51 (0.77)	0.58 (0.71)	0.92 (0.85)
Radiologist	0.58 (0.81)	0.20 (0.76)	0.23 (0.77)	0.20 (0.67)	0.20 (0.60)	0.17 (0.57)	0.12 (0.56)	0.099 (0.36)	0.093 (0.35)	0.26 (0.64)
Other	0.31 (0.94)	0.48 (1.23)	0.56 (1.30)	0.42 (1.07)	0.45 (1.32)	0.44 (1.35)	0.38 (1.29)	0.45 (1.14)	0.49 (1.82)	0.34 (1.05)
Blood tests*	1.65 (1.22)	1.86 (1.87)	1.67 (1.45)	1.44 (1.47)	1.41 (1.48)	1.26 (1.54)	1.29 (1.37)	1.17 (1.27)	1.22 (1.10)	1.03 (0.64)
X-ray exams*	0.94 (1.19)	0.34 (0.96)	0.36 (0.89)	0.39 (1.16)	0.26 (0.77)	0.19 (0.61)	0.23 (0.66)	0.25 (0.83)	0.18 (0.46)	0.47 (0.89)
Physical therapy*	4.91 (11.8)	5.59 (10.0)	4.82 (8.24)	4.68 (8.35)	4.32 (8.29)	4.12 (8.02)	3.47 (7.46)	3.93 (8.05)	3.81 (7.42)	3.24 (6.16)
Work days missed*	11.3 (25.7)	15.9 (83.3)	5.01 (18.5)	6.11 (51.8)	4.21 (15.1)	3.01 (13.0)	2.98 (12.2)	2.66 (12.8)	1.73 (8.88)	5.45 (15.6)

* Data are expressed as mean (SD); mean number of each type of visit or examination

15.14.2 Work productivity loss assessment using the WPAI questionnaire

The WPAI yields four types of scores: absenteeism (work time missed), presenteeism (impairment at work/work capacity limitation), overall work productivity limitation (overall work limitation / absenteeism plus presenteeism), and limitation of activities [28]. The sum of specific health problem impairment and impairment due to other health reasons is equal to impairment due to all health reasons. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes.

- **Rheumatoid arthritis (RA)**

The change over time in productivity loss assessed using the WPAI questionnaire is presented in Table 112. The number of questionnaires received decreased gradually over time: 157 at inclusion compared to 85 at the 13th injection and 47 at the 25th injection.
At inclusion, about one third (35.0%) of the RA patients declared having a job, for whom “work time missed” in the previous week was 14.9%, “work capacity limitation” was 30.4% and “overall work productivity limitation” was 33.2%. Limitation of activities due to a health problem was 46.4% in RA patients at baseline.
At the 13th and 25th injection, a similar proportion of RA patients were working: 31.8% and 31.9%, respectively. However, the four scores had decreased. “Work time missed” dropped to 11.2% after 13 injections and to 7.69% after 25 injections. Looking at the same time points “work capacity limitation” fell to 16.1% and 6.36%, and “overall work productivity limitation” decreased to 17.4% and 6.36%. “Limitation of activities” reduced to 27.5% and 26.5%, at year 1 and 2, compared to baseline.
ANOVA analysis showed a statistically significant improvement of the four scores over study duration (p=.0002 for “work time missed” and p <.0001 for the three others). WPAI questionnaire data at permanent golimumab discontinuation was available for 10 patients.
For these, all four scores tended to be similar or higher to the baseline scores.

- **Psoriatic arthritis (PsA)**

The change over time in productivity loss assessed is presented in Table 113. The number of questionnaires received decreased gradually over time: 98 at inclusion vs. 51 at the 13th injection and 26 at the 25th injection.
At inclusion, half (50.0%) of the PsA patients declared having a job, for whom the “work time missed” in the previous week was 30.7%, “work capacity limitation” was 41.4%, “overall work productivity limitation” was 46.5%. “Limitation of activities due to a health problem” was 55.6% for all PsA patients.
The proportion of employed PsA patients was 41.2% at year 1, but increased to 53.8% at year 2.
All four scores had decreased during golimumab treatment. At the time point of the 13th and the 25th injections, the scores had dropped to: 4.12%and 2.19%, respectively for “work time missed”, 27.9% and 13.0%, respectively, for “work capacity limitation”, and 29.6% and 14.1%, respectively, for “overall work productivity limitation”. “Limitation of activities due to a health problem” lowered to 34.9% and 25.7% at year 1 and year 2, correspondingly.
ANOVA analysis showed that the improvement in the four scores over time was statistically significant (p =.0007 for “work time missed” and p <.0001 for the three others).
WPAI data at permanent golimumab discontinuation was available for 7 patients, for whom all four scores were higher to the baseline scores (except for work time missed).

- **Ankylosing spondylitis (AS)**

The change over time in productivity loss is presented in Table 114. The number of questionnaires received decreased gradually over time: 454 at inclusion, 218 at the 13th injection and 125 at the 25th injection.

At baseline, 62.3% of the AS patients were employed, for whom “work time missed” was 25.4%, “work capacity limitation” was 42.7%, and “overall work productivity limitation” was 45.6%. “Limitation of activities due to a health problem” was 57.2%.

The proportion of employed AS patients remained rather stable over the course of the study. Similarly, to the RA and the PsA population, the four scores decreased over time. Looking at the time point of the 13th and the 25th injection, the scores had dropped to: 8.80 % and 5.74%, respectively, for “work time missed”, 26.3% and 23.8%, respectively for “work capacity limitation”, and 27.2% and 23.3%, respectively, for “overall work productivity limitation”. “Limitation of activities due to a health problem” was 32.5% and 30.2% at year 1 and year 2, correspondingly.
The corresponding ANOVA analysis showed a statistically significant improvement of the four scores over study duration (p <.0001 for all scores).
WPAI data at permanent golimumab discontinuation was available for 36 AS patients, and all four scores tended to be higher than those at baseline.

Table 112 : The change over time in productivity loss assessed using the WPAI questionnaire in RA patients, from inclusion to year-2

Rheumatoid arthritis (RA)	Injection 1 (baseline)	Injection 7	Injection 13 (Year-1)	Injection 19	Injection 25 (year-2)	Golimumab discontinuation
	n = 157	n = 110	n = 85	n = 68	n = 47	n = 10
Currently employed, n (%)	55 (35.0)	44 (40.0)	27 (31.8)	20 (29.4)	15 (31.9)	4 (40.0)
Time missed at work in the previous week (%)	n = 43	n = 35	n = 23	n = 16	n = 13	n = 3
Mean (SD)	14.9 (32.6)	8.55 (22.1)	11.2 (28.8)	3.13 (12.5)	7.69 (27.7)	33.3 (57.7)
Median	0	0	0	0	0	0
Range	0 - 100	0 - 100	0 - 100	0 - 50.0	0 - 100	0 - 100
Work capacity limitation due to a health problem (%)	n = 46	n = 39	n = 23	n = 17	n = 11	n = 2
Mean (SD)	30.4 (25.0)	17.7 (22.2)	16.1 (13.7)	9.41 (13.4)	6.36 (8.09)	40.0 (28.3)
Median	25.0	10.0	20.0	0	0	40.0
Range	0 - 80.0	0 - 100	0 - 50.0	0 - 50.0	0 - 20.0	20.0 - 60.0
Overall work productivity limitation due to a health problem (%)	n = 38	n = 35	n = 21	n = 15	n = 11	n = 2
Mean (SD)	33.2 (25.2)	24.1 (25.1)	17.4 (13.7)	12.3 (19.4)	6.36 (8.09)	40.0 (28.3)
Median	30.0	19.0	20.0	10.0	0	40.0
Range	0 - 85.0	0 - 100	0 - 48.3	0 - 75.0	0 - 20.0	20.0 - 60.0
Limitation of activities due to a health problem (%)	n = 133	n = 97	n = 72	n = 54	n = 40	n = 8
Mean (SD)	46.4 (24.8)	31.4 (24.3)	27.5 (22.3)	25.2 (23.8)	26.5 (23.8)	46.3 (21.3)
Median	50.0	30.0	20.0	20.0	20.0	45.0
Range	0 - 100	0 - 90.0	0 - 80.0	0 - 80.0	0 - 90.0	10.0 - 80.0

Table 113 : The change over time in productivity loss assessed using the WPAI questionnaire in PsA patients, from inclusion to year-2

Psoriatic arthritis (PsA)	Injection 1 (baseline)	Injection 7	Injection 13 (Year-1)	Injection 19	Injection 25 (year-2)	Golimumab discontinuation
	n = 98	n = 73	n = 51	n = 39	n = 26	n = 7
Currently employed, n (%)	49 (50.0)	37 (50.7)	21 (41.2)	17 (43.6)	14 (53.8)	4 (57.1)
Time missed at work in the previous week (hours)	n = 43	n = 27	n = 17	n = 10	n = 10	n = 3
Mean (SD)	30.7 (43.1)	16.9 (29.0)	4.12 (12.8)	9.01 (21.9)	2.19 (6.92)	0 (0)
Median	0	0	0	0	0	0
Range	0 - 100	0 - 100	0 - 50.0	0 - 68.2	0 - 21.9	0 - 0
Work capacity limitation due to a health problem	n = 37	n = 31	n = 19	n = 13	n = 10	n = 4
Mean (SD)	41.4 (28.5)	32.9 (28.2)	27.9 (22.0)	24.6 (26.7)	13.0 (15.7)	47.5 (33.0)
Median	40.0	30.0	30.0	20.0	10.0	50.0
Range	0 - 100	0 - 90.0	0 - 70.0	0 - 80.0	0 - 50.0	10.0 - 80.0
Overall work productivity limitation due to a health problem	n = 34	n = 26	n = 17	n = 10	n = 10	n = 3
Mean (SD)	46.5 (29.0)	34.4 (32.3)	29.6 (23.8)	29.9 (32.4)	14.1 (18.6)	60.0 (26.5)
Median	50.0	33.9	30.0	25.0	10.0	70.0
Range	0 - 100	0 - 95.7	0 - 85.0	0 - 84.1	0 - 60.9	30.0 - 80.0
Limitation of activities due to a health problem	n = 88	n = 68	n = 47	n = 37	n = 23	n = 6
Mean (SD)	55.6 (24.2)	36.5 (24.6)	34.9 (24.8)	35.1 (29.6)	25.7 (22.7)	65.0 (32.7)
Median	50.0	30.0	30.0	30.0	20.0	80.0
Range	0 - 100	0 - 90.0	0 - 80.0	0 - 100	0 - 80.0	10.0 - 90.0

Table 114 : The change over time in productivity loss assessed using the WPAI questionnaire in AS patients, from inclusion to year-2

Ankylosing spondylitis (AS)	Injection 1 (baseline)	Injection 7	Injection 13 (Year-1)	Injection 19	Injection 25 (year-2)	Golimumab discontinuation
	n = 454	n = 295	n = 218	n = 182	n = 125	n = 36
Currently employed, n (%)	283 (62.3)	185 (62.7)	134 (61.5)	113 (62.1)	77 (61.6)	21 (58.3)
Time missed at work in the previous week (%)	n = 235	n = 144	n = 101	n = 81	n = 61	n = 20
Mean (SD)	25.4 (39.2)	9.03 (24.2)	8.80 (24.9)	4.54 (15.7)	5.74 (21.5)	30.4 (42.2)
Median	0	0	0	0	0	8.33
Range	0 - 100	0 - 100	0 - 100	0 - 100	0 - 100	0 - 100
Work capacity limitation due to a health problem (%)	n = 222	n = 160	n = 120	n = 102	n = 72	n = 18
Mean (SD)	42.7 (28.0)	28.7 (25.2)	26.3 (24.9)	24.0 (24.2)	23.8 (23.5)	59.4 (35.7)
Median	40.0	20.0	20.0	20.0	20.0	65.0
Range	0 - 100	0 - 100	0 - 90.0	0 - 100	0 - 100	0 - 100
Overall work productivity limitation due to a health problem (%)	n = 200	n = 139	n = 96	n = 79	n = 60	n = 17
Mean (SD)	45.6 (29.6)	30.3 (26.7)	27.2 (27.5)	21.7 (23.7)	23.3 (24.7)	58.6 (35.7)
Median	40.0	20.0	20.0	10.0	15.0	60.0
Range	0 - 100	0 - 100	0 - 100	0 - 85.0	0 - 100	0 - 100
Limitation of activities due to a health problem (%)	n = 435	n = 277	n = 198	n = 173	n = 119	n = 33
Mean (SD)	57.2 (25.0)	34.6 (26.4)	32.5 (26.2)	30.4 (25.8)	30.2 (24.9)	64.5 (26.6)
Median	60.0	30.0	30.0	30.0	30.0	70.0
Range	0 - 100	0 - 90.0	0 - 90.0	0 - 90.0	0 - 100	0 - 100

16 ADVERSE EVENTS/ADVERSE REACTIONS

The pharmacovigilance data presented here include all the adverse events (AEs) that occurred since the start of the study and reported from January 15, 2015 to 10/12/2018, for all patients included in the study during this time period (n=754).

These data are presented below in 2 sets:

- Adverse events reported by the patients.
- Adverse events reported by the physicians

It is worth noting that both, a physician and a patient may have declared the same AE. These AEs were analyzed separately in the database.

16.1 AEs reported by patients

Each event reported by patients has been taken into account. Since the seriousness of AEs were not provided by the patients, it was assessed based on the known criteria for defining a serious adverse event (ICH Topic E2A). Time to onset was not assessable as patients did not report any accurate date.

16.1.1 Total number of patient-reported AEs/SAEs

Total population: 1291 AEs were reported for the entire study population. Among these, 196 (15.2%) were considered as serious adverse events (SAEs). The total number of AEs by disease group and prior biotherapy status of patient are presented in Table 115.

Patients with rheumatoid arthritis: 259 AEs were reported for the RA cohort, of which 39 (15.1%) were SAEs.

Patients with psoriatic arthritis: 272 AEs were reported for PsA patients, of which 32 (11.8%) were considered as SAEs.

Patients with ankylosing spondylitis: 760 AEs were reported for AS patients, of which 125 (16.4%) were SAEs

Table 115: Total number of AEs and SAEs reported by the patient for each rheumatic disease

	RA (n=170) [a]		PsA (n=106)		AS (n=478)		Total (n=754) [a]	
	BT-n (n=110)	BT-p (n=59)	BT-n (n=70)	BT-p (n=36)	BT-n (n=291)	BT-p (n=187)	BT-n (n=471)	BT-p (n=282)
Total number of AEs	259		272		760		1291	
	135	124	213	59	135	124	213	59
Total number of SAEs n, (% of AEs)	39 (15.1%)		32 (11.8%)		125 (16.4%)		196 (15.2%)	
	19 (14.1%)	20 (16.1%)	17 (7.98%)	15 (25.4%)	45 (12.4%)	80 (20.1%)	81 (11.4%)	115 (19.8%)

a: prior biotherapy data was missing for on RA patient

16.1.2 Number of patients with at least one AEs/SAEs (reported by patients)

Total population: Among 754 patients included in the study, 258 patients (34.2%) experienced at least one AE and 73 (9.68%) patients experienced at least one SAE. AEs were reported in a higher proportion of BT-p patients (37.6%) compared to BT-n patients (32.2%), and SAEs were reported in 41 BT-p patients (14.5%) and 32 BT-n patients (6.79%). These results are detailed in Table 116.

Patients with rheumatoid arthritis: of 170 RA patients included in the study, 56 (32.9%) experienced at least one AE and 16 (9.41%) patients experienced at least one SAE, between BT-n and BT-p patients: 29.1% vs. 40.7% experienced one AE and 8.18% vs. 11.9% experienced at least one SAE, respectively.

Patients with psoriatic arthritis: among the 106 PsA patients included in the study, 33 patients (31.1%) experienced at least one AE and 11 (10.4%) patients experienced at least one SAE; 32.8% of BT-n and 27.8% of BT-p patients had experienced at least one AE, and 8.57% of BT-n vs. 13.9% of BT-p patients had experienced at least one SAE.

Patients with ankylosing spondylitis: Among 478 AS patients, 169 patients (35.4%) experienced at least one AE and 46 (9.68%) patients experienced at least one SAE. BT-p AS patients were more likely to report AEs and SAEs than BT-n AS patients: 33.3% of BT-n vs. 38.5% of BT-p patients reported at least one AE and 5.84% vs. 15.5% had experienced at least one SAE, respectively.

Table 116: Number of patients in whom at least 1 AE/SAE was reported, by rheumatic disease

	RA (n=170) [a]		PsA (n=106)		AS (n=478)		Total (n=754) [a]	
	BT-n (n=110)	BT-p (n=59)	BT-n (n=70)	BT-p (n=36)	BT-n (n=291)	BT-p (n=187)	BT-n (n=471)	BT-p (n=282)
Patients with at least 1 AE [b]	56 (32.9%)		33 (31.1%)		169 (35.4%)		258 (34.2%)	
	32 (29.1%)	24 (40.7%)	23 (32.9%)	10 (27.8%)	97 (33.3%)	72 (38.5%)	152 (32.2%)	106 (37.6%)
Patients with at least 1 SAE [b]	16 (9.41%)		11 (10.4%)		46 (9.62%)		73 (9.68%)	
	9 (8.18%)	7 (11.9%)	6 (8.57%)	5 (13.9%)	17 (5.84%)	29 (15.5%)	32 (6.79%)	41 (14.5%)

a: prior biotherapy data was missing for on RA patient

b: percentage calculated over the total number of patients in total, BT-n and BT-p groups, respectively

16.1.3 Action taken concerning golimumab prescription

Table 117: Action taken concerning golimumab prescription by rheumatic disease

	RA (n=259)	PsA (n=272)	AS (n=760)	Total (n=1291)
Action taken with golimumab (AEs)				
n	242	240	698	1180
Golimumab temporary withdrawal	76 (31.4)	92 (38.3)	279 (40.0)	447 (37.9)
Golimumab permanent discontinuation	43 (17.8)	10 (4.17)	58 (8.31)	111 (9.41)
Dosage change	1 (0.41)	5 (2.08)	14 (2.01)	20 (1.69)
Unchanged dosage	118 (48.8)	131 (54.6)	340 (48.7)	589 (49.9)
Unknown	4 (1.65)	2 (0.83)	7 (1.00)	13 (1.10)
Action taken with golimumab (SAEs)				
n	32	29	110	171
Golimumab temporary withdrawal	12 (37.5)	16 (55.2)	35 (31.8)	63 (36.8)
Golimumab permanent discontinuation	2 (6.25)	1 (3.45)	12 (10.9)	15 (8.77)
Unchanged dosage	17 (53.1)	12 (41.4)	59 (53.6)	88 (51.5)
Unknown	1 (3.13)	0 (0)	4 (3.64)	5 (2.92)

Total population

The action that was taken concerning golimumab prescription was provided for 1180/1291 AEs (91.4%) and 171/196 SAEs (87.2%). Golimumab dosage remained unchanged following most AEs (n=589, 49.9%) and SAEs (n=88, 51.5%).

Overall, 111 AEs (9.41%) led to golimumab permanent discontinuation, the majority (3 most frequent) belonging to the SOCs:

- “General disorders and administration site conditions” (n=58, 52.3%), under which the three most common PTs were “drug ineffective” (n=21, 36.2%), “pain” (n=6, 10.3%) and “drug intolerance” (n=5, 8.62%).
- “Gastrointestinal disorders” (n=8, 7.21%)
- “Infections and infestations” (n=8, 7.21%)

Additionally, 15 SAEs (8.77%) led to permanent golimumab discontinuation, most of them belonging to SOC “Surgical and Medical” (n=5, 33.3%).

Temporary golimumab discontinuation was reported following 447 AEs (37.9%), for which the three most frequent SOCs were:

- “Infections and infestations” (n=131, 29.3%), including mainly bronchitis (n=25, 19.1%), nasopharyngitis (n=17, 13.0%) and influenza (n=15, 11.5%)
- “General disorders and administration site conditions” (n=127, 28.4%), including mainly ill-defined disorder (n=45, 35.4%), pyrexia (n=15, 11.8%) and fatigue (n=13, 10.2%)
- “Surgical and Medical procedures” (n=60, 13.4%), including mainly cataract operation, hospitalization and knee operation (n=5, 8.33%, for each).

SAEs leading to temporary golimumab discontinuation were 63 (36.8%), most of them belonging to SOC “Surgical and Medical procedures” (n=27, 42.9%), infections and infestations (n=5, 7.94%) and “musculoskeletal and connective tissue disorders” (n=5, 7.94%).

Patients with rheumatoid arthritis

Action taken concerning golimumab prescription was provided for 242/259 AEs (93.4%) and 32/39 SAEs (82.1%). Golimumab dosage remained unchanged in RA patients following most AEs (n=118, 48.8%) and SAEs (n=17, 53.1%).

Overall, 43 AEs (17.8%) led to golimumab permanent discontinuation, the majority belonging to the SOC "General disorders and administration site conditions" (n=21, 48.8%). Only 2 SAEs (6.25%) led to permanent golimumab discontinuation, 1 each due to lung abscess (SOC: infections and infestations) and respiratory disorder (SOC: Respiratory, thoracic and mediastinal disorders).

Temporary golimumab discontinuations in RA patients were attributed to 76 AEs (31.4%), for which the three most frequent SOCs were:

- "Infections and infestations" (n=25, 32.9%), including mainly bronchitis (n=7, 28.0%), influenza (n=5, 20.0%) and jointly, nasopharyngitis and tonsillitis (n=3, 12.0%, for each).
- "General disorders and administration site conditions" (n=16, 21.1%), including mainly ill-defined disorder (n=4, 25.0%), pyrexia (n=4, 25.0%) and inflammation (n=2, 12.5%)
- "Surgical and Medical procedures" (n=16, 21.1%), including mainly shoulder arthroplasty (n=3, 18.8%), and jointly, bunion operation, cataract operation and surgery (n=2, 12.5% for each).

In RA patients 12 SAEs (37.5%) led to temporary golimumab discontinuation, half of which (n=6, 50.0%) were due to "Surgical and medical procedures".

Patients with psoriatic arthritis

Action taken regarding golimumab prescription was provided for 240/272 AEs (88.2%) and 29/32 SAEs (90.6%). Golimumab dosage remained unchanged in PsA patients following most AEs (n=131, 54.6%). However, most SAEs led to temporary golimumab withdrawal in patients (n=16, 55.2%), with fewer patients (n=12, 41.4%) experiencing no dosage change.

Only 10 AEs (4.17%) led to permanent golimumab discontinuation in PsA patients, most of them belonging to SOC "General disorders and administration site conditions" (n=4, 40.0%) including the AEs drug ineffective, drug intolerance, pain and treatment failure. Only 1 SAE led to permanent golimumab discontinuation, it being psoriatic arthropathy.

Temporary golimumab discontinuation in was reported following 92 AEs (38.3%), for which the three most frequent SOCs were:

- "Infections and infestations" (n=24, 26.1%), including mainly bronchitis (n=5, 20.8%), and jointly ear infection, nasopharyngitis, tonsillitis and tracheitis (n=2, 8.33%, for each).
- "General disorders and administration site conditions" (n=20, 21.7%), including mainly ill-defined disorder (n=8, 40.0%), pyrexia (n=3, 15.0%) and jointly fatigue, malaise, peripheral oedema and pain (n=2, 10.0% for each).
- "Surgical and Medical procedures" (n=15, 16.3%), including mainly knee operation (n=4, 26.7%), and jointly, hip surgery and surgery (n=2, 13.3% for each).

In PsA patients 16 SAEs (55.2%) led to temporary golimumab discontinuation, the majority (n=11, 68.8%) belonging to SOC "Surgical and medical procedures", including 4 knee operations (36.4%).

Patients with ankylosing spondylitis

Action taken regarding golimumab prescription was provided for 698/760 AEs (91.8%) and 110/196 SAEs (88.0%). Golimumab dosage remained unchanged in PsA patients following most AEs (n=340, 48.7%) and most SAEs (n=59, 53.6%).

Overall, 58 AEs (8.31%) led to permanent golimumab discontinuation, the majority belonging to the SOC "General disorders and administration site conditions" (n=33, 56.9%), which included mainly "drug ineffective" (n=14, 42.4%).

Only 12 SAEs (10.9%) led to permanent golimumab discontinuation, most of which belonged to the SOC "Surgical and medical procedures" (n=5, 41.7%).

Temporary golimumab discontinuations in AS patients were attributed to 279 AEs (40.0%), for which the three most frequent SOCs were:

- "General disorders and administration site conditions" (n=91, 32.6%), including mainly ill-defined disorder (n=33, 36.3%), fatigue (n=10, 11.0%) and drug intolerance (n=9, 9.89%).
- "Infections and infestations" (n=82, 29.4%), including mainly bronchitis (n=13, 15.9%), nasopharyngitis (n=12, 14.6%) and influenza (n=10, 12.2%)
- "Surgical and Medical procedures" (n=29, 10.4%), including mainly surgery (n=9, 31.0%), dental care (n=4, 13.8%) and jointly, antibiotic therapy, hospitalization and tooth extraction (n=3, 10.3% for each).

In AS patients 35 SAEs (31.8%) led to temporary golimumab discontinuation, most of which (n=10, 28.6%) were under the SOC "Surgical and medical procedures", including mainly surgery (n=5, 50.0%) and hospitalization (n=3, 30.0%) followed by the SOC "Infections and infestations" (n=5, 14.3%), and jointly 4 SAEs (11.4%) each from the SOC "musculoskeletal and connective tissue disorders" and "nervous system disorders".

16.1.4 Deaths

No deaths were reported for patients during the study.

16.1.5 Patient-reported AE/SAE outcomes

Total population: Outcomes were available for 167 (12.9%) of AEs and 33 (16.8%) of SAEs. Of 167 AEs, 88 (52.7%) were resolved, and of 33 SAEs, 23 (69.7%) were resolved at the time of reporting.

Rheumatoid arthritis (RA): Outcomes were available for 37 AEs (14.3%) of and 5 SAEs (12.8%). Of these, 20 AEs (54.1%) and 4 SAEs (80.0%) were resolved at the time of reporting.

Psoriatic arthritis (PsA): Outcomes were available for 23 AEs (8.46%) of and 5 SAEs (15.6%) of. Of these, 11 AEs (47.8%) and all SAEs were resolved at the time of reporting.

Ankylosing spondylitis (AS): Outcomes were provided for 107 (14.1%) AEs and 23 SAEs (18.4%). Of these, 57 AEs (53.3%) and 14 SAEs (60.9%) were resolved at the time of reporting.

Table 118 : Patient-reported AEs/SAEs outcomes by rheumatic disease

	RA (n=259)	PsA (n=272)	AS (n=760)	Total (n=1291)
AE outcomes	37	23	107	167
Ongoing	17 (45.9)	12 (52.2)	50 (46.7)	79 (47.3)
Resolved	20 (54.1)	11 (47.8)	57 (53.3)	88 (52.7)
SAE outcomes	5	5	23	33
Ongoing	1 (20.0)	0 (0)	9 (39.1)	10 (30.3)
Resolved	4 (80.0)	5 (100)	14 (60.9)	23 (69.7)

16.1.6 Description of patient-reported AEs and SAEs by preferred terms and system organ class

All the serious and non-serious AEs are presented by system organ class (SOC) and preferred terms (PT) in Table 119. Only SOCs and PTs with a frequency more than 10% are listed in this section. In decreasing order of frequency, all AEs in the total study population were affiliated with the following SOCs and PTs:

- *"General disorders and administration site conditions"* (391/1291 AEs; 30.3%)
  - Pain (67/391, 17.1%)
  - Ill-defined disorder (51/391, 13.0%)
  - Fatigue (46/391, 11.8%)
- *"Infections and infestations"* (193/1291 AEs; 14.9%)
  - Bronchitis (31/193, 16.1%)
  - Nasopharyngitis (27/193, 14.0%)
- *"Musculoskeletal and connective tissue disorders"* (156/1291 AEs; 12.1%)
  - Arthralgia (27/156, 17.3%)
  - Pain in extremity (26/156, 16.7%)
  - Musculoskeletal pain (19/156, 12.2%)

In decreasing order of frequency, SAEs in the total population were affiliated with the following SOCs:

1) "*Surgical and medical procedures"* (79/196 SAEs; 40.3%)
   a) Hospitalization (42/79, 53.2%)
   b) Surgery (10/79, 12.7%)
2) *"General disorders and administration site conditions" 22/196, 11.2%*
   a) Condition aggravated (9/22, 40.9%)
   b) Pain (6/22, 27.3%)
   c) Fatigue & Malaise (4/22, 18.2%)
3) *"Musculoskeletal and connective tissue disorders"* (19/196 SAEs; *9.69*%)
   a) Arthralgia (3/19, 15.8%)
   b) Ankylosing spondylitis (2/19, 10.5%)
   c) Musculoskeletal pain (2/19, 10.5%)
   d) Systemic lupus erythematosus (2/19, 10.5%)

16.1.6.1 Patients with rheumatoid arthritis

In decreasing order of frequency, all AEs (serious and non-serious) were classed in the following SOCs:

1) *"General disorders and administration site conditions"* (74/259 AEs; 28.6%)
   a) Condition aggravated (11/74, 14.9%)
   b) Fatigue (10/74, 13.5%)
   c) Pain (10/74, 13.5%)
2) *"Musculoskeletal and connective tissue disorders"* (42/259 AEs; 16.2%)
   a) Arthralgia (9/42, 21.4%)
   b) Pain in extremity (9/42, 21.4%)
   c) Musculoskeletal pain (5/42, 11.9%)
3) *"Infections and infestations"* (40/259 AEs; 15.4%)
   a) Bronchitis (7/40, 17.5%)
   b) Nasopharyngitis (6/40, 15%)
   c) Urinary tract infection (5/40, 12.5%)
   d) Influenza (5/40, 12.5%)
4) *Surgical and medical (34/259, 13.1%)*

a) Joint injection (6/34, 17.6%)
b) Hospitalization (5/34, 14.7%)

In decreasing order of frequency, SAEs were affiliated in the following SOCs:

- "*Surgical and medical procedures"* (14/39 SAEs; 35.9%)
  - Hospitalization (4/14, 28.6%)
  - Shoulder arthroplasty (3/14, 21.4%)
  - Surgery (2/14, 14.3%)
- *"General disorders and administration site conditions"* (4/39 SAEs; 10.3%)
  a) Condition aggravated (2/4, 50.0%)
  b) Fatigue (1/4, 25.0%)
  c) Malaise (1/4, 25.0%)
- *"Infections and infestations"* (4/39 SAEs; 10.3%)
  a) Gastroenteritis (1/4, 25%)
  b) Lung abscess (1/4, 25%)
  c) Lung infection (1/4, 25%)
  d) Sepsis (1/4, 25%)

16.1.6.2 Patients with psoriatic arthritis

In decreasing order of frequency, all AEs (serious and non-serious) were classed under the following SOCs:

1) *"General disorders and administration site conditions"* (71/272 AEs; 26.1%)
   a) Pain (22/71, 31.0%)
   b) Ill-defined disorder (10/71, 14.1%)
2) *"Musculoskeletal and connective tissue disorders"* (52/272 AEs; 19.1%)
   a) Pain in extremity (7/52, 13.5%)
   b) Arthralgia (6/49, 11.5%)
   c) Musculoskeletal pain (6/49, 11.5%)
3) *"Infections and infestations"* (33/272 AEs; 12.1%)
   a) Bronchitis (7/33, 21.2%)

In decreasing order of frequency, SAEs were affiliated in the following SOCs:

1) "*Surgical and medical procedures"* (14/32 SAEs; 43.8% %)
   a) Knee operation (4/14, 28.6%)
   b) Hospitalization (2/14, 14.3%)
   c) Hip surgery (2/14, 14.3%)
2) *"Musculoskeletal and connective tissue disorders"* (6/32 SAEs; 18.8%)
   a) Systemic lupus erythematosus (2/6, 33.3%)
   b) Arthropathy (1/6, 16.7%)
   c) Intervertebral disc protrusion (1/6, 16.7%)
   d) Psoriatic arthropathy (1/6, 16.7%)
   e) Rheumatic disorder (1/6, 16.7%)

16.1.6.3 Patients with ankylosing spondylitis

In decreasing order of frequency, all AEs (serious and non-serious) were classed in the following SOCs:

1) *"General disorders and administration site conditions"* (246/760 AEs; 32.4%)
   a) Ill-defined disorder (37/246, 15%)

b) Pain (35/246, 14.2%)
c) Fatigue (31/246, 12.6%)

2) *"Infections and infestations"* (120/760 AEs; 15.8%)
a) Nasopharyngitis (19/120, 15.8%)
b) Bronchitis (17/120, 14.2%)
c) Influenza (12/120, 15.8%)

In decreasing order of frequency, SAEs were affiliated in the following SOCs:

1) "*Surgical and medical procedures"* (51/125 SAEs; 40.8%)
a) Hospitalization (36/51, 70.6%)
b) Surgery (7/51, 13.7%)

2) *"General disorders and administration site conditions"* (15/125 SAEs; 12.0 %)
a) Pain 6/15, 40%)
b) Condition aggravated (5/15, 33.3%)

Table 119 : Patient-reported non-serious AEs and SAEs classified by Preferred Term (PT) and System Organ Class (SOC) for each indication

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Blood and lymphatic system	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**5 (0.79)**	**1 (0.80)**	**6 (0.79)**	**5 (0.46)**	**1 (0.51)**	**6 (0.46)**
Haemorrhagic anaemia	-	-	-	-	-	-	0 (0)	1 (100)	1 (16.7)	0 (0)	1 (100)	1 (16.7)
Lymphadenopathy	-	-	-	-	-	-	5 (100)	0 (0)	5 (83.3)	5 (100)	0 (0)	5 (83.3)
Cardiac disorders	**3 (1.36)**	**1 (2.56)**	**4 (1.54)**	**0 (0)**	**0 (0)**	**0 (0)**	**3 (0.47)**	**0 (0)**	**3 (0.39)**	**6 (0.55)**	**1 (0.51)**	**7 (0.54)**
Atrial fibrillation	0 (0)	0 (0)	0 (0)	-	-	-	1 (33.3)	0 (0)	1 (33.3)	1 (16.7)	0 (0)	1 (14.3)
Cardiac amyloidosis	1 (33.3)	0 (0)	1 (25.0)	-	-	-	-	-	-	1 (16.7)	0 (0)	1 (14.3)
Cardiac discomfort	0 (0)	0 (0)	0 (0)	-	-	-	1 (33.3)	0 (.)	1 (33.3)	1 (16.7)	0 (0)	1 (14.3)
Cardiomyopathy	0 (0)	1 (100)	1 (25.0)	-	-	-	-	-	-	0 (0)	1 (100)	1 (14.3)
Palpitations	1 (33.3)	0 (0)	1 (25.0)	-	-	-	1 (33.3)	0 (.)	1 (33.3)	2 (33.3)	0 (0)	2 (28.6)
Tachycardia	1 (33.3)	0 (0)	1 (25.0)	-	-	-	-	-	-	1 (16.7)	0 (0)	1 (14.3)
Ear and labyrinth disorders	**0 (0)**	**0 (0)**	**0 (0)**	**5 (2.08)**	**0 (0)**	**5 (1.84)**	**3 (0.47)**	**0**	**3 (0.39)**	**8 (0.73)**	**0**	**8 (0.62)**
Ear disorder	-	-	-	0	-	0	1 (33.3)	0 (0)	1 (33.3)	1 (12.5)	0 (.)	1 (12.5)
Tinnitus	-	-	-	0	-	0	1 (33.3)	0 (0)	1 (33.3)	1 (12.5)	0 (.)	1 (12.5)
Vertigo	-	-	-	5 (100)	0 (0)	5 (100)	1 (33.3)	0 (0)	1 (33.3)	6 (75.0)	0 (.)	6 (75.0)
Eye disorders	**0 (0)**	**0 (0)**	**0 (0)**	**3 (1.25)**	**0 (0)**	**3 (1.10)**	**4 (0.63)**	**3 (2.40)**	**7 (0.92)**	**7 (0.64)**	**3 (1.53)**	**10 (0.77)**
Cataract	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (14.3)	1 (14.3)	0 (0)	1 (10.0)
Blepharitis	-	-	-	1 (33.3)	0 (0)	1 (33.3)	-	-	-	1 (14.3)	0 (0)	1 (10.0)
Chalazion	-	-	-	1 (33.3)	0 (0)	1 (33.3)	-	-	-	1 (14.3)	0 (0)	1 (10.0)
Eye pain	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (14.3)	1 (14.3)	0 (0)	1 (10.0)
Retinal detachment	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (14.3)	1 (14.3)	0 (0)	1 (10.0)
Uveitis	-	-	-	-	-	-	0 (0)	3 (100)	3 (42.9)	0 (0)	3 (100)	3 (30.0)
Visual impairment	-	-	-	1 (33.3)	0 (0)	1 (33.3)	1 (25.0)	0 (0)	1 (14.3)	2 (28.6)	0 (0)	2 (20.0)
Gastrointestinal disorders	**5 (2.27)**	**3 (7.69)**	**8 (3.09)**	**7 (2.92)**	**1 (3.13)**	**8 (2.94)**	**43 (6.77)**	**5 (4.00)**	**48 (6.32)**	**55 (5.02)**	**9 (4.59)**	**64 (4.96)**
Abdominal pain	1 (20.0)	0 (0)	1 (12.5)	-	-	-	6 (14.0)	0 (0)	6 (12.5)	7 (12.7)	0 (0)	7 (10.9)
Abdominal pain lower	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Abdominal pain upper	-	-	-	1 (14.3)	0 (0)	1 (12.5)	3 (6.98)	0 (0)	3 (6.25)	4 (7.27)	0 (0)	4 (6.25)
Aphthous ulcer	-	-	-	-	-	-	8 (18.6)	0 (0)	8 (16.7)	8 (14.5)	0 (0)	8 (12.5)
Chronic gastritis	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.08)	0 (0)	1 (11.1)	1 (1.56)
Colitis	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)
Colitis microscopic	-	-	-	0 (0)	1 (100)	1 (12.5)	-	-	-	0 (0)	1 (11.1)	1 (1.56)
Constipation	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)
Diarrhoea	1 (20.0)	0 (0)	1 (12.5)	2 (28.6)	0 (0)	2 (25.0)	3 (6.98)	0 (0)	3 (6.25)	6 (10.9)	0 (0)	6 (9.38)
Dyspepsia	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)
Enterocolitis	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.08)	0 (0)	1 (11.1)	1 (1.56)
Gastritis	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)
Gastrointestinal disorder	1 (20.0)	0 (0)	1 (12.5)	-	-	-	5 (11.6)	0 (0)	5 (10.4)	6 (10.9)	0 (0)	6 (9.38)
Gastrointestinal pain	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)
Gastrointestinal tract irritation	-	-	-	1 (14.3)	0 (0)	1 (12.5)	0	0	0	1 (1.82)	0 (0)	1 (1.56)
Inguinal hernia	0 (0)	1 (33.3)	1 (12.5)	-	-	-	-	-	-	0 (0)	1 (11.1)	1 (1.56)
Irritable bowel syndrome	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.08)	0 (0)	1 (11.1)	1 (1.56)
Mouth ulceration	-	-	-	-	-	-	1 (2.33)	1 (20.0)	2 (4.17)	1 (1.82)	1 (11.1)	2 (3.13)
Nausea	2 (40.0)	1 (33.3)	3 (37.5)	2 (28.6)	0 (0)	2 (25.0)	6 (14.0)	0 (0)	6 (12.5)	10 (18.2)	1 (11.1)	11 (17.2)
Oral pain	-	-	-	-	-	-	1 (2.33)	0 (0)	1 (2.08)	1 (1.82)	0 (0)	1 (1.56)
Tooth disorder	-	-	-	-	-	-	1 (2.33)	1 (20.0)	2 (4.17)	1 (1.82)	1 (11.1)	2 (3.13)
Toothache	-	-	-	1 (14.3)	0 (0)	1 (12.5)	-	-	-	1 (1.82)	0 (0)	1 (1.56)
Vomiting	0 (0)	1 (33.3)	1 (12.5)	-	-	-	3 (6.98)	0 (0)	3 (6.25)	3 (5.45)	1 (11.1)	4 (6.25)
General disorders and administration site conditions	**70 (31.8)**	**4 (10.3)**	**74 (28.6)**	**68 (28.3)**	**3 (9.38)**	**71 (26.1)**	**231 (36.4)**	**15 (12.0)**	**246 (32.4)**	**369 (33.7)**	**22 (11.2)**	**391 (30.3)**
Adverse drug reaction	1 (1.43)	0 (0)	1 (1.35)	-	-	-	1 (0.43)	0 (0)	1 (0.41)	2 (0.54)	0 (0)	2 (0.51)
Adverse event	2 (2.86)	0 (0)	2 (2.70)	-	-	-	-	-	-	2 (0.54)	0 (0)	2 (0.51)
Adverse reaction	2 (2.86)	0 (0)	2 (2.70)	-	-	-	4 (1.73)	0 (0)	4 (1.63)	6 (1.63)	0 (0)	6 (1.53)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Asthenia	1 (1.43)	0 (0)	1 (1.35)	-	-	-	10 (4.33)	0 (0)	10 (4.07)	11 (2.98)	0 (0)	11 (2.81)
Chest discomfort	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
Chest pain	-	-	-	-	-	-	3 (1.30)	0 (0)	3 (1.22)	3 (0.81)	0 (0)	3 (0.77)
Condition aggravated	9 (12.9)	2 (50.0)	11 (14.9)	3 (4.41)	2 (66.7)	5 (7.04)	9 (3.90)	5 (33.3)	14 (5.69)	21 (5.69)	9 (40.9)	30 (7.67)
Device defective	0	0	0	1 (1.47)	0 (0)	1 (1.41)	1 (0.43)	0 (0)	1 (0.41)	2 (0.54)	0 (0)	2 (0.51)
Device malfunction	3 (4.29)	0 (0)	3 (4.05)	3 (4.41)	0 (0)	3 (4.23)	7 (3.03)	0 (0)	7 (2.85)	13 (3.52)	0 (0)	13 (3.32)
Disease recurrence	-	-	-	-	-	-	0 (0)	1 (6.67)	1 (0.41)	0 (0)	1 (4.55)	1 (0.26)
Drug effect decreased	-	-	-	-	-	-	5 (2.16)	0 (0)	5 (2.03)	5 (1.36)	0 (0)	5 (1.28)
Drug effect incomplete	-	-	-	1 (1.47)	0 (0)	1 (1.41)	-	-	-	1 (0.27)	0 (0)	1 (0.26)
Drug ineffective	6 (8.57)	0 (0)	6 (8.11)	1 (1.47)	0 (0)	1 (1.41)	21 (9.09)	1 (6.67)	22 (8.94)	28 (7.59)	1 (4.55)	29 (7.42)
Drug intolerance	4 (5.71)	0 (0)	4 (5.41)	2 (2.94)	0 (0)	2 (2.82)	15 (6.49)	1 (6.67)	16 (6.50)	21 (5.69)	1 (4.55)	22 (5.63)
Face oedema	0 (0)	0 (0)	0 (0)	-	-	-	3 (1.30)	0 (0)	3 (1.22)	3 (0.81)	0 (0)	3 (0.77)
Fatigue	9 (12.9)	1 (25.0)	10 (13.5)	5 (7.35)	0 (0)	5 (7.04)	30 (13.0)	1 (6.67)	31 (12.6)	44 (11.9)	2 (9.09)	46 (11.8)
Feeling abnormal	-	-	-	1 (1.47)	0 (0)	1 (1.41)	1 (0.43)	0 (0)	1 (0.41)	2 (0.54)	0 (0)	2 (0.51)
Feeling cold	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
Fibrosis	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
Gait disturbance	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
General physical health deterioration	-	-	-	-	-	-	3 (1.30)	0 (0)	3 (1.22)	3 (0.81)	0 (0)	3 (0.77)
Hernia	1 (1.43)	0 (0)	1 (1.35)	-	-	-	-	-	-	1 (0.27)	0 (0)	1 (0.26)
Ill-defined disorder	4 (5.71)	0 (0)	4 (5.41)	10 (14.7)	0 (0)	10 (14.1)	37 (16.0)	0 (0)	37 (15.0)	51 (13.8)	0 (0)	51 (13.0)
Inflammation	2 (2.86)	0 (0)	2 (2.70)	-	-	-	2 (0.87)	0 (0)	2 (0.81)	4 (1.08)	0 (0)	4 (1.02)
Influenza like illness	1 (1.43)	0 (0)	1 (1.35)	-	-	-	5 (2.16)	0 (0)	5 (2.03)	6 (1.63)	0 (0)	6 (1.53)
Injection site haemorrhage	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
Injection site pain	-	-	-	1 (1.47)	0 (0)	1 (1.41)	-	-	-	1 (0.27)	0 (0)	1 (0.26)
Injection site paraesthesia	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
Injection site reaction	-	-	-	-	-	-	2 (0.87)	0 (0)	2 (0.81)	2 (0.54)	0 (0)	2 (0.51)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Injection site swelling	-	-	-	-	-	-	1 (0.43)	0 (0)	1 (0.41)	1 (0.27)	0 (0)	1 (0.26)
Local swelling	-	-	-	1 (1.47)	0 (0)	1 (1.41)	-	-	-	1 (0.27)	0 (0)	1 (0.26)
Malaise	2 (2.86)	1 (25.0)	3 (4.05)	1 (1.47)	1 (33.3)	2 (2.82)	1 (0.43)	0 (0)	1 (0.41)	4 (1.08)	2 (9.09)	6 (1.53)
Oedema	-	-	-	2 (2.94)	0 (0)	2 (2.82)	-	-	-	2 (0.54)	0 (0)	2 (0.51)
Oedema peripheral	2 (2.86)	0 (0)	2 (2.70)	4 (5.88)	0 (0)	4 (5.63)	7 (3.03)	0 (0)	7 (2.85)	13 (3.52)	0 (0)	13 (3.32)
Pain	10 (14.3)	0 (0)	10 (13.5)	22 (32.4)	0 (0)	22(31.0)	29 (12.6)	6 (40.0)	35 (14.2)	61 (16.5)	6 (27.3)	67 (17.1)
Peripheral swelling	2 (2.86)	0 (0)	2 (2.70)	3 (4.41)	0 (0)	3 (4.23)	2 (0.87)	0 (0)	2 (0.81)	7 (1.90)	0 (0)	7 (1.79)
Pyrexia	6 (8.57)	0 (0)	6 (8.11)	4 (5.88)	0 (0)	4 (5.63)	13 (5.63)	0 (0)	13 (5.28)	23 (6.23)	0 (0)	23 (5.88)
Similar reaction on previous exposure to drug	1 (1.43)	0 (0)	1 (1.35)	-	-	-	-	-	-	1 (0.27)	0 (0)	1 (0.26)
Therapeutic response shortened	-	-	-	-	-	-	3 (1.30)	0 (0)	3 (1.22)	3 (0.81)	0 (0)	3 (0.77)
Treatment failure	-	-	-	2 (2.94)	0 (0)	2 (2.82)	1 (0.43)	0 (0)	1 (0.41)	3 (0.81)	0 (0)	3 (0.77)
Unevaluable event	2 (2.86)	0 (0)	2 (2.70)	1 (1.47)	0 (0)	1 (1.41)	9 (3.90)	0 (0)	9 (3.66)	12 (3.25)	0 (0)	12 (3.07)
Hepatobiliary disorders	**0 (0)**	**1 (2.56)**	**1 (0.39)**	**0 (0)**	**1 (3.13)**	**1 (0.37)**	**4 (0.63)**	**0 (0)**	**4 (0.53)**	**4 (0.37)**	**2 (1.02)**	**6 (0.46)**
Bile duct stone	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (25.0)	1 (25.0)	0 (0)	1 (16.7)
Biliary tract disorder	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (25.0)	1 (25.0)	0 (0)	1 (16.7)
Cholelithiasis	0 (0)	1 (100)	1 (100)	0 (0)	1 (100)	1 (100)	-	-	-	0 (0)	2 (100)	2 (33.3)
Liver disorder	0 (0)	0 (0)	0 (0)	-	-	-	2 (50.0)	0 (0)	2 (50.0)	2 (50.0)	0 (0)	2 (33.3)
Immune system disorders	**2 (0.91)**	**0**	**2 (0.77)**	**0 (0)**	**0 (0)**	**0 (0)**	**2 (0.31)**	**1 (0.80)**	**3 (0.39)**	**4 (0.37)**	**1 (0.51)**	**5 (0.39)**
Drug hypersensitivity	1 (50.0)	0 (0)	1 (50.0)	-	-	-	1 (50.0)	0 (0)	1 (33.3)	2 (50.0)	0 (0)	2 (40.0)
Hypersensitivity	1 (50.0)	0 (0)	1 (50.0)	-	-	-	1 (50.0)	1 (100)	2 (66.7)	2 (50.0)	1 (100)	3 (60.0)
Infections and infestations	**36 (16.4)**	**4 (10.3)**	**40 (15.4)**	**32 (13.3)**	**1 (3.13)**	**33 (12.1)**	**112 (17.6)**	**8 (6.40)**	**120 (15.8)**	**180 (16.4)**	**13 (6.63)**	**193 (14.9)**
Abscess	-	-	-	-	-	-	2 (1.79)	0 (0)	2 (1.67)	2 (1.11)	0 (0)	2 (1.04)
Alveolar osteitis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Appendicitis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Bacterial infection	-	-	-	-	-	-	2 (1.79)	0 (0)	2 (1.67)	2 (1.11)	0 (0)	2 (1.04)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Bacterial vaginosis	1 (2.78)	0 (0)	1 (2.50)	-	-	-	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Bartholinitis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Bronchitis	7 (19.4)	0 (0)	7 (17.5)	7 (21.9)	0 (0)	7 (21.2)	16 (14.3)	1 (12.5)	17 (14.2)	30 (16.7)	1 (7.69)	31 (16.1)
Cellulitis	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (0.83)	0 (0)	1 (7.69)	1 (0.52)
Cyst	-	-	-	1 (3.13)	0 (0)	1 (3.03)	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Cystitis	1 (2.78)	0 (0)	1 (2.50)	-	-	-	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Ear infection	-	-	-	2 (6.25)	0 (0)	2 (6.06)	3 (2.68)	0 (0)	3 (2.50)	5 (2.78)	0 (0)	5 (2.59)
Fungal skin infection	-	-	-	1 (3.13)	0 (0)	1 (3.03)	1 (0.89)	0 (0)	1 (0.83)	2 (1.11)	0 (0)	2 (1.04)
Gastroenteritis	1 (2.78)	1 (25.0)	2 (5.00)	1 (3.13)	0 (0)	1 (3.03)	3 (2.68)	0 (0)	3 (2.50)	5 (2.78)	1 (7.69)	6 (3.11)
Herpes simplex	1 (2.78)	0 (0)	1 (2.50)	1 (3.13)	0 (0)	1 (3.03)	1 (0.89)	0 (0)	1 (0.83)	3 (1.67)	0 (0)	3 (1.55)
Herpes virus infection	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Herpes zoster	1 (2.78)	0 (0)	1 (2.50)	1 (3.13)	0 (0)	1 (3.03)	1 (0.89)	0 (0)	1 (0.83)	3 (1.67)	0 (0)	3 (1.55)
Infection	-	-	-	2 (6.25)	1 (100)	3 (9.09)	6 (5.36)	0 (0)	6 (5.00)	8 (4.44)	1 (7.69)	9 (4.66)
Infective exacerbation of chronic obstructive ai	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Influenza	5 (13.9)	0 (0)	5 (12.5)	-	-	-	12 (10.7)	0 (0)	12 (10.0)	17 (9.44)	0 (0)	17 (8.81)
Laryngitis	-	-	-	1 (3.13)	0 (0)	1 (3.03)	1 (0.89)	0 (0)	1 (0.83)	2 (1.11)	0 (0)	2 (1.04)
Localised infection	-	-	-	1 (3.13)	0 (0)	1 (3.03)	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Lung abscess	0 (0)	1 (25.0)	1 (2.50)	-	-	-	-	-	-	0 (0)	1 (7.69)	1 (0.52)
Lung infection	1 (2.78)	1 (25.0)	2 (5.00)	1 (3.13)	0 (0)	1 (3.03)	-	-	-	2 (1.11)	3 (23.1)	5 (2.59)
Lyme disease	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Lymph node tuberculosis	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (0.83)	0 (0)	1 (7.69)	1 (0.52)
Meningitis viral	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (0.83)	0 (0)	1 (7.69)	1 (0.52)
Mumps	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (0.83)	0 (0)	1 (7.69)	1 (0.52)
Nasopharyngitis	6 (16.7)	0 (0)	6 (15.0)	2 (6.25)	0 (0)	2 (6.06)	19 (17.0)	0 (0)	19 (15.8)	27 (15.0)	0 (0)	27 (14.0)
Oral herpes	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Paronychia	-	-	-	1 (3.13)	0 (0)	1 (3.03)	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Pharyngitis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Pneumonia	-	-	-	1 (3.13)	0 (0)	1 (3.03)	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Post procedural infection	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (0.83)	0 (0)	1 (7.69)	1 (0.52)
Pyelonephritis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Rhinitis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Salmonellosis	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Sepsis	0 (0)	1 (25.0)	1 (2.50)	-	-	-	-	-	-	0 (0)	1 (7.69)	1 (0.52)
Sinusitis	1 (2.78)	0 (0)	1 (2.50)	1 (3.13)	0 (0)	1 (3.03)	6 (5.36)	0 (0)	6 (5.00)	8 (4.44)	0 (0)	8 (4.15)
Superinfection	0 (0)	0 (0)	0 (0)	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Tonsillitis	4 (11.1)	0 (0)	4 (10.0)	2 (6.25)	0 (0)	2 (6.06)	9 (8.04)	0 (0)	9 (7.50)	15 (8.33)	0 (0)	15 (7.77)
Tooth abscess	1 (2.78)	0 (0)	1 (2.50)	1 (3.13)	0 (0)	1 (3.03)	-	-	-	2 (1.11)	0 (0)	2 (1.04)
Tooth infection	1 (2.78)	0 (0)	1 (2.50)	-	-	-	2 (1.79)	0 (0)	2 (1.67)	3 (1.67)	0 (0)	3 (1.55)
Tracheitis	-	-	-	2 (6.25)	0 (0)	2 (6.06)	1 (0.89)	0 (0)	1 (0.83)	3 (1.67)	0 (0)	3 (1.55)
Upper respiratory tract infection	-	-	-	-	-	-	7 (6.25)	0 (0)	7 (5.83)	7 (3.89)	0 (0)	7 (3.63)
Urinary tract infection	5 (13.9)	0 (0)	5 (12.5)	2 (6.25)	0 (0)	2 (6.06)	7 (6.25)	0 (0)	7 (5.83)	14 (7.78)	0 (0)	14 (7.25)
Vulvovaginal mycotic infection	-	-	-	-	-	-	1 (0.89)	0 (0)	1 (0.83)	1 (0.56)	0 (0)	1 (0.52)
Wound infection	-	-	-	1 (3.13)	0 (0)	1 (3.03)	-	-	-	1 (0.56)	0 (0)	1 (0.52)
Injury, poisoning and procedural complications	**8 (3.63)**	**2 (5.12)**	**10 (3.86)**	**20 (8.33)**	**1 (3.13)**	**21 (7.72)**	**36 (5.67)**	**5 (4.00)**	**41 (5.39)**	**64 (5.84)**	**8 (4.08)**	**72 (5.58)**
Asbestosis	-	-	-	1 (5.00)	0 (0)	1 (4.76)	-	-	-	1 (1.56)	0 (0)	1 (1.39)
Chest injury	-	-	-	-	-	-	1 (2.78)	0 (0)	1 (2.44)	1 (1.56)	0 (0)	1 (1.39)
Drug dose omission	2 (25.0)	0 (0)	2 (20.0)	-	-	-	-	-	-	2 (3.13)	0 (0)	2 (2.78)
Epicondylitis	-	-	-	-	-	-	1 (2.78)	0 (0)	1 (2.44)	1 (1.56)	0 (0)	1 (1.39)
Excoriation	-	-	-	1 (5.00)	0 (0)	1 (4.76)	-	-	-	1 (1.56)	0 (0)	1 (1.39)
Facial bones fracture	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.44)	0 (0)	1 (12.5)	1 (1.39)
Fall	-	-	-	4 (20.0)	0 (0)	4 (19.0)	1 (2.78)	0 (0)	1 (2.44)	5 (7.81)	0 (0)	5 (6.94)
Gastrointestinal disorder	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.44)	0 (0)	1 (12.5)	1 (1.39)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Hand fracture	0 (0)	1 (50.0)	1 (10.0)	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (1.39)
Humerus fracture	1 (12.5)	0 (0)	1 (10.0)	-	-	-	1 (2.78)	0 (0)	1 (2.44)	2 (3.13)	0 (0)	2 (2.78)
Inappropriate schedule of drug administration	1 (12.5)	0 (0)	1 (10.0)	-	-	-	12 (33.3)	0 (0)	12 (29.3)	13 (20.3)	0 (0)	13 (18.1)
Incorrect dosage administered	-	-	-	1 (5.00)	0 (0)	1 (4.76)	-	-	-	1 (1.56)	0 (0)	1 (1.39)
Incorrect dose administered	-	-	-	2 (10.0)	0 (0)	2 (9.52)	-	-	-	2 (3.13)	0 (0)	2 (2.78)
Ligament rupture	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.44)	0 (0)	1 (12.5)	1 (1.39)
Limb injury	-	-	-	-	-	-	1 (2.78)	0 (0)	1 (2.44)	1 (1.56)	0 (0)	1 (1.39)
Muscle rupture	-	-	-	1 (5.00)	0 (0)	1 (4.76)	1 (2.78)	0 (0)	1 (2.44)	2 (3.13)	0 (0)	2 (2.78)
Off label use	3 (37.5)	0 (0)	3 (30.0)	2 (10.0)	0 (0)	2 (9.52)	18 (50.0)	0 (0)	18 (43.9)	23 (35.9)	0 (0)	23 (31.9)
Post procedural haemorrhage	0 (0)	0 (0)	0 (0)	-	-	-	0 (0)	1 (20.0)	1 (2.44)	0 (0)	1 (12.5)	1 (1.39)
Post vaccination syndrome	1 (12.5)	0 (0)	1 (10.0)	-	-	-	-	-	-	1 (1.56)	0 (0)	1 (1.39)
Post-traumatic neck	-	-	-	1 (5.00)	0 (0)	1 (4.76)	-	-	-	1 (1.56)	0 (0)	1 (1.39)
Product use issue	-	-	-	1 (5.00)	0 (0)	1 (4.76)	-	-	-	1 (1.56)	0 (0)	1 (1.39)
Rib fracture	-	-	-	2 (10.0)	0 (0)	2 (9.52)	-	-	-	2 (3.13)	0 (0)	2 (2.78)
Road traffic accident	-	-	-	2 (10.0)	1 (100)	3 (14.3)	-	-	-	2 (3.13)	1 (12.5)	3 (4.17)
Spinal compression fracture	-	-	-	2 (10.0)	0 (0)	2 (9.52)	-	-	-	2 (3.13)	0 (0)	2 (2.78)
Stress fracture	-	-	-	-	-	-	0 (0)	1 (20.0)	1 (2.44)	0 (0)	1 (12.5)	1 (1.39)
Tendon rupture	0 (0)	1 (50.0)	1 (10.0)	-	-	-	-	-	-	0 (0)	1 (12.5)	1 (1.39)
Injury, poisoning and procedural complications / infections and infestations / gastrointestinal disorders	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**2 (1.60)**	**2 (0.26)**	**0**	**2 (1.02)**	**2 (0.15)**
Peritoneal haemorrhage	-	-	-	-	-	-	0 (0)	1 (50.0)	1 (50.0)	0	1 (50.0)	1 (50.0)
Post procedural	-	-	-	-	-	-	0 (0)	1 (50.0)	1 (50.0)	0	1 (50.0)	1 (50.0)
Investigations	**6 (2.73)**	**2 (5.13)**	**8 (3.09)**	**3 (1.25)**	**1 (3.13)**	**4 (1.47)**	**12 (1.89)**	**6 (4.80)**	**18 (2.37)**	**21**	**9**	**30**

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Blood cholesterol abnormal	1 (16.7)	0 (0)	1 (12.5)	-	-	-	-	-	-	1 (4.76)	0 (0)	1 (3.33)
Blood pressure abnormal	1 (16.7)	0 (0)	1 (12.5)	-	-	-	-	-	-	1 (4.76)	0 (0)	1 (3.33)
Blood pressure decreased	-	-	-	-	-	-	1 (8.33)	0 (0)	1 (5.56)	1 (4.76)	0 (0)	1 (3.33)
Blood pressure increased	-	-	-	-	-	-	1 (8.33)	0 (0)	1 (5.56)	1 (4.76)	0 (0)	1 (3.33)
Blood test abnormal	1 (16.7)	0 (0)	1 (12.5)	-	-	-	-	-	-	1 (4.76)	0 (0)	1 (3.33)
Colonoscopy	1 (16.7)	0 (0)	1 (12.5)	-	-	-	3 (25.0)	3 (50.0)	6 (33.3)	4 (19.0)	3 (33.3)	7 (23.3)
Diagnostic procedure	0 (0)	0 (0)	0 (0)	-	-	-	0 (0)	1 (16.7)	1 (5.56)	0 (0)	1 (11.1)	1 (3.33)
Endoscopy	1 (16.7)	0 (0)	1 (12.5)	-	-	-	1 (8.33)	2 (33.3)	3 (16.7)	2 (9.52)	2 (22.2)	4 (13.3)
Heart rate irregular	-	-	-	-	-	-	1 (8.33)	0 (0)	1 (5.56)	1 (4.76)	0 (0)	1 (3.33)
International normalised ratio abnormal	-	-	-	1 (33.3)	0 (0)	1 (25.0)	-	-	-	1 (4.76)	0 (0)	1 (3.33)
Liver function test abnormal	0 (0)	0 (0)	0 (0)	-	-	-	1 (8.33)	0 (0)	1 (5.56)	1 (4.76)	0 (0)	1 (3.33)
Platelet count decreased	0 (0)	1 (50.0)	1 (12.5)	-	-	-	-	-	-	0 (0)	1 (11.1)	1 (3.33)
Ultrasound Doppler	-	-	-	1 (33.3)	0 (0)	1 (25.0)	-	-	-	1 (4.76)	0 (0)	1 (3.33)
Unevaluable investigation	-	-	-	0 (0)	1 (100)	1 (25.0)	-	-	-	0 (0)	1 (11.1)	1 (3.33)
Weight decreased	1 (16.7)	1 (50.0)	2 (25.0)	-	-	-	3 (25.0)	0 (0)	3 (16.7)	4 (19.0)	1 (11.1)	5 (16.7)
Weight increased	-	-	-	-	-	-	1 (8.33)	0 (0)	1 (5.56)	1 (4.76)	0 (0)	1 (3.33)
X-ray limb abnormal	-	-	-	1 (33.3)	0 (0)	1 (25.0)	-	-	-	1 (4.76)	0 (0)	1 (3.33)
Metabolism and nutrition	**2 (0.91)**	**0 (0)**	**2 (0.77)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.16)**	**0 (0)**	**1 (0.13)**	**3 (0.27)**	**0**	**3 (0.23)**
Decreased appetite	2 (100)	0 (0)	2 (100)	-	-	-	-	-	-	2 (66.7)	0 (.)	2 (66.7)
Diabetes mellitus inadequate control	-	-	-	-	-	-	1 (100)	0 (0)	1 (100)	1 (33.3)	0 (.)	1 (33.3)
Musculoskeletal and connective tissue disorders	**40 (18.2)**	**2 (5.13)**	**42 (16.2)**	**46 (19.2)**	**6 (18.8)**	**52 (19.1)**	**51 (8.03)**	**11 (8.80)**	**62 (8.16)**	**137 (12.5)**	**19 (9.69)**	**156 (12.1)**
Ankylosing spondylitis	-	-	-	-	-	-	0 (0)	2 (18.2)	2 (3.23)	0 (0)	2 (10.5)	2 (1.28)
Arthralgia	8 (20.0)	1 (50.0)	9 (21.4)	6 (13.0)	0 (0)	6 (11.5)	10 (19.6)	2 (18.2)	12 (19.4)	24 (17.5)	3 (15.8)	27 (17.3)
Arthritis	2 (5.00)	0 (0)	2 (4.76)	1 (2.17)	0 (0)	1 (1.92)	-	-	-	3 (2.19)	0 (0)	3 (1.92)
Arthropathy	1 (2.50)	0 (0)	1 (2.38)	0 (0)	1 (16.7)	1 (1.92)	-	-	-	1 (0.73)	1 (5.26)	2 (1.28)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Back disorder	1 (2.50)	0 (0)	1 (2.38)	-	-	-	1 (1.96)	0 (0)	1 (1.61)	2 (1.46)	0 (0)	2 (1.28)
Back pain	3 (7.50)	0 (0)	3 (7.14)	3 (6.52)	0 (0)	3 (5.77)	6 (11.7)	0 (0)	6 (9.68)	12 (8.76)	0 (0)	12 (7.69)
Bone pain	-	-	-	-	-	-	2 (3.92)	0 (0)	2 (3.23)	2 (1.46)	0 (0)	2 (1.28)
Fibromyalgia	-	-	-	-	-	-	0 (0)	1 (9.09)	1 (1.61)	0 (0)	1 (5.26)	1 (0.64)
Foot deformity	-	-	-	3 (6.52)	0 (0)	3 (5.77)	-	-	-	3 (2.19)	0 (0)	3 (1.92)
Groin pain	-	-	-	1 (2.17)	0 (0)	1 (1.92)	3 (5.88)	0 (0)	3 (4.84)	4 (2.92)	0 (0)	4 (2.56)
Intervertebral disc protrusion	-	-	-	0 (0)	1 (16.7)	1 (1.92)	-	-	-	0 (0)	1 (5.26)	1 (0.64)
Joint ankylosis	-	-	-	-	-	-	1 (1.96)	0 (0)	1 (1.61)	1 (0.73)	0 (0)	1 (0.64)
Joint effusion	-	-	-	-	-	-	0 (0)	1 (9.09)	1 (1.61)	0 (0)	1 (5.26)	1 (0.64)
Joint swelling	-	-	-	3 (6.52)	0 (0)	3 (5.77)	1 (1.96)	1 (9.09)	2 (3.23)	4 (2.92)	1 (5.26)	5 (3.20)
Lumbar spinal stenosis	0 (0)	1 (50.0)	1 (2.38)	-	-	-	-	-	-	0 (0)	1 (5.26)	1 (0.64)
Mobility decreased	1 (2.50)	0 (0)	1 (2.38)	1 (2.17)	0 (0)	1 (1.92)	-	-	-	2 (1.46)	0 (0)	2 (1.28)
Muscle contracture	-	-	-	1 (2.17)	0 (0)	1 (1.92)	-	-	-	1 (0.73)	0 (0)	1 (0.64)
Muscular weakness	-	-	-	1 (2.17)	0 (0)	1 (1.92)	1 (1.96)	0 (0)	1 (1.61)	2 (1.46)	0 (0)	2 (1.28)
Musculoskeletal chest pain	-	-	-	-	-	-	0 (0)	1 (9.09)	1 (1.61)	0 (0)	1 (5.26)	1 (0.64)
Musculoskeletal pain	5 (12.5)	0 (0)	5 (11.9)	6 (13.0)	0 (0)	6 (11.5)	6 (11.7)	2 (18.2)	8 (12.9)	17 (12.4)	2 (10.5)	19 (12.2)
Musculoskeletal stiffness	-	-	-	1 (2.17)	0 (0)	1 (1.92)	1 (1.96)	0 (0)	1 (1.61)	2 (1.46)	0 (0)	2 (1.28)
Myalgia	2 (5.00)	0 (0)	2 (4.76)	3 (6.52)	0 (0)	3 (5.77)	1 (1.96)	0 (0)	1 (1.61)	6 (4.38)	0 (0)	6 (3.85)
Neck pain	3 (7.50)	0 (0)	3 (7.14)	3 (6.52)	0 (0)	3 (5.77)	2 (3.92)	0 (0)	2 (3.23)	8 (5.84)	0 (0)	8 (5.13)
Osteoarthritis	-	-	-	1 (2.17)	0 (0)	1 (1.92)	1 (1.96)	0 (0)	1 (1.61)	2 (1.46)	0 (0)	2 (1.28)
Pain in extremity	9 (22.5)	0 (0)	9 (21.4)	7 (15.2)	0 (0)	7 (13.5)	10 (19.6)	0 (0)	10 (16.1)	26 (19.0)	0 (0)	26 (16.7)
Pain in jaw	1 (2.50)	0 (0)	1 (2.38)	-	-	-	1 (1.96)	0 (0)	1 (1.61)	2 (1.46)	0 (0)	2 (1.28)
Patellofemoral pain	-	-	-	-	-	-	1 (1.96)	0 (0)	1 (1.61)	1 (0.73)	0 (0)	1 (0.64)
Psoriatic arthropathy	-	-	-	1 (2.17)	1 (16.7)	2 (3.85)	-	-	-	1 (0.73)	1 (5.26)	2 (1.28)
Rheumatic disorder	-	-	-	0 (0)	1 (16.7)	1 (1.92)	-	-	-	0 (0)	1 (5.26)	1 (0.64)
Rotator cuff syndrome	1 (2.50)	0 (0)	1 (2.38)	1 (2.17)	0 (0)	1 (1.92)	-	-	-	2 (1.46)	0 (0)	2 (1.28)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Sacroiliitis	-	-	-	-	-	-	1 (1.96)	0 (0)	1 (1.61)	1 (0.73)	0 (0)	1 (0.64)
Scoliosis	-	-	-	-	-	-	0 (0)	1 (9.09)	1 (1.61)	0 (0)	1 (5.26)	1 (0.64)
Shoulder deformity	-	-	-	1 (2.17)	0 (0)	1 (1.92)	-	-	-	1 (0.73)	0 (0)	1 (0.64)
Sjogren's syndrome	1 (2.50)	0 (0)	1 (2.38)	-	-	-	-	-	-	1 (0.73)	0 (0)	1 (0.64)
Spinal disorder	-	-	-	-	-	-	1 (1.96)	0 (0)	1 (1.61)	1 (0.73)	0 (0)	1 (0.64)
Spinal osteoarthritis	-	-	-	1 (2.17)	0 (0)	1 (1.92)	-	-	-	1 (0.73)	0 (0)	1 (0.64)
Spinal pain	-	-	-	1 (2.17)	0 (0)	1 (1.92)	-	-	-	1 (0.73)	0 (0)	1 (0.64)
Synovial cyst	2 (5.00)	0 (0)	2 (4.76)	-	-	-	-	-	-	2 (1.46)	0 (0)	2 (1.28)
Systemic lupus erythematosus	-	-	-	0 (0)	2 (33.3)	2 (3.85)	-	-	-	0 (0)	2 (10.5)	2 (1.28)
Tendon calcification	-	-	-	-	-	-	1 (1.96)	0 (0)	1 (1.61)	1 (0.73)	0 (0)	1 (0.64)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1 (0.45)**	**1 (2.56)**	**2 (0.77)**	**0 (0)**	**0 (0)**	**0 (0)**	**3 (0.47)**	**2 (1.60)**	**5 (0.66)**	**4 (0.37)**	**3 (1.53)**	**7 (0.54)**
Basal cell carcinoma	0 (0)	1 (100)	1 (50.0)	-	-	-	0 (0)	1 (50.0)	1 (20.0)	0 (0)	2 (66.7)	2 (28.6)
Benign gastrointestinal neoplasm	-	-	-	-	-	-	1 (33.3)	0 (0)	1 (20.0)	1 (25.0)	0 (0)	1 (14.3)
Haemangioma of skin	1 (100)	0 (0)	1 (50.0)	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (14.3)
Leukaemia	-	-	-	-	-	-	1 (33.3)	0 (0)	1 (20.0)	1 (25.0)	0 (0)	1 (14.3)
Prostate cancer	-	-	-	-	-	-	0 (0)	1 (50.0)	1 (20.0)	0 (0)	1 (33.3)	1 (14.3)
Skin papilloma	-	-	-	-	-	-	1 (33.3)	0 (0)	1 (20.0)	1 (25.0)	0 (0)	1 (14.3)
Nervous system disorders	**5 (2.27)**	**2 (5.13)**	**7 (2.70)**	**14 (5.83)**	**2 (6.25)**	**16 (5.88)**	**34 (5.35)**	**6 (4.80)**	**40 (5.26)**	**53 (4.84)**	**10 (5.10)**	**63 (4.87)**
Amnesia	-	-	-	-	-	-	0 (0)	1 (16.7)	1 (2.50)	0 (0)	1 (10.0)	1 (1.59)
Apraxia	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Balance disorder	-	-	-	2 (14.3)	0 (0)	2 (12.5)	2 (5.88)	0 (0)	2 (5.00)	4 (7.55)	0 (0)	4 (6.35)
Burning sensation	1 (20.0)	0 (0)	1 (14.3)	-	-	-	-	-	-	1 (1.89)	0 (0)	1 (1.59)
Carpal tunnel syndrome	0 (0)	1 (50.0)	1 (14.3)	-	-	-	-	-	-	0 (0)	1 (10.0)	1 (1.59)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Cerebrovascular accident	-	-	-	0 (0)	1 (50.0)	1 (6.25)	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	1 (10.0)	2 (3.17)
Complex regional pain syndrome	-	-	-	1 (7.14)	0 (0)	1 (6.25)	-	-	-	1 (1.89)	0 (0)	1 (1.59)
Disturbance in attention	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Dizziness	-	-	-	1 (7.14)	0 (0)	1 (6.25)	2 (5.88)	0 (0)	2 (5.00)	3 (5.66)	0 (0)	3 (4.76)
Dysesthesia	-	-	-	1 (7.14)	0 (0)	1 (6.25)	2 (5.88)	0 (0)	2 (5.00)	3 (5.66)	0 (0)	3 (4.76)
Dysgeusia	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Dysgraphia	-	-	-	1 (7.14)	0 (0)	1 (6.25)	0	0	0	1 (1.89)	0 (0)	1 (1.59)
Formication	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Headache	2 (40.0)	0 (0)	2 (28.6)	3 (21.4)	0 (0)	3 (18.8)	10 (29.4)	2 (33.3)	12 (30.0)	15 (28.3)	2 (20.0)	17 (27.0)
Hypoaesthesia	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Hypokinesia	-	-	-	1 (7.14)	0 (0)	1 (6.25)	-	-	-	1 (1.89)	0 (0)	1 (1.59)
Intercostal neuralgia	1 (20.0)	1 (50.0)	2 (28.6)	-	-	-	-	-	-	1 (1.89)	1 (10.0)	2 (3.17)
Memory impairment	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Migraine	1 (20.0)	0 (0)	1 (14.3)	1 (7.14)	0 (0)	1 (6.25)	5 (14.7)	0 (0)	5 (12.5)	7 (13.2)	0 (0)	7 (11.1)
Movement disorder	-	-	-	1 (7.14)	0 (0)	1 (6.25)	-	-	-	1 (1.89)	0 (0)	1 (1.59)
Paraesthesia	-	-	-	-	-	-	3 (8.82)	1 (16.7)	4 (10.0)	3 (5.66)	1 (10.0)	4 (6.35)
Paralysis	-	-	-	-	-	-	1 (2.94)	1 (16.7)	2 (5.00)	1 (1.89)	1 (10.0)	2 (3.17)
Sciatica	-	-	-	0 (0)	1 (50.0)	1 (6.25)	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	1 (10.0)	2 (3.17)
Seizure	-	-	-	-	-	-	0 (0)	1 (16.7)	1 (2.50)	0 (0)	1 (10.0)	1 (1.59)
Sensory loss	-	-	-	1 (7.14)	0 (0)	1 (6.25)	-	-	-	1 (1.89)	0 (0)	1 (1.59)
Tremor	-	-	-	-	-	-	1 (2.94)	0 (0)	1 (2.50)	1 (1.89)	0 (0)	1 (1.59)
Visual field defect	-	-	-	1 (7.14)	0 (0)	1 (6.25)	-	-	-	1 (1.89)	0 (0)	1 (1.59)
Product issues	**1 (0.45)**	**0**	**1 (0.39)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.16)**	**0 (0)**	**1 (0.13)**	**2 (0.18)**	**0 (0)**	**2 (0.15)**
Device difficult to use	1 (100)	0 (0)	1 (100)	-	-	-	0	0	0	1 (50.0)	0 (0)	1 (50.0)
Device malfunction	-	-	-	-	-	-	1 (100)	0 (0)	1 (100)	1 (50.0)	0 (0)	1 (50.0)
Psychiatric disorders	**8 (3.64)**	**1 (2.56)**	**9 (3.47)**	**9 (3.75)**	**1 (3.13)**	**10 (3.68)**	**22 (3.46)**	**2 (1.60)**	**24 (3.16)**	**39 (3.29)**	**4 (2.04)**	**43 (3.33)**

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Affective disorder	1 (12.5)	0 (0)	1 (11.1)	-	-	-	-	-	-	1 (2.56)	0 (0)	1 (2.33)
Aggression	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Anxiety	1 (12.5)	0 (0)	1 (11.1)	-	-	-	3 (13.6)	0 (0)	3 (12.5)	4 (10.3)	0 (0)	4 (9.30)
Bipolar disorder	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Decreased interest	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Depressed mood	-	-	-	2 (22.2)	0 (0)	2 (20.0)	-	-	-	2 (5.13)	0 (0)	2 (4.65)
Depression	3 (37.5)	0 (0)	3 (33.3)	-	-	-	5 (22.7)	1 (50.0)	6 (25.0)	8 (20.5)	1 (25.0)	9 (20.9)
Emotional disorder	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Fear of injection	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Insomnia	1 (12.5)	0 (0)	1 (11.1)	2 (22.2)	1 (100)	3 (30.0)	4 (18.2)	0 (0)	4 (16.7)	7 (17.9)	1 (25.0)	8 (18.6)
Middle insomnia	1 (12.5)	0 (0)	1 (11.1)	3 (33.3)	0 (0)	3 (30.0)	1 (4.55)	0 (0)	1 (4.17)	5 (12.8)	0 (0)	5 (11.6)
Nightmare	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Panic attack	0 (0)	1 (100)	1 (11.1)	-	-	-	-	-	-	0 (0)	1 (25.0)	1 (2.33)
Sleep disorder	1 (12.5)	0 (0)	1 (11.1)	2 (22.2)	0 (0)	2 (20.0)	2 (9.09)	0 (0)	2 (8.33)	5 (12.8)	0 (0)	5 (11.6)
Stress	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.17)	1 (2.56)	0 (0)	1 (2.33)
Suicide attempt	-	-	-	-	-	-	0 (0)	1 (50.0)	1 (4.17)	0 (0)	1 (25.0)	1 (2.33)
Renal and urinary disorders	**1 (0.45)**	**0**	**1 (0.39)**	**0 (0)**	**0 (0)**	**0 (0)**	**3 (0.47)**	**2 (1.60)**	**5 (0.66)**	**4 (0.37)**	**2 (1.02)**	**6 (0.46)**
Bladder disorder	-	-	-	-	-	-	1 (33.3)	0 (0)	1 (20.0)	1 (25.0)	0 (0)	1 (16.7)
Pollakiuria	-	-	-	-	-	-	0 (0)	1 (50.0)	1 (20.0)	0 (0)	1 (50.0)	1 (16.7)
Renal disorder	-	-	-	-	-	-	1 (33.3)	0 (0)	1 (20.0)	1 (25.0)	0 (0)	1 (16.7)
Renal failure	-	-	-	-	-	-	0 (0)	1 (50.0)	1 (20.0)	0 (0)	1 (50.0)	1 (16.7)
Renal Pain	1 (100)	0 (0)	1 (100)	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (16.7)
Urinary tract inflammation	-	-	-	-	-	-	1 (33.3)	0 (0)	1 (20.0)	1 (25.0)	0 (0)	1 (16.7)
Reproductive system and breast disorders	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.42)**	**0 (0)**	**1 (0.37)**	**1 (0.16)**	**1 (0.80)**	**2 (0.26)**	**2 (0.18)**	**1 (0.51)**	**3 (0.23)**
Endometriosis	-	-	-	-	-	-	0 (0)	1 (100)	1 (50.0)	0 (0)	1 (100)	1 (33.3)
Menorrhagia	-	-	-	-	-	-	1 (100)	0 (0)	1 (50.0)	1 (50.0)	0 (0)	1 (33.3)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Pelvic pain	-	-	-	1 (100)	0 (0)	1 (100)	-	-	-	1 (50.0)	0 (0)	1 (33.3)
Respiratory, thoracic and mediastinal disorders	**3 (1.36)**	**2 (5.13)**	**5 (1.93)**	**6 (2.50)**	**1 (3.13)**	**7 (2.57)**	**17 (2.68)**	**3 (2.40)**	**20 (2.63)**	**26 (2.37)**	**6 (3.06)**	**32 (2.48)**
Asthma	-	-	-	-	-	-	1 (5.88)	0 (0)	1 (5.00)	1 (3.85)	0 (0)	1 (3.13)
Bronchial obstruction	-	-	-	-	-	-	0 (0)	1 (33.3)	1 (5.00)	0 (0)	1 (16.7)	1 (3.13)
Cough	1 (33.3)	0 (0)	1 (20.0)	2 (33.3)	0 (0)	2 (28.6)	7 (41.2)	0 (0)	7 (35.0)	10 (38.5)	0 (0)	10 (31.3)
Dyspnoea	-	-	-	1 (16.7)	0 (0)	1 (14.3)	3 (17.6)	1 (33.3)	4 (20.0)	4 (15.4)	1 (16.7)	5 (15.6)
Emphysema	0 (0)	1 (50.0)	1 (20.0)	-	-	-	-	-	-	0 (0)	1 (16.7)	1 (3.13)
Epistaxis	-	-	-	2 (33.3)	0 (0)	2 (28.6)	1 (5.88)	0 (0)	1 (5.00)	3 (11.5)	0 (0)	3 (9.38)
Lung disorder	-	-	-	-	-	-	1 (5.88)	0 (0)	1 (5.00)	1 (3.85)	0 (0)	1 (3.13)
Nasal crusting	-	-	-	1 (16.7)	0 (0)	1 (14.3)	-	-	-	1 (3.85)	0 (0)	1 (3.13)
Oropharyngeal pain	1 (33.3)	0 (0)	1 (20.0)	-	-	-	1 (5.88)	0 (0)	1 (5.00)	2 (7.69)	0 (0)	2 (6.25)
Pulmonary fibrosis	1 (33.3)	0 (0)	1 (20.0)	-	-	-	-	-	-	1 (3.85)	0 (0)	1 (3.13)
Respiratory disorder	0 (0)	1 (50.0)	1 (20.0)	-	-	-	2 (11.8)	0 (0)	2 (10.0)	2 (7.69)	1 (16.7)	3 (9.38)
Respiratory failure	-	-	-	0 (0)	1 (100)	1 (14.3)	-	-	-	0 (0)	1 (16.7)	1 (3.13)
Sleep apnoea syndrome	-	-	-	-	-	-	0 (0)	1 (33.3)	1 (5.00)	0 (0)	1 (16.7)	1 (3.13)
Wheezing	-	-	-	-	-	-	1 (5.88)	0 (0)	1 (5.00)	1 (3.85)	0 (0)	1 (3.13)
Skin and subcutaneous tissue disorders	**8 (3.64)**	**0 (0)**	**8 (3.09)**	**15 (6.25)**	**0 (0)**	**15 (5.51)**	**22 (3.46)**	**1 (0.80)**	**23 (3.03)**	**45 (4.11)**	**1 (0.51)**	**46 (3.56)**
Alopecia	1 (12.5)	0 (0)	1 (12.5)	-	-	-	2 (9.09)	0 (0)	2 (8.70)	3 (6.67)	0 (0)	3 (6.52)
Angioedema	1 (12.5)	0 (0)	1 (12.5)	-	-	-	-	-	-	1 (2.22)	0 (0)	1 (2.17)
Blister	-	-	-	-	-	-	2 (9.09)	0 (0)	2 (8.70)	2 (4.44)	0 (0)	2 (4.35)
Dermatitis allergic	1 (12.5)	0 (0)	1 (12.5)	-	-	-	-	-	-	1 (2.22)	0 (0)	1 (2.17)
Diffuse alopecia	1 (12.5)	0 (0)	1 (12.5)	1 (6.67)	0 (0)	1 (6.67)	-	-	-	2 (4.44)	0 (0)	2 (4.35)
Eczema	-	-	-	-	-	-	4 (18.2)	0 (0)	4 (17.4)	4 (8.89)	0 (0)	4 (8.70)
Erythema	-	-	-	-	-	-	2 (9.09)	0 (0)	2 (8.70)	2 (4.44)	0 (0)	2 (4.35)
Hyperkeratosis	-	-	-	1 (6.67)	0 (0)	1 (6.67)	-	-	-	1 (2.22)	0 (0)	1 (2.17)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Ingrowing nail	-	-	-	2 (13.3)	0 (0)	2 (13.3)	-	-	-	2 (4.44)	0 (0)	2 (4.35)
Nail discolouration	-	-	-	1 (6.67)	0 (0)	1 (6.67)	-	-	-	1 (2.22)	0 (0)	1 (2.17)
Nail hypertrophy	-	-	-	1 (6.67)	0 (0)	1 (6.67)	-	-	-	1 (2.22)	0 (0)	1 (2.17)
Night sweats	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.35)	1 (2.22)	0 (0)	1 (2.17)
Onychoclasis	-	-	-	1 (6.67)	0 (0)	1 (6.67)	-	-	-	1 (2.22)	0 (0)	1 (2.17)
Pruritus	2 (25.0)	0 (0)	2 (25.0)	1 (6.67)	0 (0)	1 (6.67)	1 (4.55)	0 (0)	1 (4.35)	4 (8.89)	0 (0)	4 (8.70)
Pruritus generalised	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.35)	1 (2.22)	0 (0)	1 (2.17)
Psoriasis	-	-	-	7 (46.7)	0 (0)	7 (46.7)	4 (18.2)	1 (100)	5 (21.7)	11 (24.4)	1 (100)	12 (26.1)
Rash	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.35)	1 (2.22)	0 (0)	1 (2.17)
Skin disorder	1 (12.5)	0 (0)	1 (12.5)	-	-	-	1 (4.55)	0 (0)	1 (4.35)	2 (4.44)	0 (0)	2 (4.35)
Skin reaction	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.35)	1 (2.22)	0 (0)	1 (2.17)
Skin ulcer	1 (12.5)	0 (0)	1 (12.5)	-	-	-	-	-	-	1 (2.22)	0 (0)	1 (2.17)
Urticaria chronic	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.35)	1 (2.22)	0 (0)	1 (2.17)
Vasculitic rash	-	-	-	-	-	-	1 (4.55)	0 (0)	1 (4.35)	1 (2.22)	0 (0)	1 (2.17)
Social circumstances	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.42)**	**0 (0)**	**1 (0.37)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.09)**	**0 (0)**	**1 (0.08)**
Impaired driving ability	-	-	-	1 (100)	0 (0)	1 (100)	-	-	-	1 (100)	0 (0)	1 (100)
Surgical and medical	**20 (9.09)**	**14 (35.9)**	**34 (13.1)**	**7 (2.92)**	**14 (43.8)**	**21 (7.72)**	**21 (3.31)**	**51 (40.8)**	**72 (9.47)**	**48 (4.38)**	**79 (40.3)**	**127 (9.84)**
Adrenocortical steroid therapy	-	-	-	-	-	-	1 (4.76)	0 (0)	1 (1.39)	1 (2.08)	0 (0)	1 (0.79)
Antibiotic therapy	-	-	-	-	-	-	3 (14.3)	0 (0)	3 (4.17)	3 (6.25)	0 (0)	3 (2.36)
Bladder operation	-	-	-	0 (0)	1 (7.14)	1 (4.76)	-	-	-	0 (0)	1 (1.27)	1 (0.79)
Bunion operation	2 (10.0)	0 (0)	2 (5.88)	-	-	-	-	-	-	2 (4.17)	0 (0)	2 (1.57)
Cataract operation	2 (10.0)	0 (0)	2 (5.88)	1 (14.3)	0 (0)	1 (4.76)	1 (4.76)	1 (1.96)	2 (2.78)	4 (8.33)	1 (1.27)	5 (3.94)
Cholecystectomy	1 (5.00)	0 (0)	1 (2.94)	1 (14.3)	0 (0)	1 (4.76)	-	-	-	2 (4.17)	0 (0)	2 (1.57)
Cyst removal	1 (5.00)	0 (0)	1 (2.94)	-	-	-	-	-	-	1 (2.08)	0 (0)	1 (0.79)
Dental care	-	-	-	-	-	-	4 (19.0)	0 (0)	4 (5.56)	4 (8.33)	0 (0)	4 (3.15)
Epidural injection	-	-	-	0 (0)	1 (7.14)	1 (4.76)	-	-	-	0 (0)	1 (1.27)	1 (0.79)

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Gastrectomy	-	-	-	-	-	-	0 (0)	2 (3.92)	2 (2.78)	0 (0)	2 (2.53)	2 (1.57)
Gastric banding	-	-	-	0 (0)	1 (7.14)	1 (4.76)	-	-	-	0 (0)	1 (1.27)	1 (0.79)
Hip arthroplasty	-	-	-	0 (0)	1 (7.14)	1 (4.76)	-	-	-	0 (0)	1 (1.27)	1 (0.79)
Hip surgery	-	-	-	0 (0)	2 (14.3)	2 (9.52)	-	-	-	0 (0)	2 (2.53)	2 (1.57)
Hospitalization	1 (5.00)	4 (28.6)	5 (14.7)	0 (0)	2 (14.3)	2 (9.52)	0 (0)	36 (70.6)	36 (50.0)	1 (2.08)	42 (53.2)	43 (33.9)
Hysterectomy	-	-	-	-	-	-	1 (4.76)	1 (1.96)	2 (2.78)	1 (2.08)	1 (1.27)	2 (1.57)
Influenza immunisation	1 (5.00)	0 (0)	1 (2.94)	-	-	-	-	-	-	1 (2.08)	0 (0)	1 (0.79)
Injection	1 (5.00)	0 (0)	1 (2.94)	-	-	-	-	-	-	1 (2.08)	0 (0)	1 (0.79)
Intervertebral disc operation	-	-	-	0 (0)	1 (7.14)	1 (4.76)	-	-	-	0 (0)	1 (1.27)	1 (0.79)
Joint arthroplasty	1 (5.00)	0 (0)	1 (2.94)	-	-	-	-	-	-	1 (2.08)	0 (0)	1 (0.79)
Joint injection	5 (25.0)	1 (7.14)	6 (17.6)	-	-	-	1 (4.76)	0 (0)	1 (1.39)	6 (12.5)	1 (1.27)	7 (5.51)
Kinesitherapy	0 (0)	1 (7.14)	1 (2.94)	-	-	-	-	-	-	0 (0)	1 (1.27)	1 (0.79)
Knee arthroplasty	1 (5.00)	1 (7.14)	2 (5.88)	-	-	-	-	-	-	1 (2.08)	1 (1.27)	2 (1.57)
Knee operation	1 (5.00)	1 (7.14)	2 (5.88)	0 (0)	4 (28.6)	4 (19.0)	-	-	-	1 (2.08)	5 (6.33)	6 (4.72)
Limb operation	-	-	-	-	-	-	0 (0)	1 (1.96)	1 (1.39)	0 (0)	1 (1.27)	1 (0.79)
Metabolic surgery	-	-	-	-	-	-	0 (0)	1 (1.96)	1 (1.39)	0 (0)	1 (1.27)	1 (0.79)
Mole excision	-	-	-	-	-	-	1 (4.76)	0 (0)	1 (1.39)	1 (2.08)	0 (0)	1 (0.79)
Muscle operation	0 (0)	1 (7.14)	1 (2.94)	-	-	-	-	-	-	0 (0)	1 (1.27)	1 (0.79)
Papilloma excision	1 (5.00)	0 (0)	1 (2.94)	-	-	-	-	-	-	1 (2.08)	0 (0)	1 (0.79)
Shoulder arthroplasty	0 (0)	3 (21.4)	3 (8.82)	-	-	-	-	-	-	0 (0)	3 (3.80)	3 (2.36)
Shoulder operation	-	-	-	1 (14.3)	0 (0)	1 (4.76)	0 (0)	1 (1.96)	1 (1.39)	1 (2.08)	1 (1.27)	2 (1.57)
Surgery	1 (5.00)	2 (14.3)	3 (8.82)	1 (14.3)	1 (7.14)	2 (9.52)	4 (19.0)	7 (13.7)	11 (15.3)	6 (12.5)	10 (12.7)	16 (12.6)
'Therapy cessation	-	-	-	-	-	-	1 (4.76)	0 (0)	1 (1.39)	1 (2.08)	0 (0)	1 (0.79)
Therapy change	-	-	-	1 (14.3)	0 (0)	1 (4.76)	0 (0)	1 (1.96)	1 (1.39)	1 (2.08)	1 (1.27)	2 (1.57)
Tooth extraction	-	-	-	2 (28.6)	0 (0)	2 (9.52)	4 (19.0)	0 (0)	4 (5.56)	6 (12.5)	0 (0)	6 (4.72)
Varicose vein operation	1 (5.00)	0 (0)	1 (2.94)	-	-	-	-	-	-	1 (2.08)	0 (0)	1 (0.79)
Vascular disorders	**1 (0.45)**	**0**	**1 (0.39)**	**3 (1.25)**	**0 (0)**	**3 (1.10)**	**4 (0.63)**	**0 (0)**	**4 (0.53)**	**8 (0.73)**	**0 (0)**	**8 (0.62)**

SOC PT	RA			PsA			AS			Total		
	Non-SAEs (n=220)	SAEs (n=39)	All AEs (n=259)	Non-SAEs (n=240)	SAEs (n=32)	All AEs (n=272)	Non-SAEs (n=635)	SAEs (n=125)	All AEs (n=760)	Non-SAEs (n=1095)	SAEs (n=196)	All AEs (n=1291)
Bloody discharge	-	-	-	1 (33.3)	0 (0)	1 (33.3)	-	-	-	1 (12.5)	0 (0)	1 (12.5)
Haematoma	-	-	-	1 (33.3)	0 (0)	1 (33.3)	1 (25.0)	0 (0)	1 (25.0)	2 (25.0)	0 (0)	2 (25.0)
Hypertension	1 (100)	0 (0)	1 (100)	1 (33.3)	0 (0)	1 (33.3)	1 (25.0)	0 (0)	1 (25.0)	3 (37.5)	0 (0)	3 (37.5)
Hypotension	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (25.0)	1 (12.5)	0 (0)	1 (12.5)
Peripheral coldness	-	-	-	-	-	-	1 (25.0)	0 (0)	1 (25.0)	1 (12.5)	0 (0)	1 (12.5)

16.2 AEs reported by the physicians

16.2.1 Total number of physician-reported AEs/SAEs

Total population: 1055 AEs were reported by the physician in the total population of which 189 (17.9%) were considered as SAEs. The number of AEs and SAEs reported by disease type and prior biotherapy status of the patient is presented in Table 120 below.
Patients with rheumatoid arthritis: among 220 AEs reported, 43 (19.5%) were considered as SAEs.
Patients with psoriatic arthritis: among the 146 AEs reported, 30 (20.5%) were considered as SAEs.
Patients with ankylosing spondylitis: among 689 reported AEs, 116 (16.8%) were deemed as SAEs.

Table 120 : Total number of physician-reported AEs/SAEs by rheumatic disease

	RA (n=170)		PsA (n=106)		AS (n=478)		Total (n=754)	
	BT-n (n=110)	BT-p (n=59)	BT-n (n=70)	BT-p (n=36)	BT-n (n=291)	BT-p (n=187)	BT-n (n=471)	BT-p (n=282)
Total number of AEs	220		146		689		1055	
	141	79	89	57	362	327	592	463
Total number of SAEs	43 (19.5%)		30 (20.5%)		116 (16.8%)		189 (17.9%)	
	21 (14.9%)	22 (27.8%)	13 (14.6%)	17 (29.8%)	43 (11.9%)	73 (22.3%)	77 (13.0%)	112 (24.2%)

16.2.2 Number of patients with at least one AE/SAE (physician-reported)

Total population: among 754 patients included in the study, 352 (46.7%) experienced at least one AE, of which 215 (45.6%) BT-n and 137 (48.6%) BT-p patients. 79 (10.5%) patients experienced at least one SAE, comprising 41 (8.70%) BT-n and 38 (13.5%) BT-p patients. The number of patients with at least one AE and SAE are reported by disease type and prior biotherapy status in Table 121 below.

Patients with rheumatoid arthritis: among the 170 RA patients included in the study, 79 patients (46.5%) experienced at least one AE, including 52 (47.3%) BT-n and 27 (45.8%) BT-p patients. 19 (11.2%) patients experienced at least one SAE, including 11 (10.0%) BT-n and 8 (13.6%) BT- p patients.

Patients with psoriatic arthritis: of 106 PsA patients in the study, 46 patients (43.4%) experienced at least one AE, including 26 (37.1%) BT-n and 20 (55.5%) BT-p patients. Also, 18 (17.0%) patients experienced at least one SAE [8 BT-n patients (11.4%) vs. 10 BT-p patients (27.8%)].

Patients with ankylosing spondylitis: of the 478 AS patients included in the study, 227 (47.5%) experienced at least one AE, including 137 (47.1%) BT-n and 90 (48.1%) BT-p patients. Also, 42 AS patients (8.79%) had at least one SAE, comprising 22 (7.56%) BT-n and 20 (10.7%) BT-p patients.

Table 121: Number of patients in whom at least 1 AE/SAE was reported by the physician, by rheumatic disease

	RA (n=170) [a]		PsA (n=106)		AS (n=478)		Total (n=754) [a]	
	BT-n (n=110)	BT-p (n=59)	BT-n (n=70)	BT-p (n=36)	BT-n (n=291)	BT-p (n=187)	BT-n (n=471)	BT-p (n=282)
Patients with at least 1 AE [b]	79 (46.5%)		46 (43.4%)		227 (47.5%)		352 (46.7%)	
	52 (47.3%)	27 (45.8%)	26 (37.1%)	20 (55.5%)	137 (47.1%)	90 (48.1%)	215 (45.6%)	137 (48.6%)
Patients with at least 1 SAE [b]	19 (11.2%)		18 (17.0%)		42 (8.79%)		79 (10.5%)	
	11 (10.0%)	8 (13.6%)	8 (11.4%)	10 (27.8%)	22 (7.56%)	20 (10.7%)	41 (8.70%)	38 (13.5%)

a: prior biotherapy data was missing for on RA patient

b: percentage calculated over the total number of patients in total, BT-n and BT-p groups, respectively

16.2.3 Total number of AEs/SAEs and relationship with golimumab

Total population: among the 1055 physician reported AEs, 375 (35.5%) were considered to be related to golimumab and 292 (27.7%) as not related to golimumab. The relationship to golimumab was not known for 388 AEs (36.8%). Among 189 reported SAEs, 61 (32.3%) were considered as related to golimumab, 82 (43.4%) as not related, and the relationship to golimumab was not known for 46 (24.3%) AEs. Data of the link between golimumab treatment and physician reported AEs are presented in Table 122 for each disease group and the total study population.

Patients with rheumatoid arthritis: of 220 AEs reported in RA patients, 70 (31.8%) were considered to be related to golimumab, 72 (32.7%) as not related to golimumab, and 78 (35.5%) were of unknown relationship. Among the 43 reported SAEs in RA patients, 12 (27.9%) were deemed to be related to golimumab, 19 (44.2%) as not related to golimumab and 12 (27.9%) were of unknown relationship.

Patients with psoriatic arthritis: among 146 AEs reported in PsA patients, 45 (30.8%) were deemed to be related to golimumab, 46 (31.5%) as not related to golimumab and the relationship for 55 (37.7%) AEs were unknown. Of the 30 reported SAEs, 6 (20.0 %) were considered to be related to golimumab, 13 (43.3%) as not related and 11 (36.7%) for which the relationship was not known.

Patients with ankylosing spondylitis: 689 AEs were reported in AS patients, of which 260 (37.7%) were considered as related to golimumab, 174 (25.3%) as not related to golimumab and 255 (37.0%) with unknown relationship. Of the 116 SAEs reported in AS patients, 43 (37.1%) were deemed to be related to golimumab, 50 (43.1%) as not related to golimumab and 23 (19.8%) with unknown relationship.

Table 122: Total number of AEs/SAEs and their relationship to golimumab treatment, by rheumatic disease

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)
Total AEs	220	146	689	1055
Total AEs related to golimumab	70 (31.8)	45 (30.8)	260 (37.7)	375 (35.5)
Total AEs not related to golimumab	72 (32.7)	46 (31.5)	174 (25.3)	292 (27.7)
Total AEs for which relationship is not stated	78 (35.5%)	55 (37.7%)	255 (37.0%)	388 (36.8%)
Total SAEs	43	30	116	189
Total SAEs related to golimumab	12 (27.9)	6 (20.0)	43 (37.1%)	61 (32.3)
Total SAEs not related to golimumab	19 (44.2)	13 (43.3)	50 (43.1%)	82 (43.4)
Total SAEs for which relationship is not stated	12 (27.9%)	11 (36.7%)	23 (19.8%)	46 (24.3%)

16.2.4 Number of patients who experienced at least one AE/SAE related to golimumab

Total population: of the 754 patients included in the study, 174 (23.1%) underwent at least one of the 375 AEs reported as related to golimumab, and 29 (3.85%) patients experienced at least one of the 61 SAEs related to golimumab. These data are presented in Table 123 for each disease group and the total study population.

Patients with rheumatoid arthritis: among the 170 RA patients included in the study, 38 patients (22.4%) experienced at least one of the 70 AEs reported as related to golimumab, and 7 (4.12%) patients experienced at least one of the 12 SAEs reported as related to golimumab.

Patients with psoriatic arthritis: of 106 PsA patients included in the study, 26 (24.5%) experienced at least one of the 45 AEs related to golimumab, and 6 (5.66%) patients experienced the 6 SAEs reported as related to golimumab.

Patients with ankylosing spondylitis: among the 478 AS patients included in the study, 110 (23.0%) experienced at least one of the 260 AEs related to golimumab, and 16 (3.34%) experienced at least one of the 43 SAEs reported as related to golimumab.

Table 123 : Patients in whom AEs/SAEs and their relationship to golimumab were reported, by rheumatic disease

	RA (n=170)	PsA (n=106)	AS (n=478)	Total (n=754)
Total number of AEs related to golimumab	70	45	260	375
Total number of patients concerned [a]	38 (22.4%)	26 (24.5%)	110 (23.0%)	174 (23.1%)
Total number of SAEs related to golimumab	12	6	43	61
Total number of patients concerned [a]	7 (4.12%)	6 (5.66%)	16 (3.34%)	29 (3.85%)

a: percentage calculated based on total number of patients in the cohort

16.2.5 Action taken with golimumab

Table 124 : Action taken with golimumab for physician reported AEs/SAEs, by rheumatic disease

	RA (n=167)	PsA (n=101)	AS (n=486)	Total (n=754)
Total number of AEs	207	136	645	988
Golimumab temporary discontinuation	36 (17.4)	31 (22.8)	92 (14.3)	159 (16.1)
Golimumab permanent discontinuation	94 (45.4)	61 (44.9)	314 (48.7)	469 (47.5)
Dosage change	8 (3.86)	8 (5.88)	19 (2.95)	35 (3.54)
Unchanged dosage	65 (31.4)	34 (25.0)	210 (32.6)	309 (31.3)
Unknown	4 (1.93)	2 (1.47)	10 (1.55)	16 (1.62)
Total number of SAEs	38	27	108	173
Golimumab temporary discontinuation	9 (23.7)	10 (37.0)	24 (22.2)	43 (24.9)
Golimumab permanent discontinuation	15 (39.5)	7 (25.9)	62 (57.4)	84 (48.6)
Dosage change	3 (7.89)	2 (7.41)	1 (0.93)	6 (3.47)
Unchanged dosage	11 (28.9)	8 (29.6)	21 (19.4)	40 (23.1)

Total population

Action taken concerning golimumab prescription was provided for 988/1055 AEs (93.6%) and 173/189 SAEs (91.5%). Golimumab dosage remained unchanged following 31.3% of AEs (n=309) and 23.1% of SAEs (n=40).

Almost half the AEs (n=469, 47.5%) led to permanent golimumab discontinuation, with the three most common SOC affiliations being:

- "General disorders and administration site conditions" (n=292, 62.3%), including most commonly "treatment failure (n=116, 39.7%), "drug effect decreased" (n=98, 33.6%), and "condition aggravated" (n=16, 5.48%).
- "Infections and infestations" (n=35, 7.46%), including "bronchitis" (n=5, 14.3%) and "influenza" (n=3, 8.57%).
- "Nervous system disorders" (n=21, 4.48%), including mainly "headache" (n=9, 42.9%), "dizziness" (n=4, 19.0%) and jointly "migraine" and "paraesthesia" (n=2, 9.52% for each).

Similarly, almost half the SAEs led to permanent golimumab discontinuation (n=84, 48.6%), with the three most common SOC affiliations being:

- "General disorders and administration site conditions" (n=33, 39.3%), under which the three most common PTs were jointly "condition aggravated", "drug effect decreased" and "treatment failure (n=8, 24.2%).
- "Injury poisoning and procedural complications" (n=6, 7.14%), including "multiple injuries", "post procedural haemorrhage", "pulmonary contusion", "road traffic accident", "upper limb fracture" and "venous injury".
- Jointly, "Neoplasms benign, malignant and unspecified (incl. cysts and polyps)" and "Nervous system disorders" (n=5, 5.95% for each)

Temporary golimumab discontinuation was reported following 159 AEs (16.1%), for which the three most frequent SOCs were:

- "Infections and infestations" (n=70, 44.0%), including most frequently "bronchitis" (n=13, 18.6%)
- "General disorders and administration site conditions" (n=23, 14.5%), in which most frequently "adverse event" (n=6, 26.1%).

- "Surgical and Medical procedures" (n=17, 10.7%), consisting mainly of minor or local surgeries.

A quarter of SAEs led to temporary golimumab discontinuation (n=43, 24.9%), for which the three most frequent SOCs were:

- "General disorders and administration site conditions" (n=9, 20.9%), including most often "adverse event" and "drug intolerance" (n=2, 22.2%, for each)
- "Infections and infestations" (n=9, 20.9%), including most often "pyelonephritis" (n=3, 33.3%)
- "Surgical and Medical procedures" (n=7, 16.3%)

- **Patients with rheumatoid arthritis**

Action taken with golimumab prescription was provided for 207/220 AEs (94.1%) and 38/43 SAEs (88.4%). Golimumab dosage remained unchanged following 31.4% of AEs (n=65) and 28.9% of SAEs (n=11).

Almost half the AEs (n=94, 45.4%) led to permanent golimumab discontinuation, a majority of which were affiliated with the SOC "General disorders and administration site conditions" (n=64, 68.1%), including most commonly "treatment failure (n=28, 43.8%), "drug effect decreased" (n=18, 28.1%), and "drug intolerance" (n=5, 7.81%).

Additionally, 15 SAEs led to permanent golimumab discontinuation (39.5%), over half belong to the SOC "General disorders and administration site conditions" (n=8, 53.3%), and including mainly "treatment failure" (n=4, 50.0%).

Temporary golimumab discontinuation was reported following 36 AEs (17.4%), most of which belonged to the SOC "Infections and Infestations" (n=14, 38.9%), including 6 patients with "bronchitis" (42.9%), and the SOC "General disorders and administration site conditions" (n=5, 13.9%), including "fatigue" (n=2), and one case each of "adverse event", "influenza like illness" and "treatment failure".

About a quarter of SAEs led to temporary golimumab discontinuation (n=9, 23.7%), a third of which belonged to the SOC "Musculoskeletal and connective tissue disorders" (n=3, 33.3%) and 2 each (22.2%) under "Surgical and Medical procedures" and "Infections and infestations".

- **Patients with psoriatic arthritis**

Action taken regarding golimumab prescription was given for 136/146 AEs (93.2%) and 27/30 SAEs (90.0%). Golimumab dosage remained unchanged for a quarter of the AEs (n=34) and 29.6% of SAEs (n=8).

Most AEs in PsA patients led to permanent golimumab discontinuation (n=61, 44.9%). A large proportion of these AEs were classed under the SOC "General disorders and administration site conditions" (n=43, 70.5%), including predominantly "drug effect decreased" (n=22, 51.2%) and "treatment failure" (n=15, 34.9%).

A quarter of the SAEs led to permanent golimumab discontinuation (n=7, 25.9%), most of which were also under "General disorders and administration site conditions" (n=4, 57.1%), including "drug effect decreased" (n=2), and 1 each of "drug intolerance" and "treatment failure".

Temporary golimumab discontinuation was reported following 31 AEs (22.8%), most belonging to the SOC "Infections and infestations" (n=13, 41.9%) and "surgery and medical procedures" (n=5, 16.1%).

Temporary golimumab discontinuation followed 10 SAEs (37.0%), which came under 7 different SOCs, the most common ones being "General disorders and administration site conditions", "psychiatric disorders" and ""surgery and medical procedures" (n=2, 20.0%, for each).

- **Patients with ankylosing spondylitis**

Action taken regarding golimumab prescription was given for 645/689 AEs (93.6%) and 108/116 SAEs (93.1%). Golimumab dosage remained unchanged following almost a third of the AEs (n=210, 32.6%) and 19.4% of the SAEs (n=21).

Most AEs in AS patients led to permanent golimumab discontinuation (n=314, 48.7%). A large proportion of these AEs were classed under the SOC "General disorders and administration site conditions" (n=185, 58.9%), including mainly "treatment failure" (n=73, 39.5%) "drug effect decreased" (n=58, 31.4%) and "condition aggravated" (n=10, 5.41%). The next most frequent SOC was "infections and infestations" (n=25, 7.96), most often including "urinary tract infection" (n=5, 20.0%), bronchitis (n=3, 12.0%) and "influenza" (n=3, 12.0%).
Likewise, most SAEs led to permanent golimumab discontinuation (n=62, 57.4%). The three most frequent SOCs for these SAEs were:

- "General disorders and administration site conditions" (n=21, 33.9%), comprising mainly of "condition aggravated" (n=6, 28.6%), "drug effect decreased" (n=5, 23.8%) and "treatment failure" (n=3, 14.3%).
- "Injury poisoning and procedural complications" (n=6, 9.68%)
- Jointly, "gastrointestinal disorders" and "nervous system disorders" (n=5, 8.06% for each).

AEs leading to temporary golimumab discontinuation (n=92, 14.3%) belonged predominantly to the SOC "Infections and infestations" (n=43, 46.7%), including most commonly "bronchitis" (n=7, 16.3%), "nasopharyngitis" (n=3, 6.98%) and "urinary tract infection" (n=3, 6.98%). The next most frequent SOC was "General disorders and administration site conditions" (n=14, 15.2%).
SAEs leading to temporary golimumab discontinuation (n=24, 22.2%) mostly came under the SOCs "General disorders and administration site conditions" (n=6, 25.0%) and "Infections and infestations" (n=6, 25.0%).

16.2.6 Death

Two deaths were reported by physicians during the study. One was classed under the SOC "General disorders and administration site conditions", PT, "death", which was reported as not related to golimumab. The second was classed under the SOC "Psychiatric disorders", PT "completed suicide", reported as not related to golimumab (Table 127).

16.2.7 Time to onset of AEs and SAEs

The average time to onset of AEs was of 8.68 months overall, and longest in PsA patients (9.69 months), followed by AS patient (8.69 months) and RA patients (8.01 months). Mean time to onset was higher for BT-n AS patients compared to BT-p AS patients (9.32 vs. 7.97 months, p = .024)

Mean time to onset of SAEs was 8.75 months overall, and was longer for PsA patients (10.5 months) followed by AS and RA patients (9.32 and 6.09 months, respectively). The average time to onset of SAEs was significantly longer in BT-n RA patients compared to BT-p patients (8.65 vs. 3.89 months, p < .001) and also in BT-n PsA patients than BT-p patients (15.4 months vs. 7.67 months, p = .006).

Table 125 : Time to onset of AEs and SAEs since inclusion by rheumatic disease

	RA (n=220) [a]	PsA (n=146) [a]	AS (n=689) [a]	Total (n=1055) [a]
Time to onset of AEs (n)	186	119	592	897
Mean (SD) (Months)	8.01 (6.62)	9.69 (6.91)	8.69 (7.28)	8.68 (7.11)
Median	6.11	8.23	6.48	7.11
Range	0 - 31.4	0 - 28.7	0 - 39.1	0 - 39.1
Time to onset of SAEs (n)	41	27	107	175
Mean (SD) (Months)	6.09 (4.74)	10.5 (7.39)	9.32 (7.31)	8.75 (6.95)
Median	5.38	10.1	7.97	7.97
Range	0 - 20.4	0.46 - 22.8	0 - 24.8	0 - 24.8

a: n = total number of AEs declared by the physician

16.2.8 Physician-reported AE/SAE outcomes

Outcomes for most AEs and SAEs were resolved at the time of reporting (60.8% and 58.1% respectively overall), with no significant difference between the disease groups. The outcomes by disease type are presented in Table 126 below.

Table 126 : Physician-reported AE/SAE outcomes by rheumatic disease

	(RA) (n=220) [a]	(PsA) (n=146) [a]	(AS) (n=689) [a]	Total (n=1055) [a]
AEs outcome				
n	162	110	517	789
Ongoing	55 (34.0)	37 (33.6)	217 (42.0)	309 (39.2)
Resolved	107 (66.0)	73 (66.4)	300 (58.0)	480 (60.8)
SAEs outcome				
n	36	28	103	167
Ongoing	14 (38.9)	10 (35.7)	46 (44.7)	70 (41.9)
Resolved	22 (61.1)	18 (64.3)	57 (55.3)	97 (58.1)

a: n = total number of AEs declared by the physician

16.2.9 Description of non-serious AEs and SAEs related to golimumab by preferred terms and system organ class

16.2.9.1 All physician reported AEs in the total population

All serious and non-serious AEs are presented by system organ class and preferred terms in Table 127, and according to their relationship to golimumab. Only SOCs/PTs with a frequency more than 10% are listed hereafter.

In decreasing order of frequency, all AEs (both serious and non-serious) were affiliated to the following SOCs/PTs in the overall population:

1) *"General disorders and administration site conditions"* (382/1055 AEs; 36.2%)
   - Treatment failure (123/382, 32.2%)
   - Drug effect decreased (107/382, 28.0%)
2) *"Infections and infestations"* (220/1055 AEs; 20.9%)
   - Bronchitis (35/220, 15.9%)
   - Urinary tract infection (26/220, 11.8%)

In decreasing order of frequency, SAEs were affiliated to the following SOCs:

1) *"General disorders and administration site conditions"* (55/189 SAEs; 29.1%)
   - Condition aggravated (14/41, 29.3%)
   - Treatment failure (9/41, 16.4%)
   - Drug effect decreased (8/41, 14.5%)

16.2.9.2 Non-serious AEs (NSAEs) related to golimumab

Overall, 314 NSAEs were identified to be related to golimumab (Table 127), which were most frequently affiliated to the following SOCs:

1) *"General disorders and administration site conditions"* (137/314 AEs; 43.6%)
   - Drug effect decreased (45/137, 32.8%)

- Treatment failure (42/137, 30.7%)
- Jointly, “adverse event” and “drug ineffective” (9/137, 6.57%, for each)

2) *“Infections and infestations”* (81/314 AEs; 25.8%)
   - Bronchitis (10/81, 12.3%)
   - Tonsillitis (8/81, 9.88%)
   - Sinusitis (7/81, 8.64%)

16.2.9.3 SAEs related to golimumab

Overall, 61 SAEs were identified to be related to golimumab (Table 127), which were most frequently affiliated to the following SOCs:

1) *“General disorders and administration site conditions”* (27/61 AEs; 44.3%)
   - Condition aggravated (7/27, 25.9%)
   - Drug effect decreased (7/27, 25.9%)
   - Treatment failure (6/27, 22.2%)
   - Jointly, “adverse event” and “drug ineffective” (, 6.57%, for each)
2) *“Infections and infestations”* (10/61 AEs; 16.4%), including 1 each of “anal abscess”, “bacterial pyelonephritis”, “Escherichia pyelonephritis”, “furuncle”, “lung infection”, “meningitis enteroviral”, “papilloma viral infection”, “pulmonary tuberculosis”, “pyelonephritis” and “sinusitis”.

Table 127 : All non-serious AEs/SAEs by their relationship with golimumab, classified by Preferred Term (PT) and System Organ Class (SOC)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Blood and lymphatic system disorders	**2 (0.64)**	**2 (0.95)**	**2 (0.58)**	**2 (3.58)**	**0 (0)**	**0 (0)**	**8 (0.76)**
Neutropenia	1 (50.0)	0 (0)	1 (50.0)	0 (0)	-	-	2 (25.0)
Immune thrombocytopenic purpura	0 (0)	1 (50.0)	0 (0)	0 (0)	-	-	1 (12.5)
Iron deficiency anaemia	0 (0)	1 (50.0)	0 (0)	0 (0)	-	-	1 (12.5)
Lymphadenopathy	0 (0)	0 (0)	1 (50.0)	0 (0)	-	-	1 (12.5)
Thrombocytopenia	1 (50.0)	0 (0)	0 (0)	2 (100)	-	-	3 (37.5)
Cardiac disorders	**2 (0.64)**	**2 (0.95)**	**0 (0)**	**1 (1.64)**	**3 (3.66)**	**0 (0)**	**8 (0.76)**
Cardiac amyloidosis	0 (0)	0 (0)	-	0 (0)	1 (33.3)	-	1 (12.5)
Extrasystoles	0 (0)	1 (50.0)	-	0 (0)	0 (0)	-	1 (12.5)
Myocardial infarction	0 (0)	0 (0)	-	0 (0)	1 (33.3)	-	1 (12.5)
Palpitations	1 (50.0)	1 (50.0)	-	0 (0)	1 (33.3)	-	3 (37.5)
Pericarditis	0 (0)	0 (0)	-	1 (100)	0 (0)	-	1 (12.5)
Tachycardia	1 (50.0)	0 (0)	-	0 (0)	0 (0)	-	1 (12.5)
Ear and labyrinth disorders	**1 (0.32)**	**0 (0)**	**1 (0.29)**	**0 (0)**	**0 (0)**	**0 (0)**	**2 (0.19)**
Vertigo positional	0 (0)	-	1 (100)	-	-	-	1 (50.0)
Vertigo	1 (100)	-	0 (0)	-	-	-	1 (50.0)
Endocrine disorders	**0 (0)**	**2 (0.95)**	**1 (0.29)**	**0 (0)**	**0 (0)**	**0 (0)**	**3 (0.28)**
Hyperthyroidism	-	1 (50.0)	0 (0)	-	-	-	1 (33.3)
Hypothyroidism	-	1 (50.0)	0 (0)	-	-	-	1 (33.3)
Thyroid mass	-	0 (0)	1 (100)	-	-	-	1 (33.3)
Eye disorders	**1 (0.32)**	**5 (2.38)**	**1 (0.29)**	**0 (0)**	**1 (1.22)**	**2 (4.35)**	**10 (0.95)**
Macular oedema	0 (0)	1 (20.0)	0 (0)	-	0 (0)	0 (0)	1 (10.0)
Periorbital oedema	0 (0)	0 (0)	0 (0)	-	0 (0)	1 (50.0)	1 (10.0)
Retinal detachment	0 (0)	0 (0)	0 (0)	-	1 (100)	0 (0)	1 (10.0)
Scleritis	0 (0)	0 (0)	0 (0)	-	0 (0)	1 (50.0)	1 (10.0)
Uveitis	0 (0)	4 (80.0)	1 (100)	-	0 (0)	0 (0)	5 (50.0)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Vision blurred	1 (100)	0 (0)	0 (0)	-	0 (0)	0 (0)	1 (10.0)
Gastrointestinal disorders	**14 (4.46)**	**20 (9.52)**	**9 (2.63)**	**2 (3.28)**	**4 (4.88)**	**5 (10.9)**	**54 (5.12)**
Abdominal pain	1 (7.14)	3 (15.0)	0 (0)	0 (0)	0 (0)	2 (40.0)	6 (11.1)
Abdominal pain upper	1 (7.14)	2 (10.0)	1 (11.1)	0 (0)	1 (25.0)	0 (0)	5 (9.26)
Anal fistula	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)	0 (0)	1 (1.85)
Aphthous ulcer	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	1 (1.85)
Colitis	0 (0)	1 (5.00)	2 (22.2)	0 (0)	0 (0)	0 (0)	3 (5.56)
Colitis microscopic	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	1 (1.85)
Colitis ulcerative	0 (0)	0 (0)	2 (22.2)	0 (0)	1 (25.0)	0 (0)	3 (5.56)
Constipation	0 (0)	1 (5.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Dental caries	0 (0)	1 (5.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Diarrhoea	4 (28.6)	3 (15.0)	0 (0)	0 (0)	1 (25.0)	1 (20.0)	9 (16.7)
Diarrhoea haemorrhagic	0 (0)	1 (5.00)	0 (0)	0 (0)	1 (25.0)	0 (0)	2 (3.70)
Enterocolitis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	1 (1.85)
Gastric mucosal lesion	0 (0)	1 (5.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Gastrointestinal disorder	2 (14.3)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	3 (5.56)
Gastrooesophageal reflux disease	0 (0)	2 (10.0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (3.70)
Haemorrhoids	0 (0)	1 (5.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Hiatus hernia	0 (0)	1 (5.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Large intestine polyp	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	1 (1.85)
Mouth ulceration	1 (7.14)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Nausea	3 (21.4)	0 (0)	0 (0)	1 (50.0)	0 (0)	0 (0)	4 (7.41)
Pancreatic disorder	1 (7.14)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Subileus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	1 (1.85)
Toothache	0 (0)	1 (5.00)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.85)
Vomiting	1 (7.14)	2 (10.0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (5.56)
Gastrointestinal disorders / general disorders and administration site conditions	**0 (0)**	**1 (0.48)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.09)**

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Diarrhoea / adverse drug reaction	0 (.)	1 (100)	-	-	-	-	1 (100)
General disorders and administration site conditions	**137 (43.6)**	**40 (19.1)**	**150 (43.9)**	**27 (44.3)**	**14 (17.1)**	**14 (30.4)**	**382 (36.2)**
Adverse drug reaction	0 (0)	0 (0)	0 (0)	1 (3.70)	0 (0)	0 (0)	1 (0.26)
Adverse event	9 (6.57)	8 (20.0)	5 (3.33)	0 (0)	1 (7.14)	3 (21.4)	26 (6.81)
Asthenia	4 (2.92)	3 (7.50)	4 (2.67)	0 (0)	1 (7.14)	1 (7.14)	13 (3.40)
Chest pain	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.14)	0 (0)	1 (0.26)
Condition aggravated	5 (3.65)	6 (15.0)	3 (2.00)	7 (25.9)	5 (35.7)	2 (14.3)	28 (7.33)
Death	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.14)	0 (0)	1 (0.26)
Discomfort	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	0 (0)	1 (0.26)
Disease recurrence	1 (0.73)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.26)
Drug effect decreased	45 (32.8)	9 (22.5)	45 (30.0)	7 (25.9)	1 (7.14)	0 (0)	107 (28.0)
Drug ineffective	9 (6.57)	0 (0)	5 (3.33)	0 (0)	0 (0)	0 (0)	14 (3.66)
Drug intolerance	8 (5.84)	2 (5.00)	5 (3.33)	1 (3.70)	0 (0)	3 (21.4)	19 (4.97)
Face oedema	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	1 (7.14)	2 (0.52)
Fatigue	2 (1.46)	1 (2.50)	4 (2.67)	0 (0)	0 (0)	0 (0)	7 (1.83)
Feeling abnormal	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	0 (0)	1 (0.26)
Gait disturbance	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.14)	0 (0)	1 (0.26)
General physical health deterioration	0 (0)	0 (0)	0 (0)	1 (3.70)	0 (0)	0 (0)	1 (0.26)
Hyperthermia	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	0 (0)	1 (0.26)
Induration	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	0 (0)	1 (0.26)
Influenza like illness	2 (1.46)	2 (5.00)	1 (0.67)	0 (0)	0 (0)	0 (0)	5 (1.31)
Injection site pain	1 (0.73)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.26)
Injection site rash	0 (0)	0 (0)	0 (0)	1 (3.70)	0 (0)	0 (0)	1 (0.26)
Injection site reaction	2 (1.46)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.52)
Injection site scar	1 (0.73)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.26)
Malaise	0 (0)	0 (0)	1 (0.67)	0 (0)	1 (7.14)	0 (0)	2 (0.52)
Oedema peripheral	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	1 (7.14)	2 (0.52)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Pain	0 (0)	1 (2.50)	0 (0)	0 (0)	1 (7.14)	0 (0)	2 (0.52)
Paradoxical drug reaction	1 (0.73)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.26)
Peripheral swelling	0 (0)	0 (0)	1 (0.67)	0 (0)	0 (0)	0 (0)	1 (0.26)
Pyrexia	0 (0)	1 (2.50)	2 (1.33)	1 (3.70)	0 (0)	0 (0)	4 (1.05)
Similar reaction on previous exposure to drug	5 (3.65)	0 (0)	2 (1.33)	2 (7.41)	0 (0)	1 (7.14)	10 (2.62)
Treatment failure	42 (30.7)	6 (15.0)	66 (44.0)	6 (22.2)	1 (7.14)	2 (14.3)	123 (32.2)
Unevaluable event	0 (0)	1 (2.50)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.26)
Hepatobiliary disorders	**2 (0.64)**	**1 (0.48)**	**2 (0.58)**	**0 (0)**	**0 (0)**	**5 (10.9)**	**10 (0.95)**
Cholangitis	0 (0)	0 (0)	0 (0)	-	-	2 (40.0)	2 (20.0)
Cholecystitis acute	0 (0)	0 (0)	0 (0)	-	-	2 (40.0)	2 (20.0)
Cholelithiasis	0 (0)	0 (0)	1 (50.0)	-	-	0 (0)	1 (10.0)
Cholestasis	1 (50.0)	0 (0)	0 (0)	-	-	0 (0)	1 (10.0)
Hepatocellular injury	1 (50.0)	1 (100)	1 (50.0)	-	-	1 (20.0)	4 (40.0)
Immune system disorders	**1 (0.32)**	**2 (0.95)**	**0 (0)**	**0 (0)**	**1 (1.22)**	**0 (0)**	**4 (0.38)**
Hypersensitivity	0 (0)	1 (50.0)	-	-	0 (0)	-	1 (25.0)
Drug hypersensitivity	1 (100)	1 (50.0)	-	-	1 (100)	-	3 (75.0)
Infections and infestations	**81 (25.8)**	**60 (28.6)**	**63 (18.4)**	**10 (16.4)**	**2 (2.44)**	**4 (8.70)**	**220 (20.9)**
Anal abscess	0 (0)	0 (0)	1 (1.59)	1 (10.0)	0 (0)	0 (0)	2 (0.91)
Bacterial pyelonephritis	1 (1.23)	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	2 (0.91)
Bartholin's abscess	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Bronchitis	10 (12.3)	13 (21.7)	12 (19.0)	0 (0)	0 (0)	0 (0)	35 (15.9)
Bronchitis bacterial	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Bursitis infective staphylococcal	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)	1 (0.45)
Conjunctivitis	1 (1.23)	2 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.36)
Cystitis	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Cystitis escherichia	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Dermatophytosis	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Device related infection	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Ear infection	6 (7.41)	1 (1.67)	1 (1.59)	0 (0)	0 (0)	0 (0)	8 (3.64)
Enteritis infectious	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Erysipelas	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Erythema migrans	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Escherichia pyelonephritis	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	1 (0.45)
Fungal skin infection	3 (3.70)	0 (0)	2 (3.17)	0 (0)	0 (0)	0 (0)	5 (2.27)
Furuncle	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	1 (0.45)
Gastroenteritis	0 (0)	2 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.91)
Gastroenteritis viral	1 (1.23)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.91)
Gastrointestinal candidiasis	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Helicobacter infection	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Herpes zoster	4 (4.94)	2 (3.33)	1 (1.59)	0 (0)	0 (0)	0 (0)	7 (3.18)
Infected bite	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Infection	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Influenza	2 (2.47)	1 (1.67)	4 (6.35)	0 (0)	0 (0)	0 (0)	7 (3.18)
Laryngitis	1 (1.23)	1 (1.67)	1 (1.59)	0 (0)	0 (0)	0 (0)	3 (1.36)
Localised infection	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Lung infection	0 (0)	1 (1.67)	1 (1.59)	1 (10.0)	0 (0)	0 (0)	3 (1.36)
Meningitis enteroviral	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	1 (0.45)
Nasopharyngitis	3 (3.70)	3 (5.00)	4 (6.35)	0 (0)	0 (0)	0 (0)	10 (4.55)
Omphalitis	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Oral fungal infection	1 (1.23)	2 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.36)
Oral herpes	2 (2.47)	1 (1.67)	1 (1.59)	0 (0)	0 (0)	0 (0)	4 (1.82)
Papilloma viral infection	1 (1.23)	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	2 (0.91)
Paronychia	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Periodontitis	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Peritonitis	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	1 (25.0)	2 (0.91)
Pharyngitis	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Pneumonia	0 (0)	2 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.91)
Post procedural infection	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Pulmonary tuberculosis	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	1 (0.45)
Pyelonephritis	0 (0)	0 (0)	1 (1.59)	1 (10.0)	0 (0)	3 (75.0)	5 (2.27)
Rash pustular	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Respiratory tract infection	2 (2.47)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.91)
Rhinitis	1 (1.23)	1 (1.67)	2 (3.17)	0 (0)	0 (0)	0 (0)	4 (1.82)
Sinusitis	7 (8.64)	3 (5.00)	2 (3.17)	1 (10.0)	0 (0)	0 (0)	13 (5.91)
Staphylococcal infection	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Subcutaneous abscess	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Superinfection	0 (0)	1 (1.67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Tinea infection	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Tonsillitis	8 (9.88)	1 (1.67)	6 (9.52)	0 (0)	0 (0)	0 (0)	15 (6.82)
Tooth abscess	1 (1.23)	2 (3.33)	1 (1.59)	0 (0)	0 (0)	0 (0)	4 (1.82)
Tooth infection	1 (1.23)	2 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.36)
Tracheitis	0 (0)	1 (1.67)	1 (1.59)	0 (0)	0 (0)	0 (0)	2 (0.91)
Tracheobronchitis	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Upper respiratory tract infection	5 (6.17)	0 (0)	2 (3.17)	0 (0)	0 (0)	0 (0)	7 (3.18)
Urinary tract infection	5 (6.17)	11 (18.3)	10 (15.9)	0 (0)	0 (0)	0 (0)	26 (11.8)
Viral infection	3 (3.70)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1.36)
Viral pharyngitis	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Viral upper respiratory tract infection	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Vulvovaginal candidiasis	1 (1.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.45)
Vulvovaginal mycotic infection	0 (0)	0 (0)	1 (1.59)	0 (0)	0 (0)	0 (0)	1 (0.45)
Injury, poisoning and procedural complications	**8 (2.55)**	**11 (5.24)**	**45 (13.2)**	**0 (0)**	**7 (8.54)**	**1 (2.17)**	**72 (6.82)**
Animal scratch	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Arthropod bite	0 (0)	0 (0)	1 (2.22)	-	1 (14.3)	0 (0)	2 (2.78)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Bone fissure	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Fall	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Foot fracture	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Fracture	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Humerus fracture	0 (0)	2 (18.2)	0 (0)	-	0 (0)	0 (0)	2 (2.78)
Inappropriate schedule of drug administration	0 (0)	0 (0)	9 (20.0)	-	0 (0)	0 (0)	9 (12.5)
Incorrect dose administered	0 (0)	0 (0)	1 (2.22)	-	0 (0)	0 (0)	1 (1.39)
Multiple injuries	0 (0)	0 (0)	0 (0)	-	1 (14.3)	0 (0)	1 (1.39)
Muscle strain	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Off label use	8 (100)	1 (9.09)	31 (68.9)	-	0 (0)	1 (100)	41 (56.9)
Post procedural haemorrhage	0 (0)	0 (0)	0 (0)	-	1 (14.3)	0 (0)	1 (1.39)
Product use issue	0 (0)	0 (0)	3 (6.67)	-	0 (0)	0 (0)	3 (4.17)
Pulmonary contusion	0 (0)	0 (0)	0 (0)	-	1 (14.3)	0 (0)	1 (1.39)
Rib fracture	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Road traffic accident	0 (0)	0 (0)	0 (0)	-	1 (14.3)	0 (0)	1 (1.39)
Tooth avulsion	0 (0)	1 (9.09)	0 (0)	-	0 (0)	0 (0)	1 (1.39)
Upper limb fracture	0 (0)	0 (0)	0 (0)	-	1 (14.3)	0 (0)	1 (1.39)
Venous injury	0 (0)	0 (0)	0 (0)	-	1 (14.3)	0 (0)	1 (1.39)
Investigations	**4 (1.27)**	**2 (0.95)**	**5 (1.46)**	**1 (1.64)**	**1 (1.22)**	**0 (0)**	**13 (1.23)**
Alanine aminotransferase increased	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	-	1 (7.69)
Arthroscopy	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	-	1 (7.69)
Aspartate aminotransferase increased	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	-	1 (7.69)
Blood bilirubin increased	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	-	1 (7.69)
Weight decreased	0 (0)	2 (100)	1 (20.0)	1 (100)	0 (0)	-	4 (30.8)
Weight increased	1 (25.0)	0 (0)	4 (80.0)	0 (0)	0 (0)	-	5 (38.5)
Metabolism and nutrition disorders	**1 (0.32)**	**5 (2.38)**	**0 (0)**	**0 (0)**	**1 (1.22)**	**0 (0)**	**7 (0.66)**
Cell death	0 (0)	1 (20.0)	-	-	0 (0)	-	1 (14.3)
Decreased appetite	1 (100)	2 (40.0)	-	-	0 (0)	-	3 (42.9)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Diabetes mellitus inadequate control	0 (0)	1 (20.0)	-	-	1 (100)	-	2 (28.6)
Hypoglycaemia	0 (0)	1 (20.0)	-	-	0 (0)	-	1 (14.3)
Malnutrition							
Musculoskeletal and connective tissue disorders	**2 (0.64)**	**11 (5.24)**	**4 (1.17)**	**1 (1.64)**	**15 (18.3)**	**2 (4.35)**	**35 (3.32)**
Ankylosing spondylitis	1 (50.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Arthralgia	0 (0)	1 (9.09)	0 (0)	1 (100)	2 (13.3)	0 (0)	4 (11.4)
Arthritis	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)
Arthropathy	0 (0)	0 (0)	0 (0)	0 (0)	2 (13.3)	0 (0)	2 (5.71)
Back pain	0 (0)	0 (0)	0 (0)	0 (0)	3 (20.0)	0 (0)	3 (8.57)
Bone fistula	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	1 (2.86)
Bone loss	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Interspinous osteoarthritis	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)
Joint effusion	0 (0)	2 (18.2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5.71)
Joint swelling	0 (0)	1 (9.09)	1 (25.0)	0 (0)	0 (0)	0 (0)	2 (5.71)
Muscle contracture	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Muscular weakness	1 (50.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Musculoskeletal chest pain	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)
Musculoskeletal pain	0 (0)	1 (9.09)	1 (25.0)	0 (0)	0 (0)	0 (0)	2 (5.71)
Osteoarthritis	0 (0)	1 (9.09)	0 (0)	0 (0)	1 (6.67)	0 (0)	2 (5.71)
Pain in extremity	0 (0)	1 (9.09)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Periarthritis	0 (0)	1 (9.09)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Rheumatic disorder	0 (0)	1 (9.09)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Rheumatoid arthritis	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)
Rheumatoid nodule	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)
Rotator cuff syndrome	0 (0)	1 (9.09)	0 (0)	0 (0)	0 (0)	1 (50.0)	2 (5.71)
Spinal column stenosis	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)
Spinal osteoarthritis	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.67)	0 (0)	1 (2.86)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Synovial cyst	0 (0)	1 (9.09)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.86)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0 (0)**	**2 (0.95)**	**1 (0.29)**	**0 (0)**	**5 (6.10)**	**3 (6.52)**	**11 (1.04)**
Adenocarcinoma of colon	0 (.)	0 (0)	0 (0)	-	1 (20.0)	0 (0)	1 (9.09)
Basal cell carcinoma	0 (.)	0 (0)	1 (100)	-	0 (0)	1 (33.3)	2 (18.2)
Chronic lymphocytic leukaemia	0 (.)	0 (0)	0 (0)	-	1 (20.0)	0 (0)	1 (9.09)
Fibroma	0 (.)	1 (50.0)	0 (0)	-	0 (0)	0 (0)	1 (9.09)
Invasive ductal breast carcinoma	0 (.)	0 (0)	0 (0)	-	1 (20.0)	1 (33.3)	2 (18.2)
Kidney angiomyolipoma	0 (.)	0 (0)	0 (0)	-	1 (20.0)	0 (0)	1 (9.09)
Lacrimal duct neoplasm	0 (.)	1 (50.0)	0 (0)	-	0 (0)	0 (0)	1 (9.09)
Pancreatic carcinoma	0 (.)	0 (0)	0 (0)	-	0 (0)	1 (33.3)	1 (9.09)
Prostate cancer	0 (.)	0 (0)	0 (0)	-	1 (20.0)	0 (0)	1 (9.09)
Nervous system disorders	**16 (5.10)**	**4 (1.90)**	**10 (2.92)**	**4 (6.56)**	**6 (7.32)**	**1 (2.17)**	**41 (3.89)**
Balance disorder	1 (6.25)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	2 (4.88)
Brain lesion	0 (0)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	1 (2.44)
Cerebrovascular accident	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.7)	0 (0)	1 (2.44)
Dizziness	4 (25.0)	0 (0)	1 (10.0)	0 (0)	0 (0)	0 (0)	5 (12.2)
Dysgeusia	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.44)
Headache	9 (56.3)	2 (50.0)	3 (30.0)	2 (50.0)	1 (16.7)	0 (0)	17 (41.5)
Hyperaesthesia	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	0 (0)	1 (2.44)
Ischaemic stroke	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.7)	0 (0)	1 (2.44)
Loss of consciousness	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.7)	0 (0)	1 (2.44)
Migraine	0 (0)	1 (25.0)	2 (20.0)	1 (25.0)	0 (0)	0 (0)	4 (9.76)
Paraesthesia	1 (6.25)	0 (0)	2 (20.0)	0 (0)	0 (0)	0 (0)	3 (7.32)
Paralysis	0 (0)	0 (0)	1 (10.0)	0 (0)	0 (0)	0 (0)	1 (2.44)
Restless legs syndrome	1 (6.25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.44)
Sciatica	0 (0)	0 (0)	0 (0)	0 (0)	2 (33.3)	0 (0)	2 (4.88)
Nervous system disorders / respiratory, thoracic and mediastinal disorders	**0 (0)**	**0 (0)**	**1 (0.29)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.09)**

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Headache / nasal obstruction	-	-	1 (100)	-	-	-	1 (100)
Nervous system disorders / vascular disorders	**0 (0)**	**0 (0)**	**0 (0)**	**2 (3.28)**	**0 (0)**	**0 (0)**	**2 (0.19)**
Headache / hypertension	-	-	-	1 (50.0)	-	-	1 (50.0)
Hypertension	-	-	-	1 (50.0)	-	-	1 (50.0)
Plasms benign, malignant and unspecified (incl. cysts and polyps)	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (2.17)**	**1 (0.09)**
Glioblastoma	-	-	-	-	-	1 (100)	1 (100)
Pregnancy, puerperium and perinatal conditions	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (1.22)**	**0 (0)**	**1 (0.09)**
Ectopic pregnancy	-	-	-	-	1 (100)	-	1 (100)
Psychiatric disorders	**8 (2.55)**	**4 (1.90)**	**5 (1.46)**	**1 (1.64)**	**2 (2.44)**	**2 (4.35)**	**22 (2.09)**
Affective disorder	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	1 (4.55)
Agitation	1 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.55)
Anxiety	1 (12.5)	2 (50.0)	0 (0)	0 (0)	0 (0)	1 (50.0)	4 (18.2)
Completed suicide	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)	1 (4.55)
Depersonalisation/derealisation disorder	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	1 (4.55)
Depression	2 (25.0)	1 (25.0)	0 (0)	0 (0)	1 (50.0)	0 (0)	4 (18.2)
Depression suicidal	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (4.55)
Insomnia	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.55)
Irritability	2 (25.0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	3 (13.6)
Mental disorder	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	1 (4.55)
Middle insomnia	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	1 (4.55)
Morbid thoughts	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	1 (4.55)
Sleep disorder	2 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9.09)
Psychiatric disorders	**0 (0)**	**0 (0)**	**1 (0.29)**	**0 (0)**	**0 (0)**	**0 (0)**	**1 (0.09)**
Insomnia / depression	-	-	1 (100)	-	-	-	1 (100)
Renal and urinary disorders	**0 (0)**	**2 (0.95)**	**0 (0)**	**0 (0)**	**4 (4.88)**	**0 (0)**	**6 (0.57)**
Acute kidney injury	-	0 (0)	-	-	1 (25.0)	-	1 (16.7)
Glomerulonephropathy	-	0 (0)	-	-	1 (25.0)	-	1 (16.7)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Nephropathy	-	0 (0)	-	-	1 (25.0)	-	1 (16.7)
Renal colic	-	2 (100)	-	-	0 (0)	-	2 (33.3)
Renal failure	-	0 (0)	-	-	1 (25.0)	-	1 (16.7)
Reproductive system and breast disorders	**4 (1.27)**	**1 (0.48)**	**4 (1.17)**	**1 (1.64)**	**0 (0)**	**0 (0)**	**10 (0.95)**
Bartholinitis	0 (0)	0 (0)	1 (25.0)	0 (0)	-	-	1 (10.0)
Breast pain	0 (0)	1 (100)	0 (0)	0 (0)	-	-	1 (10.0)
Cervical dysplasia	1 (25.0)	0 (0)	0 (0)	1 (100)	-	-	2 (20.0)
Erectile dysfunction	0 (0)	0 (0)	2 (50.0)	0 (0)	-	-	2 (20.0)
Metrorrhagia	1 (25.0)	0 (0)	0 (0)	0 (0)	-	-	1 (10.0)
Ovarian cyst	0 (0)	0 (0)	1 (25.0)	0 (0)	-	-	1 (10.0)
Vaginal ulceration	1 (25.0)	0 (0)	0 (0)	0 (0)	-	-	1 (10.0)
Vulvovaginal pruritus	1 (25.0)	0 (0)	0 (0)	0 (0)	-	-	1 (10.0)
Respiratory, thoracic and mediastinal disorders	**4 (1.27)**	**3 (1.43)**	**12 (3.51)**	**2 (3.28)**	**5 (6.10)**	**0 (0)**	**26 (2.46)**
Asthma	0 (0)	0 (0)	1 (8.33)	1 (50.0)	0 (0)	-	2 (7.69)
Bronchopneumopathy	1 (25.0)	0 (0)	1 (8.33)	0 (0)	0 (0)	-	2 (7.69)
Cough	0 (0)	1 (33.3)	1 (8.33)	1 (50.0)	0 (0)	-	3 (11.5)
Dyspnoea	3 (75.0)	0 (0)	2 (16.7)	0 (0)	1 (20.0)	-	6 (23.1)
Dyspnoea at rest	0 (0)	0 (0)	1 (8.33)	0 (0)	0 (0)	-	1 (3.85)
Dyspnoea exertional	0 (0)	0 (0)	2 (16.7)	0 (0)	0 (0)	-	2 (7.69)
Eosinophilic rhinitis	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	-	1 (3.85)
Epistaxis	0 (0)	1 (33.3)	3 (25.0)	0 (0)	0 (0)	-	4 (15.4)
Nasal obstruction	0 (0)	0 (0)	1 (8.33)	0 (0)	0 (0)	-	1 (3.85)
Pneumothorax	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	-	1 (3.85)
Productive cough	0 (0)	0 (0)	0 (0)	0 (0)	2 (40.0)	-	2 (7.69)
Respiratory distress	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	-	1 (3.85)
Skin and subcutaneous tissue disorders	**16 (5.10)**	**17 (8.10)**	**19 (5.56)**	**5 (8.20)**	**0 (0)**	**3 (6.52)**	**60 (5.69)**
Acne	0 (0)	0 (0)	2 (10.5)	0 (0)	-	0 (0)	2 (3.33)
Alopecia	1 (6.25)	2 (11.8)	2 (10.5)	0 (0)	-	1 (33.3)	6 (10.0)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Diffuse alopecia	0 (0)	1 (5.88)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Eczema	1 (6.25)	1 (5.88)	1 (5.26)	0 (0)	-	0 (0)	3 (5.00)
Erythema	0 (0)	2 (11.8)	0 (0)	0 (0)	-	0 (0)	2 (3.33)
Erythema annulare	0 (0)	1 (5.88)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Erythrodermic psoriasis	0 (0)	0 (0)	1 (5.26)	0 (0)	-	0 (0)	1 (1.67)
Hidradenitis	0 (0)	1 (5.88)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Hyperhidrosis	0 (0)	0 (0)	2 (10.5)	0 (0)	-	0 (0)	2 (3.33)
Ingrowing nail	0 (0)	1 (5.88)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Intertrigo	0 (0)	0 (0)	1 (5.26)	0 (0)	-	0 (0)	1 (1.67)
Nail disorder	1 (6.25)	0 (0)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Nail psoriasis	0 (0)	0 (0)	1 (5.26)	0 (0)	-	0 (0)	1 (1.67)
Parapsoriasis	1 (6.25)	0 (0)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Peau d'orange	1 (6.25)	0 (0)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Pruritus	2 (12.5)	1 (5.88)	0 (0)	0 (0)	-	0 (0)	3 (5.00)
Psoriasis	6 (37.5)	1 (5.88)	2 (10.5)	4 (80.0)	-	2 (66.7)	15 (25.0)
Pustular psoriasis	1 (6.25)	1 (5.88)	1 (5.26)	0 (0)	-	0 (0)	3 (5.00)
Rash	0 (0)	3 (17.6)	1 (5.26)	1 (20.0)	-	0 (0)	5 (8.33)
Rash pruritic	1 (6.25)	0 (0)	1 (5.26)	0 (0)	-	0 (0)	2 (3.33)
Skin disorder	0 (0)	0 (0)	1 (5.26)	0 (0)	-	0 (0)	1 (1.67)
Skin fissures	0 (0)	1 (5.88)	0 (0)	0 (0)	-	0 (0)	1 (1.67)
Skin lesion	0 (0)	0 (0)	1 (5.26)	0 (0)	-	0 (0)	1 (1.67)
Urticaria	1 (6.25)	1 (5.88)	2 (10.5)	0 (0)	-	0 (0)	4 (6.67)
Social circumstances	**1 (0.32)**	**0 (0)**	**1 (0.29)**	**0 (0)**	**0 (0)**	**0 (0)**	**2 (0.19)**
Impaired work ability	0 (0)	-	1 (100)	-	-	-	1 (50.0)
Treatment noncompliance	1 (100)	-	0 (0)	-	-	-	1 (50.0)
Surgical and medical procedures	**3 (0.96)**	**12 (5.71)**	**1 (0.29)**	**1 (1.64)**	**10 (12.2)**	**3 (6.52)**	**30 (2.84)**
Antibiotic therapy	2 (66.7)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	3 (10.0)
Carpal tunnel decompression	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)

SOC PT	Non-Serious AEs			Serious AEs			Total
	Related (n=314)	Not related (n=210)	Not stated (n=342)	Related (n=61)	Not related (n=82)	Not stated (n=46)	Total (n=1055)
Cervical conisation	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (3.33)
Cholecystectomy	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Cyst removal	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Foot operation	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Gastrectomy	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Gastric banding	0 (0)	1 (8.33)	0 (0)	0 (0)	1 (10.0)	0 (0)	2 (6.67)
Hip arthroplasty	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	1 (33.3)	2 (6.67)
Infusion	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Intervertebral disc operation	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Knee arthroplasty	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Metabolic surgery	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Middle ear operation	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Osteotomy	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Pilonidal sinus repair	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Rotator cuff repair	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Salpingectomy	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Shoulder arthroplasty	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Shoulder operation	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)	1 (3.33)
Suture insertion	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Tooth extraction	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Umbilical hernia repair	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)	1 (3.33)
Uterine polypectomy	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)	1 (3.33)
Varicose vein operation	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Wisdom teeth removal	0 (0)	1 (8.33)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.33)
Vascular disorders	**4 (1.27)**	**1 (0.48)**	**4 (1.17)**	**1 (1.64)**	**0 (0)**	**0 (0)**	**10 (0.95)**
Hot flush	3 (75.0)	0 (0)	0 (0)	0 (0)	-	-	3 (30.0)
Hypertension	1 (25.0)	0 (0)	4 (100)	1 (100)	-	-	6 (60.0)
Raynaud's phenomenon	0 (0)	1 (100)	0 (0)	0 (0)	-	-	1 (10.0)

17 DISCUSSION

17.1 Key results

Study population

Between 15/01/2015 and 29/03/2016, 770 patients were enrolled in the study. Representativeness of the patients included in the study was assessed by comparison with the eligible patients not included in the study (section 13.2): no differences were observed between included and non-included patients, thus indicating minimal selection bias.

Of 770 patients, 754 were included in the descriptive analysis of baseline characteristics. The reasons for non-inclusion were “patient did not take the treatment” (n=12), change of rheumatic disease during the study (n=1), lack of clinical evaluation at inclusion (n=1) and invalid date of birth (n=1).

Baseline description of the entire cohort

Patient characteristics (section 13.5.1 to 13.5.4)

The mean age of the study population was 46.1 years and the majority were female (60.6%). Most patients had a normal BMI (43.5%), 32.7% were overweight and 19.9% were obese. Most patients (58.7%) were full-time or part-time employees, 14.6% were retired and 10.3% reported as being unable to work.

At baseline, 37.4% of the study patients were severely ill, presenting at least 3 co-morbidities or risk factors at baseline, in addition to rheumatic disease. In particular, 51.9% of PsA patients, had ≥ 3 co-morbidities, compared to 34.7% of RA and 35.1% of AS patients.

Most patients (85.3%) had at least comorbidity, in addition to rheumatic disease, and almost half had already undergone a surgical procedure (51.2%). Psoriasis was one of the most prevalent comorbidities in the total cohort (30.6%), and the bulk of affected patients were found in the PsA cohort (92.2%), compared to 23.4% of AS patients and 7.53% of RA patients. Other common comorbidities reported in the total cohort were hypertension (20.6%), uveitis (15.0%), depressive disorder (12.0%) and thyroid disease (10.3%). Tobacco consumption was reported in 47.5% of the study population.

Most RA patients had 2 comorbidities (28.4%). The two most common ones were hypertension (29.3%) and thyroid disease (18.1%). Tobacco consumption was reported in 47.7% of RA patients.

Most PsA patients had 3 comorbidities (31.1%) The two most common comorbidities were psoriasis (92.2%) and hypertension (24.0%), the first being the most evident phenotype of the PsA disease. Tobacco consumption was reported in 29.5% of PsA patients.

Most AS patients suffered from 1 comorbidity (24.3%). Psoriasis, uveitis and IBD are known extra-articular manifestations associated with AS, and they were found in 23.4%, 23.1% and 10.2% of AS patients at baseline, respectively.

Disease history (Section 13.5.5)

- For rheumatoid arthritis (RA) patients

Of 754 patients in the cohort, 170 (22.5%) had RA, of which 110 (64.7%) were biotherapy naïve (BT-n), 59 (34.7%) were biotherapy pretreated (BT-p) and prior biotherapy data was missing for 1 patient (0.59%). Mean age of RA patients was 54.3 years and 74.1% were female; 42.3% of RA patients had a normal BMI, 36.9% were overweight and 15.5% were obese.

Mean duration of rheumatic disease at baseline (8.63 years) was higher for BT-p patients than BT-n patients (13.7 vs. 5.87 years). Rheumatoid factors were present in 72.2% of patients. CCP antibodies (67.7% of patients) were present in a greater proportion of BT-n (75.9%) than BT-p patients (52.5%). Mean ESR was 20.2 mm/h, mean CRP was 11.6 mg/l and mean baseline DAS28-CRP was 4.34.

Overall, X-ray results showed bone and joint lesions in 138 (81.7%) RA patients, of whom 35 (20.7%) had 2 lesions and 27 (16.0%) had 3 or more lesions. The lesions consisted of bone erosion, joint space loss, bone demineralization and complete joint fusion, found in 55.6%, 40.2%, 36.1% and 2.96% of patients, respectively. Extra-articular manifestations were observed in 21 (12.4%) RA patients, of whom 7 (33.3%) suffered from pleuro-pulmonary complications.

- For psoriatic arthritis (PsA) patients

Among 754 patients in the cohort, 106 (14.1%) had PsA, of which 70 (66.0%) were BT-n and 36 (34.0%) were BT-p patients. Mean patient age was 48.1 years and 66.0% were female; 30.5% of patients had a normal BMI, 32.4% were overweight and 36.2% were obese.

Mean duration of rheumatic disease at baseline (6.06 years) was higher for BT-p patients compared to BT-n patients (7.93 vs. 5.04 years). At baseline, rheumatoid factors were present in a minority of patients (8.00%), keeping in line with the disease characteristics of PsA. Mean ESR was 19.9 mm/h, mean CRP was 8.52 mg/l and mean DAS28-CRP was 3.89.

X-ray results indicated bone and joint lesions in 50 (47.2%) PsA patients, of whom 11 (22.0%) had two lesions and 6 (12.0%) had three or more lesions. The lesions consisted of joint space loss, bone erosion, bone demineralization and complete joint fusion, in 29.2%, 23.6%, 10.4% and 6.60% of PsA patients, respectively. Extra-articular manifestations were observed in only 6 (5.94%) patients.

Cutaneous psoriasis was evident for most PsA patients (83.0%), and was more prevalent in BT-n than BT-p patients (88.6% vs. 72.2%). Among patients with cutaneous psoriasis, 92.0% presented with scaly or erythematous plaques, 18.2% presented with affected nails and 9.09% with genital lesions. Peripheral forms of rheumatic disease were reported in the majority of patients (90.6%) – 82.1% with an affected peripheral joint and 46.2% with entheses. Axial forms were found in 52.8% of patients – 38.7% and 30.2% with sacroiliac and axial skeleton involvement, respectively. Both axial and peripheral forms of the disease were found in 44.3% of PsA patients.

- For Ankylosing spondylitis (AS) patients

Among 754 patients in the cohort, 478 (63.4%) had AS, of which 291 (60.9%) were BT-n and 187 (39.1%) were BT-p patients. Mean patient age was 42.8 years and 54.6% were female; 46.9% of patients had a normal BMI, 31.2% were overweight and 17.8% were obese. Mean duration of rheumatic disease at baseline (7.55 years) was higher for BT-p patients compared to BT-n patients (10.7 vs. 5.52 years). At baseline, 66.5% of patients were HLA-B27 positive, in line with the disease characteristics of AS. Mean ESR was 16.4 mm/h, mean CRP was 11.4 mg/l and mean ASDAS-CRP was 3.16.

X-ray results indicated bone and joint lesions in 273 (57.1%) AS patients, of whom 92 (33.7%) had two lesions and 9 (3.30%) had three or more lesions. The lesions consisted of bone erosion, joint space loss, complete joint fusion and bone demineralization, in 31.6%, 23.4%, 15.9% and 9.62% of AS patients, respectively. Extra-articular manifestations were observed in 129 patients (27.0%), indicating a higher disease activity in this group, compared to RA and PsA groups, in which extra-articular manifestations were less frequent (12.4% and 5.94%, respectively). The most common types of manifestations were acute anterior uveitis and IBD (in 65.9% and 25.6% of patients, respectively).

Axial forms were observed in almost all AS patients (95.6%) – 304 (63.6%) with affected axial skeleton and 414 (86.6%) with affected sacroiliac joint, the latter being more prevalent in BT-n than in BT-p patients (91.4% vs. 79.1%). Peripheral forms occurred in a higher proportion of BT-p than BT-n AS patients: entheses was found in 47.6% BT-p patients compared to 32.6% of BT-n patients and peripheral joint complications occurred in 44.4% of BT-p patients versus 34.0% of BT-n patients. Both axial and peripheral forms of the disease were also found together in a higher proportion of BT-p than BT-n participants (63.6% and 45.7%, respectively).

Prior treatments

1) Prior biotherapies: In the total study cohort, 282 patients (37.5%) had received at least one biotherapy at baseline (the BT-p patients). Of these, the majority had received 1 line of biotherapy (n=135, 47.9%), 84 (29.8%) had received 2 lines, 47 (16.7%) had received 3 lines and 16 (5.67%) had received ≥4 lines.

The three most often used prior biotherapies were etanercept, adalimumab and infliximab, in 63.5%, 59.9% and 31.9% of BT-p patients, respectively. The main reason for discontinuing these 3 biotherapies was secondary failure: 46.9% for etanercept, 45.0% for adalimumab, and 41.1% for infliximab. The second most frequent reason for discontinuation was primary non-response – 28.5% for etanercept and 31.4% for adalimumab, and intolerance in those who received infliximab (32.2%).

2) Prior DMARDs: Over half the patients (53.4%) in the study cohort had received DMARDs. The majority of RA and PsA patients, had been treated (91.8% and 79.2%, respectively), compared to only a third of AS patients (34.1%). These observations comply with standard clinical recommendations of prescribing DMARDs as an early line of treatment to RA and PsA patients.

MTX was the most commonly prescribed DMARD (84.1%). Almost all PsA and RA patients who were prescribed DMARDs received MTX (98.8% and 93.6%, respectively), compared to two-thirds of AS patients (67.5%). A higher proportion of RA patients (61.6%) were continuing MTX at baseline compared to PsA (54.2%) and AS patients (41.8%). The most common reason for stopping MTX was intolerance in RA and PsA patients (26.7% and 27.7%, respectively). Primary non-response was the most common reason for MTX discontinuation in the AS group (34.5%); primary non-response was lower in the PsA (16.9%) and RA groups (9.59%).

3) Prior corticosteroids: 29.7% of patients in the total cohort had received long term corticosteroids. Corticosteroid use was more common in RA patients (63.5%) than in PsA (34.9%) and AS patients (16.5%). The most prescribed corticosteroid was prednisone/prednisolone/methylprednisolone (in 66.5% of patients who received corticosteroids) and cortisone/Hydrocortisone (35.3%). A lower proportion of AS patients (12.0%) were continuing the treatment compared to PsA and RA patients (50.0% each). Corticosteroid discontinuations were more common in AS patients due to a higher frequency of primary non-responses.

4) Prior NSAIDs/analgesics: The majority of patients, particularly those with AS and PsA had received at least one NSAID/Analgesic (90.0% of AS and 86.8% of PsA patients versus 71.2% of RA patients). The most commonly prescribed were paracetamol (61.6%), aspirin/ ibuprofen/coxibs (37.3%) and opioids (21.2%). “Other” non-specified NSAIDs/analgesics were received by 41.1% of patients.

5) Prior local surgeries: 27.9% of patients had a history of surgery related to rheumatic disease, with a higher percentage of RA (38.8%) and PsA (39.6%) patients having undergone surgery relative to AS patients (21.3%). The main surgical procedure in the total cohort was joint injections (85.7%).

Golimumab prescription

For all chronic rheumatic inflammatory diseases, the initial golimumab prescription was comparable between BT-n and BT-p patients, and conformed to the IFU in terms of dose and frequency (50 mg once a month) in almost all cases. The average initial prescription duration was around 5 months.

Golimumab was mostly prescribed in combination with other treatments (84.1%). Concomitant treatments were DMARDs in 45.0% of patients, NSAIDs/analagesics in 84.2% and corticosteroids in 22.9% of patients.

DMARDs were mostly prescribed concomitantly in RA patients (86.7%) compared to PsA (65.9%) and AS patients (21.8%). This observation is again in conformity to the golimumab treatment associations in the IFU *("golimumab is indicated in association with MTX for RA patients; whereas in PsA patients golimumab is indicated alone or in association with MTX").*

In patients receiving co-treatments corticosteroids were prescribed to over half of RA patients (54.5%), in under a third of PsA patients (29.7%) and in a minority of AS patients (7.43%). NSAIDs/analgesics were co-prescribed to 93.4% of AS, 85.7% of PsA and 62.4% of RA patients.

Evaluation of outcomes at 2 years

CRFs were received for 391 patients of 754 at 2 years. At the end of the 2nd year, and since initial prescription, 340 patients in the cohort discontinued golimumab and 362 patients persisted on the. A total of 52 patients were lost to follow-up after inclusion of which 9 RA, 7 PsA and 36 AS participants.

Primary objective: golimumab treatment persistence (Sections 15.1 to 15.3)

At the 2nd year of follow-up, 340 of 754 patients were reported as discontinuing golimumab treatment, consisting of 72 RA, 54 PsA and 214 AS patients. 362 patients persisted on golimumab, of which 89 RA, 45 PsA and 228 AS patients.

1) Total population:

Base case (excluding patients who were lost-to-follow-up): Among the 702 patients with assessable data at 24 months, 340 stopped the treatment, of whom 183 were BT-n and 157 were BT-p. 362 patients persisted on the treatment (248 BT-n and 114 BT-p). Treatment persistence in the base case was 51.6% (362/702) for the overall population: 57.5% (248/702) for BT-n patients and 42.1% (114/702) for BT-p patients.

Two assumptions were used to assess the sensitivity of golimumab persistence results:

- Worst case: all patients lost to follow-up have definitively discontinued golimumab
- Best case: all patients lost to follow-up are still continuing golimumab at 2 years.

Worst case: Assuming that golimumab was permanently stopped for the patients lost to follow-up (n=52), persistence was 48.0% (362/754) in the total population and 52.7% (248/471) and 40.4% (114/282) in BT-n and BT-p patients, respectively.

Best case: Assuming that golimumab was ongoing for the patients lost to follow-up (n=52), persistence was 54.9% (414/754) in the total population, and 61.1% (288/754) and 44.3% (125/754) in BT-n and BT-p patients respectively.

Cumulative persistence probability, as assessed with the Kaplan-Meier method was 65.7% at 1 year (71.2% BT-n an 56.8% BT-p) and 52.4% at 2 years (58.3% BT-n and 42.7% BT-p).

2) RA patients

At year 2, 89 RA patients were continuing golimumab, 72 had discontinued and 9 were lost to follow-up.

Base case: Treatment persistence in the base case was 55.3% (89/161) for the RA group: 59.2% (61/103) for BT-n patients and 48.3% (28/58) for BT-p patients.

Worst case: Assuming that golimumab was permanently stopped for the patients lost to follow-up (n=9), persistence was 52.7% (89/170) in the RA cohort and 55.5% (61/110) and 47.5% (28/59) in BT-n and BT-p patients, respectively.

Best case: Assuming that golimumab was ongoing for the patients lost to follow-up (n=9), persistence was 57.6% (98/170) in the RA cohort, and 61.8% (68/110) and 49.2% (29/59) in BT-n and BT-p patients respectively.

Cumulative persistence probability, as assessed with the Kaplan-Meier method was 65.4% at 1 year (69.6% BT-n an 56.9% BT-p) and 56.5% at 2 years (60.6% BT-n and 48.2% BT-p).

3) PsA patients

At year 2, 45 PsA patients were continuing golimumab, 54 had discontinued and 7 were lost to follow-up.

Base case: Treatment persistence in the base case was 45.5% (45/99) for the PsA group: 51.6% (33/64) for BT-n patients and 34.3% (12/35) for BT-p patients.

Worst case: Assuming that golimumab was permanently stopped for the patients lost to follow-up (n=7), persistence was 42.5% (45/106) in the PsA cohort and 47.1% (33/70) and 33.3% (12/36) in BT-n and BT-p patients, respectively.

Best case: Assuming that golimumab was ongoing for the patients lost to follow-up (n=7), persistence was 49.1% (52/106) in the PsA cohort, and 55.7% (39/70) and 36.1% (13/36) in BT-n and BT-p patients respectively.

Cumulative persistence probability, as assessed with the Kaplan-Meier method was 66.0% at 1 year (72.3% BT-n an 54.3% BT-p) and 45.1% at 2 years (56.9% BT-n and 34.1% BT-p).

4) AS patients

At year 2, 228 AS patients were continuing golimumab, 214 had discontinued and 36 were lost to follow-up.

Base case: Treatment persistence in the base case was 51.6% (228/442) in the AS cohort: 58.3% (154/264) for BT-n patients and 41.6% (74/178) for BT-p patients.

Worst case: Assuming that golimumab was permanently stopped for the patients lost to follow-up (n=36), persistence was 47.7% (228/478) in the AS cohort, and 52.9% (154/291) and 39.6% (74/187) in BT-n and BT-p patients, respectively.

Best case: Assuming that golimumab was ongoing for the patients lost to follow-up (n=36), persistence was 55.2% (264/478) in the AS group, and 62.2% (181/291) and 44.4% (83/187) in BT-n and BT-p patients respectively.

Cumulative persistence probability, as assessed with the Kaplan-Meier method was 65.8% at 1 year (71.5% BT-n an 57.2% BT-p) and 52.6% at 2 years (59.2% BT-n and 42.7% BT-p).

5) Summary of findings:

The base case results indicate that golimumab persistence at year 2 was 51.6% in the overall population, with moderate sensitivity ranges between 48.0% for the worst case and 54.9% for the best case. Base case results for all BT-n patients was 57.5%, with increased sensitivity ranges between 52.7% in for worst-case and 61.8% for the best-case scenarios. For BT-p patients, the base case persistence was 42.1%, with moderate sensitivity ranges between 40.4% and 44.3%.

The difference in persistence between the total BT-n and BT-p groups were significant ($p < .001$). The difference between BT-n and BT-p patient persistence was statistically significant only in the AS group ($p < .001$), but not in the RA and PsA groups.

Golimumab prescription renewal at 1 and 2 years

Prescription renewal data was available for 523 out of 557 patients at year 1 and 373 of 391 patients at year two. For most patients, golimumab prescription renewal was consistent with the IFU in terms of dosage (50mg once monthly).

RA patients: at year 1 (n=119), 106 RA patients (89.1%) had renewed prescriptions and at year 2 (n=93), 84 patients (90.3%) got their golimumab prescriptions renewed.

PsA patients: at year-1 (n=78) golimumab was re-prescribed to 62 PsA patients (79.5%), and at year-2 (n=48), golimumab was re-prescribed to 41 patients (85.4%).

AS patients: at year 1 (n=325) golimumab was re-prescribed to 283 AS patients (87.1%), and to 213 patients (91.8%) at year 2 (n=232).

Treatment administration

The majority of patients declared that they had respected the date of the injection day, as per their golimumab prescription. The majority of injections were performed with pen. The first injection was performed mainly by a professional caregiver. After the 1st injection, the use of professional caregiver for the injection gradually decreased toward an increase in patient's autonomy up to injection 25. Most patients were generally satisfied with the golimumab injection.

Disease activity

- For RA patients, disease activity as assessed by the rheumatologists at baseline was moderate for the majority of patients (63.8%), high for 21.9% and low for 14.4% of patients, as per mean DAS28-CRP scores. Average DAS 28 CRP was 4.34 for RA patients. Average physician's global assessment (GA) of disease activity on a 100-mm visual analogic scale (VAS) was 52.2.

At 1-year follow-up, overall disease activity was low in 79.2% of patients, moderate in 19.8% patients and high in only 1 patient, as per the DAS28 CRP. Significant clinical improvement (as per the DAS28) occurred in 68.1% of RA patients continuing golimumab at year 1. The average physician's GA of disease activity was 21.3 at year 1. At year 2 follow-up DAS28-CRP was low and moderate in 86.1% and 13.9% of patients, respectively, and significant improvement from baseline was noted for 71.8% of RA patients continuing treatment. Mean physicians GA was 17.9.

The improvement in disease activity over 2 years from baseline was significant (DAS28-CRP, $p < .0001$).

The disease activity, as assessed by the RA patients using the RAPID3 score, decreased over time, from a mean score of 4.49 at baseline to 2.43 at year 1 and 1.82 at year 2 ($p < .0001$).

- For PsA patients, the level of disease activity as assessed by the rheumatologists at inclusion was moderate and high for most patients (66.0% and 11.3%, respectively), as per DAS28 CRP. Mean DAS28-CRP was 3.89. Average physician's GA of disease activity was 54.0.

At 1-year follow-up, disease activity, as evaluated by DAS28-CRP had a mean of 2.64 and was low, moderate and high in 70.7%, 25.9% and 3.45% of PsA patients, respectively. Average physician's GA of disease activity was 28.5. Significant clinical improvement occurred in 54.5% of PsA patients who attended the 1-year visit, according to the DAS28 CRP. At year 2 follow-up DAS28-CRP was low and moderate in 91.4% and 8.57% of patients, respectively, and significant improvement from baseline was noted for 72.7% of PsA patients continuing treatment. Mean physicians GA was 20.2.

The improvement in disease activity over 2 years from baseline was significant (DAS28-CRP, $p < 0.0001$), and more so for BT-n than BT-p patients ($p = .0139$).

The RAPID3 score assessed by PsA patients at baseline was 5.31, and improved to 2.97 at year 1 and 2.83 at year 2, in patients continuing the treatment ($p < .0001$).

- For AS patients, the disease activity was high and very high in nearly all patients (91.9%) as assessed via the ASDAS-CRP. The average ASDAS-CRP score was 3.16 at baseline.

At 1-year follow-up, significant clinical improvement occurred in 57.6% of AS patients. Mean ASDAS-CRP was 1.84, and disease activity was moderate and high in 33.7% and 27.8% of patients, with 32.9% of patients having a score denoting remission. At year 2 follow-up ASDAS-CRP was inactive and moderate in 38.1% and 34.0% of patients, respectively, and significant improvement from baseline was noted for 59.8% of AS patients continuing treatment. Mean ASDAS-CRP was 1.70.

The improvement in disease activity over 2 years from baseline was significant (ASDAS-CRP, $p < 0.0001$), and more so for BT-n than BT-p patients ($p < .0051$).

The BASDAI score assessed by AS patients at baseline was 5.48, and improved to 3.06 at year 1 and 2.75 at year 2, in patients continuing the treatment ($p < .0001$).

- For patients who discontinued the golimumab treatment, disease activity as assessed by the rheumatologists and the patients at treatment discontinuation, was similar or worse than baseline, for the 3 diseases.

Pain severity, assessed by patients monthly using VAS, improved significantly over 2 years compared to baseline, in all disease groups.

It is interesting to note that the results of the disease assessments performed by the physicians and the patients were in agreement with each other and evolved similarly, also concerning the differences in improvement observed between BT-n and BT-p patients. At 2 years, both physician and patient reported scores showed an improvement in disease severity. And at treatment withdrawal, both reported an equivalent or worse disease activity compared to conclusion.

Health status and functional ability

Health status assessed by the patients using EQ-5D index, showed an improvement over time in patients under golimumab over a period of 2 years. This improvement in health status was statistically significant from baseline to 2 years for all disease groups and more so for BT-n patients compared to BT-p patients ($p < .0001$).

Similarly, functional ability evaluated using the HAQ index by the patient was improved over time in patients treated with golimumab. The improvement in functional ability was statistically significant from baseline to year 2, and was more improved for BT-n than BT-p patients in all disease groups ($p < .0001$).

In patients who discontinued the golimumab treatment, health status and the functional ability scores were similar or worsened at discontinuation compared to baseline.

Quality of life

The physical component score (PCS) of the SF-12 quality of life questionnaire showed improvements from baseline to year 2 for patients in all the disease cohorts, who were continuing golimumab. Nevertheless, the mental component score (MCS) did not evolve significantly for RA and PsA patients from baseline to 2 years; the change was only significant for AS patients. PCS and MCS scores for patients who discontinued golimumab were the same or worsened upon discontinuation, compared to baseline.

Consumption of Healthcare and Health Services

Most differences in healthcare resource utilization, were observed regarding hospitalizations (≥24h and <24h) for medical reason or surgery, which appeared to decrease over time in all, RA, PsA and AS patients, compared to 3-months before study inclusion. The number of missed work days also seemed to decrease overtime from baseline in all cohorts. However, these observations should be considered with caution due to limited statistical analysis on these data.

Productivity loss at work

The productivity loss due to the disease assessed using the WPAI questionnaire overtime showed an improvement in all sub-scores. At inclusion, a majority declared having a job. For these patients, the percentage of “work time missed”, the percentage of “impairment at work” and the percentage of “overall work impairment” appeared to decrease over time. Similarly, the “global activity impairment” due to the disease appears to improve over time from baseline to 2 years, for those continuing golimumab. This observation was statistically significant in all disease groups.

17.2 Strengths and limitations

This analysis allowed for the description of patients treated with golimumab in real-life practice, for the three most common chronic rheumatic diseases: rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis.

This study has strengths and limitations. One of the strengths is the relatively large cohort of RA, PsA and AS patients who were prospectively and consecutively enrolled, to reflect the real-life prescription of golimumab among patients of 3 different rheumatic diseases. This cohort also allowed for the analysis of the persistence and treatment effects of golimumab in biotherapy naïve and biotherapy pre-treated patients. One of the key findings obtained, as a result, was that golimumab treatment had a higher persistence and overall better clinical and patient reported outcomes in BT-n patients compared to BT-p patients.

Since this study included only French patients, the cohort was relatively homogenous, but also representative of the patients encountered in current clinical practice throughout France. However, this aspect could limit the generalizability of the study outcomes to other healthcare settings. Additionally, a selection bias may be present concerning the physicians or patients, as it depends on their will and motivation to participate in this study.

Generally, the responses to golimumab as well as overall outcomes of patients in this cohort correspond to the effects observed in previous published pivotal trials and other prospective cohort studies on golimumab, such as the GO-NICE study, which externally validates the findings of this study. Golimumab was prescribed according to the IFU and recommended modalities, in terms of dosage and regimen. The golimumab prescription, in regards with prior and concomitant treatments, was also consistent with the IFU and current recommendations.

One of the limitations of this study, as is the case of most non-interventional studies was the high rate of missing data.

17.3 The claims data study (RIC SNIIRAM) and Go-PRACTICE

17.3.1 The RIC SNIIRAM study

A retrospective observational cohort study was performed using data from the ‘Système National des données de santé’ (SNDS, the French National Health Insurance) database, which lists all reimbursed outpatient and inpatient medical resource use (claims data) for individuals covered by the general health insurance scheme (Caisse Nationale de l’Assurance Maladie des Travailleurs Salariés [CNAMTS]). The beneficiaries included in the SNDS database represent 91% of the French population. In the SNDS database, anonymised data are prospectively recorded on 1) patient characteristics such as age, gender, medical diagnoses [International Classification of Diseases – 10th revision (ICD-10) codes] for severe and costly chronic diseases for which the CNAMTS provides full health insurance coverage [Long Term Disease], region of residence, and date of death, 2) ambulatory care namely detailed reimbursements for drugs with prescription and dispensing dates, corresponding codes for primary care and consultations with specialists and reimbursed medicines, medical procedures, biological tests, medical devices and healthcare from other health professionals, and 3) hospitalisations from all French public and private hospitals (PMSI database) such as discharge diagnoses [ICD-10 codes], some of the medical procedures performed during hospitalisation, date of discharge and length of stay, ambulatory visits to hospital, and medicines and medical devices included in a specific list of costly and most necessary products.

This study included patients with chronic inflammatory rheumatic diseases (CIRDs) and covered by the general scheme between 2011 and 2014, initiated the following SC TNFi(α) treatments: Etanercept (marketing authorisation year [MA]: 2000), Adalimumab (MA year: 2003), Certolizumab pegol (MA year:

2009) and/or Golimumab (MA year: 2009), identified via prescriptions delivered between July 1, 2012 and December 31, 2013.

As diagnosis information is not available in the SNDS database except in the case of hospital admissions or long-term disease status (for which patients are exempt from health insurance payor fees), patient selection was based on diagnosis and performed using the following criteria: patients hospitalised for an CIRD-related principal or related diagnosis; patients who were reimbursed at least once under the long-term disease category, or due to an CIRD-associated disability. Included patients were divided into 3 cohorts: patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Diagnoses were based on the Long Term Disease status and/or hospital admissions related to a RA (ICD-10 codes M05, M05.0, M05.1, M05.2, M05.3, M05.8, M05.9, M06.0, M06.3, M06.8, M06.9, M08.0, M08.2, M08.4, M13.0), an AS (ICD-10 codes M08.1, M08.8, M08.9, M45, M45.0, M45.1, M45.2, M45.3, M45.4, M45.5, M45.6, M45.7, M45.8, M45.9, M46, M46.1, M46.8, M46.9) or a PsA (ICD-10 codes M07, M07.0, M07.1, M07.2, M07.3, M09.0) diagnosis. The date of entry in each cohort was defined as the date of treatment initiation (i.e. first treatment dispensing).

In the RIC SNIIRAM study, 1,315 patients with RA, 2,656 patients with AS and 514 patients with PsA initiated golimumab, corresponding to a whole cohort of 4,485 patients.

17.3.2 Patients characteristics

For RA, mean age of Go-Practice patients was 54.3 years and 74.1% were female. In the RIC SNIIRAM study, females were even more represented (82.5% of RA patients), and mean age was similar (53.8 years). The results were consistent between the two studies for AS patients, regarding sex ratio (54.6% of females in the Go-Practice study and 58.5% in the RIC SNIIRAM study) and mean age (42.8 years for Go-Practice patients and 44.2 years for RIC SNIIRAM patients), as well as for the PsA cohort (sex ratio: 66.0% females versus 64%; mean age: 48.1 versus 48.9 years).

17.3.3 Prior treatments

- For rheumatoid arthritis (RA) patients:

Of 754 patients in the Go-Practice cohort, 170 (22.5%) had RA, of which 110 (64.7%) were biotherapy naïve (BT-n), 59 (34.7%) were biotherapy pretreated (BT-p) and prior biotherapy data was missing for one patient (0.59%). In the RIC SNIIRAM study, only 466 (35.4%) patients were BT-n and 849 (64.6%) were BT-p. Among the 849 BT-p, 620 received golimumab as second-line treatment.

- For Ankylosing spondylitis (AS) patients:

Among 754 patients in the Go-Practice cohort, 478 (63.4%) had AS, of which 291 (60.9%) were BT-n and 187 (39.1%) were BT-p patients. In the RIC SNIIRAM study, only 848 (32.0%) patients were BT-n and 1,808 (68.1%) were BT-p. Among the 1,808 BT-p, 1,362 received golimumab as second-line treatment.

- For psoriatic arthritis (PsA) patients:

Among 106 patients in the Go-Practice PsA cohort, 70 (66.0%) were BT-n and 36 (34.0%) were BT-p patients. In the RIC SNIIRAM study, only 140 (27.2%) patients were BT-n and 374 (68.1%) were BT-p. Among the 374 BT-p, 276 received golimumab as second-line treatment.

For the three CIRDs, the Go-Practice study included more BT-n patients, compared to the RIC SNIIRAM study. This result could be explained by the difference in the study periods. Indeed, the RIC SNIIRAM study included patients during 2012 and 2013 (just after the launch of golimumab), whereas the Go-Practice study included patients in 2015 and 2016. It is therefore likely that patients who received golimumab immediately after its launch was already treated with another SC TNFi(α), since golimumab was the last to be marketed.

The prior use of others treatments, like DMARDs and corticosteroids, cannot be compared between the two studies, as the RIC SNIIRAM study only described their utilization after the initiation of golimumab, and not before.

17.3.4 Golimumab prescription

In the Go-Practice study, golimumab was mostly prescribed in combination with other treatments (84.1%). DMARDs were mostly prescribed concomitantly in RA patients (86.7%) compared to PsA (65.9%) and AS patients (21.8%). This was also the case in the RIC SNIIRAM study, as 54.1% of the RA patients received methotrexate, against 17.0% of SA patients and 42.0% of PsA patients. This observation is in conformity to the golimumab treatment associations in the IFU ("golimumab is indicated in association with MTX for RA patients; whereas in PsA patients golimumab is indicated alone or in association with MTX").

In the Go-Practice study, corticosteroids were prescribed to over half of RA patients (54.5%), in under a third of PsA patients (29.7%) and in a minority of AS patients (7.4%). These results are in line with the RIC SNIIRAM study, as 34.0%, 11.1% and 5.6% of RA, PsA and AS patients had received long-term corticosteroids, respectively.

In both studies, NSAIDs/analgesics were co-prescribed to the majority of patients (Go-Practice study: 93.4% of AS, 85.7% of PsA and 62.4% of RA patients; RIC SNIIR AM study: 78.0% of AS, 73.7% of PsA and 64.6% of RA patients).

17.3.5 Treatment persistence

17.3.5.1 Golimumab treatment persistence at 2 years

In the Go-Practice study, the persistence of golimumab at 2 years after initial prescription was assessed for the 702 patients for whom CRFs were available at the year-2 visit (a total of 52 patients were lost to follow-up after inclusion of which 9 RA, 7 PsA and 36 AS participants).

At the end of the 2nd year, and since initial prescription, 340 patients in the cohort discontinued golimumab and 362 patients persisted on the treatment. The base case results indicate that golimumab persistence at 2 years was 51.6% in the overall population. Applying sensitivity analyses (for best and worst-case scenarios) for patients lost to follow-up at 2 years, the persistence varies between 48.0% for the worst case and 54.9% for the best-case scenarios.

In RA patients, overall treatment persistence at 2 years was 55.3%, ranging in sensitivity from 52.7% (worst case) to 57.6% (best case). In PsA patients, overall treatment persistence at 2 years was 45.5%, ranging in sensitivity from 42.5% to 49.1% in the worst-case and best-case scenarios, respectively. In AS patients, golimumab persistence at 2 years was 51.6%, ranging in sensitivity from 47.7% to 55.2%, for the worst-case and the best-case situations.

In the RIC SNIIRAM study, patients with at least one treatment gap between two administrations of 91 days or more were considered non-persistent. Furthermore, a patient who switched from one SC TNF inhibitor to another was considered as non-persistent to the first one. Patients with treatment gaps between two administrations of less than 91 days were considered persistent.

In this study, 1,062 patients had at least 24 months of available follow-up after the initiation of golimumab (289 RA patients, 653 SA patients and 120 PsA patients). In RA patients, overall treatment persistence at 2 years was 40.1%. In PsA patients, overall treatment persistence at 2 years was 35.0%. In AS patients, golimumab persistence at 2 years was 41.0%.

Whatever the disease, treatment persistence at 2 years was lower in the RIC SNIIRAM study, compared to the Go-Practice study. This result could be due to differences between the definitions of treatment discontinuation. Indeed, the definition of the discontinuation in claims data was a gap of 91 days or more between two dispensings, which includes temporary stops and definitive stops. In the Go Practice study,

discontinuation was recorded by rheumatologists at the visit date. This variable was not continually assessed during the study period, but only at 3 time-points (treatment initiation (baseline), and then at year 1 and year 2 visits for prescription renewal), which can overestimate the results.

Sensitivity analyses conducted on BT-n patients shown similar results. For BT-n RA patients, persistence rates at 24 months ranged between 48.5% (RIC SNIIRAM study) and 59.2% (Go-Practice study); for SA BT-n patients, persistence rates ranged between 44.1% and 58.3%; and for PsA BT-n, persistence rates ranged between 57.1% and 51.6%.

One of the key findings obtained in the two studies, was that golimumab treatment had a higher persistence at 24 months in BT-n patients compared to BT-p patients. Differences in persistence rates between the two studies can be explained largely by the fact that the number of BT-p patients in the RIC SNIIRAM study was higher than in the GO practice study.

17.3.5.2 Golimumab treatment persistence at 1 year

Among 715 patients with assessable data at 12 months in the Go-Practice study (a total of 39 patients were lost to follow-up between inclusion and 12 months), 249 stopped the treatment before year 1. Overall treatment persistence at year-1 was 65.2% (466 of 715 patients continuing golimumab). In RA patients, overall treatment persistence was 65.1%. In PsA patients, overall treatment persistence was 65.7%. In AS patients, golimumab persistence was 65.1%.

In the RIC SNIIRAM study, the treatment persistence at 1 year was 56.6% for the RA cohort, 50.8% for PsA cohort, and 54.5% for the AS cohort.

As for the persistence at 2 years, the RIC SNIIRAM study gave lower figures than the Go-Pratice study.

Sensitivity analyses conducted on BT-n patients shown similar results. For BT-n RA patients, persistence rates at 12 months ranged between 63.8% (RIC SNIIRAM study) and 69.2% (Go-Practice study); for SA BT-n patients, persistence rates ranged between 58.9% and 70.9%; and for PsA BT-n, persistence rates ranged between 55.9% and 71.9%.

As for the 24 months persistence, golimumab treatment had a higher persistence at 12 months in BT-n patients compared to BT-p patients.

18 TABULATED SUMMARY OF CHARACTERISTICS AND OUTCOMES BY DISEASE

18.1 Rheumatoid arthritis

	Inclusion n=170	1-year follow-up n=123	2-year follow-up n=98	Golimumab discontinuation n=72
Rheumatoid arthritis characteristics				
Duration since diagnosis – Mean (SD)	8.63 (9.86)	-	-	-
Physician's GA of RA activity – Mean (SD)	52.2 (16.7)	21.3 (18.6)	17.9 (16.0)	50.4 (21.9)
DAS 28 (CRP) – Mean (SD)	4.34 (1.11)	2.50 (0.94)	2.28 (0.80)	4.09 (1.21)
RA activity level (DAS28 CRP)	*n = 160*	*n = 96*	*n = 72*	*n = 40*
Low (DAS28<=3.2)	23 (14.4)	76 (79.2)	62 (86.1)	13 (32.5)
Moderate (3.2<DAS28<=5.1)	102 (63.8)	19 (19.8)	10 (13.9)	19 (47.5)
High (DAS28>5.1)	35 (21.9)	1 (1.04)	0 (0)	8 (20.0)
	-	*n = 95*	*n = 71*	-
Significant clinical improvement	-	64 (68.1)	51 (71.8)	-
Prior RA treatments				
Prior biotherapy	59 (34.9)	-	-	-
Number of biotherapies	n = 59	-	-	-
1	23 (39.0)	-	-	-
2	15 (25.4)	-	-	-
3	7 (11.9)	-	-	-
4 and more	14 (23.7)	-	-	-
Prior DMARDs	156 (91.8)	-	-	-
Prior Corticosteroids	108 (63.5)	-	-	-
Prior NSAIDs/Analgesics	121 (71.2)	-	-	-
Prior Local/surgical treatments	66 (38.8)	-	-	-
	n =169	*n =119*	*n =93*	
Golimumab prescription	168 (98.8%)	106 (89.1%)	84 (90.3%)	-
	n = 168	*n = 105*	*n = 85*	-
Dosage – 50 mg	166 (98.8)	105 (100.0%)	85 (100.0%)	-
Dose : 1 / month	168 (100.0)	103 (98.1)	81 (95.3)	-
Prescription duration (month), Mean(SD)	5.30 (2.63)	7.04 (2.78)	7.10 (2.96)	-
Permanent discontinuation	-	-	-	*n = 72*
Intolerance	-	-	-	13 (18.1)
Primary non-response	-	-	-	30 (41.7)
Secondary failure	-	-	-	15 (20.8)
Patient's request	-	-	-	15 (20.8)
Other reason	-	-	-	6 (8.33)
	n = 169	*n = 116*	*n = 93*	-
Concomitant treatments	165 (97.6)	99 (85.3)	77 (82.8)	-
DMARDs	143 (86.7)	91 (91.9)	71 (92.2)	-
Corticosteroids	90 (54.5)	30 (30.3)	23 (29.9)	-
NSAIDs	103 (62.4)	52 (52.5)	28 (36.4)	-

	Inclusion n=170	1-year follow-up n=123	2-year follow-up n=98	Golimumab discontinuation n=72
Golimumab treatment persistence – Worst case			89/170 (52.7%)	-
Golimumab treatment persistence – Base case	-	108/166 (65.1%)	89 (55.3%)	-
Golimumab treatment persistence – Best case	-		98/170 (57.6%)	-
Cumulative persistence probability (Kaplan Meier)	-	65.4%	56.5%	-
RAPID3 score – n / Mean (SD)	125 /4.49 (1.81)	71 / 2.43 (1.81)	38 / 1.82 (1.69)	11 / 5.09 (1.44)
PGIC scale – n / Mean (SD)	137 /3.31* (1.84)	78 / 5.46 (1.39)	46 / 6.07 (1.04)	12 / 1.92 (1.38)
Pain assessed using VAS – n / Mean (SD)	151 /50.1 (24.0)	81 / 26.6 (21.5)	45 / 20.8 (20.3)	12 / 57.6 (22.7)
Health status using EQ-5D – n / Mean (SD)	127 /0.43 (0.28)	76 / 0.64 (0.28)	42 / 0.73 (0.23)	7 / 0.39 (0.15)
Functional disability using HAQ – n / Mean (SD)	115 /1.18 (0.64)	75 / 0.76 (0.65)	44 / 0.62 (0.56)	8 / 1.06 (0.67)
QOL using SF-12 – n / Mean (SD)				
PCS	119 /35.8 (9.11)	72 / 43.1 (8.41)	36 / 47.0 (8.57)	7 / 34.5 (8.71)
MCS	119 /41.1 (10.8)	72 / 45.8 (10.4)	36 / 47.5 (9.76)	7 / 40.8 (8.37)
Productivity loss using WPAI				
Activity impairment (%)- n / Mean (SD)	133 /46.4 (24.8)	72 / 27.5 (22.3)	40 / 26.5 (23.8)	8 / 46.3 (21.3)

* At 2nd injection

18.2 Psoriatic arthritis

	Inclusion (n=106)	1-year follow-up (n=84)	2-year follow-up (n=52)	Golimumab discontinuation (n=54)
Psoriatic arthritis characteristics				
Duration since diagnosis – Mean (SD)	6.06 (7.01)	-	-	-
Physician's GA of PsA activity – Mean (SD)	54.0 (16.7)	28.5 (23.1)	20.2 (20.2)	60.4 (16.4)
DAS 28 (CRP) – Mean (SD)	3.89 (1.00)	2.64 (1.13)	2.00 (0.79)	3.78 (1.06)
PsA activity level (DAS28 CRP)	*n = 97*	*n = 58*	*n = 35*	*n = 21*
Low (DAS28<=3.2)	22 (22.7)	41 (70.7)	32 (91.4)	5 (23.8)
Moderate (3.2<DAS28<=5.1)	64 (66.0)	15 (25.9)	3 (8.57)	14 (66.7)
High (DAS28>5.1)	11 (11.3)	2 (3.45)	0 (0)	2 (9.52)
	-	*n = 55*	*n = 33*	-
Significant clinical improvement	-	30 (54.5)	24 (72.7)	-
Prior PsA treatments		-	-	-
Prior biotherapy	36 (34.0)	-	-	-
Number of biotherapies	*n = 36*	-	-	-
1	22 (61.1)	-	-	-
2	10 (27.8)	-	-	-
3	4 (11.1)	-	-	-
4 and more	0 (0)	-	-	-
Prior DMARDs	84 (79.2)	-	-	-
Prior Corticosteroids	37 (34.9)	-	-	-
Prior NSAIDs/Analgesics	92 (86.8)	-	-	-
Prior Local/surgical treatments	42 (39.6)	-	-	-
	n = 106	*n = 78*	*n = 48*	
Golimumab prescription	106 (100.0)	62 (79.5)	41 (85.4)	-
	n = 106	*n = 62*	*n = 41*	-
Dosage – 50 mg	101 (95.3)	56 (90.3)	37 (90.2)	-
Dose : 1 / month	105 (99.1)	60 (96.8)	41 (100.0)	-
Prescription duration (month), Mean(SD)	5.17 (2.57)	6.66 (2.91)	7.78 (3.07)	-
Permanent discontinuation	-	-	-	*n = 54*
Intolerance	-	-	-	8 (14.8)
Primary non-response	-	-	-	19 (35.2)
Secondary failure	-	-	-	19 (35.2)
Patient's request	-	-	-	6 (11.1)
Other reason	-	-	-	5 (9.26)
	n = 106	*n = 78*	*n = 47*	
Concomitant treatments	91 (85.8)	58 (74.4)	32 (68.1)	-
DMARDs	60 (65.9)	44 (75.9)	22 (68.8)	-
Corticosteroids	27 (29.7)	10 (17.2)	5 (15.6)	-
NSAIDs	78 (85.7)	38 (65.5)	15 (46.9)	-
Golimumab treatment persistence – Worst case	-	-	45/106 (42.5%)	-
Golimumab treatment persistence – Base case	-	65/99 (65.7%)	45/99 (45.5%)	-

	Inclusion (n=106)	1-year follow-up (n=84)	2-year follow-up (n=52)	Golimumab discontinuation (n=54)
Golimumab treatment persistence – Best case	-		52/106 (57.6%)	-
Cumulative persistence probability (Kaplan Meier)	-	66.0%	45.1%	-
RAPID3 score – n / Mean (SD)	74 / 5.31 (1.45)	43 / 2.97 (1.90)	19 / 2.83 (2.20)	6 / 6.27 (1.07)
PGIC scale – n / Mean (SD)	94 / 3.65* (2.01)	49 / 5.51 (1.53)	26 / 5.92 (1.47)	8 / 2.75 (2.05)
Pain assessed using VAS – n / Mean (SD)	97 / 63.9 (20.5)	49 / 30.4 (23.8)	26 / 26.3 (26.6)	8 / 78.0 (22.1)
Health status using EQ-5D – n / Mean (SD)	86 / 0.36 (0.27)	47 / 0.62 (0.22)	23 / 0.67 (0.27)	6 / 0.24 (0.47)
Functional disability using HAQ – n / Mean (SD)	80 / 1.14 (0.56)	49 / 0.68 (0.51)	24 / 0.59 (0.61)	7 / 1.05 (0.74)
QOL using SF-12 – n / Mean (SD)				
PCS	88 / 34.7 (7.70)	48 / 43.3 (7.81)	25 / 44.4 (9.24)	5 / 34.1 (9.48)
MCS	88 / 40.0 (10.6)	48 / 45.0 (9.01)	25 / 48.8 (10.5)	5 / 42.1 (11.1)
Productivity loss using WPAI				
Activity impairment (%)- n / Mean (SD)	88 / 55.6 (24.2)	47 / 34.9 (24.8)	23 /25.7 (22.7)	6 / 65.0 (32.7)

* At 2nd injection

18.3 Ankylosing spondylitis

	Inclusion (n=478)	1-year follow-up (n=350)	2-year follow-up (n=241)	Golimumab discontinuation (n=214)
Ankylosing spondylitis characteristics				
Duration since diagnosis – Mean (SD)	7.55 (9.24)	-	-	-
ASDAS (CRP) – Mean (SD)	3.16 (0.79)	1.84 (0.93)	1.70 (0.95)	2.96 (0.88)
AS activity level (ASDAS CRP)	*n = 447*	*n = 255*	*n = 194*	*n = 107*
Inactive (ASDAS<1.3)	1 (0.22)	84 (32.9)	74 (38.1)	6 (5.61)
Moderate (1.3<=ASDAS<2.1)	35 (7.83)	86 (33.7)	66 (34.0)	8 (7.48)
High (ASDAS>=2.1)	266 (59.5)	71 (27.8)	42 (21.6)	66 (61.7)
Very high (ASDAS ≥3.5)	145 (32.4)	14 (5.49)	12 (6.19)	27 (25.2)
	-	*n = 243*	*n = 184*	-
Significant clinical improvement	-	140 (57.6)	110 (59.8)	-
Prior AS treatments		-	-	-
Prior biotherapy	187 (39.1)	-	-	-
Number of biotherapies	*n = 187*	-	-	-
1	90 (48.1)	-	-	-
2	59 (31.6)	-	-	-
3	36 (19.3)	-	-	-
4 and more	2 (1.07)	-	-	-
Prior DMARDs	163 (34.1)	-	-	-
Prior Corticosteroids	79 (16.5)	-	-	-
Prior NSAIDs/Analgesics	430 (90.0)	-	-	-
Prior Local/surgical treatments	102 (21.3)	-	-	-
	n = 478	*n = 325*	*n = 232*	
Golimumab prescription	471 (98.5)	283 (80.9)	213 (88.4)	-
	n = 471	*n = 283*	*n = 213*	-
Dosage – 50 mg	465 (97.3)	283 (87.1)	213 (91.8)	-
Dose : 1 / month	467 (99.2)	276 (97.5)	197 (92.5)	-
Prescription duration (month), Mean (SD)	5.37 (2.69)	7.57 (3.04)	8.06 (3.10)	-
Permanent discontinuation	-	-	-	*n = 214*
Intolerance	-	-	-	46 (21.5)
Primary non-response	-	-	-	80 (37.4)
Secondary failure	-	-	-	53 (24.8)
Patient's request	-	-	-	22 (10.3)
Other reason	-	-	-	27 (12.6)
	n = 478	*n = 324*	*n = 229*	
Concomitant treatments	377 (78.9)	157 (48.5)	80 (34.9)	-
DMARDs	82 (21.8)	50 (31.8)	26 (32.5)	-
Corticosteroids	28 (7.43)	7 (4.46)	1 (1.25)	-
NSAIDs	352 (93.4)	135 (86.0)	71 (88.8)	-
Golimumab treatment persistence – Worst case	-	-	228/478 (47.7)	-

	Inclusion (n=478)	1-year follow-up (n=350)	2-year follow-up (n=241)	Golimumab discontinuation (n=214)
Golimumab treatment persistence – Base case	-	293/450 (65.1%)	228/442 (51.6)	-
Golimumab treatment persistence – Best case	-	-	264/478 (55.2)	-
Cumulative persistence probability (Kaplan Meier)	-	65.8%	52.6%	-
BASDAI score – n / Mean (SD)	430 / 5.48 (1.64)	178 / 3.06 (1.94)	112 / 2.75 (1.92)	34 / 5.72 (2.00)
PGIC scale – n / Mean (SD)	413 / 3.59* (2.01)	211 / 5.40 (1.48)	123 / 5.62 (1.43)	39 / 2.62 (1.74)
Pain assessed using VAS – n / Mean (SD)	436 / 64.6 (22.5)	214 / 31.5 (24.5)	125 / 28.5 (23.7)	39 / 66.0 (27.3)
Health status using EQ-5D – n / Mean (SD)	422 / 0.38 (0.27)	204 / 0.62 (0.28)	123 / 0.64 (0.27)	36 / 0.29 (0.26)
Functional disability using HAQ – n / Mean (SD)	446 / 0.97 (0.56)	210 / 0.56 (0.53)	123 / 0.50 (0.52)	38 / 1.15 (0.59)
QOL using SF-12 – n / Mean (SD)				
PCS	412 / 34.4 (9.11)	194 / 43.7 (9.08)	117 / 44.5 (8.48)	37 / 33.1 (9.44)
MCS	412 / 40.5 (10.0)	194 / 44.8 (10.5)	117 / 46.4 (9.49)	37 / 38.3 (11.1)
Productivity loss using WPAI				
Activity impairment (%)- n / Mean (SD)	435 / 57.2 (25.0)	198 / 32.5 (26.2)	119 / 30.2 (24.9)	33 / 64.5 (26.6)

* At 2nd injection

19 PHARMACOVIGILANCE

The pharmacovigilance data presented in this report include all the adverse events (AEs) reported from January 15, 2015 to December 10, 2018, for all patients included in the study (n=754).

These data are presented in 2 sets:

- Adverse events reported by the physicians
- Adverse events reported by the patients.

It is worth noting that the same AE might be declared by both, the physician and the patient. Patient and physician-reported AEs were analyzed separately (see section 16).

AEs according to the patients, 258 patients (34.2%) experienced at least one AE and 73 (9.68%) patients experienced at least one SAE, in similar proportions across each disease group. In total, 1291 AEs were reported, of which 196 (15.2%) were considered to be SAEs. The frequency of SAEs were similar among all disease groups.

Most patient-declared AEs (both serious and non-serious) were grouped under the following SOCs: *"General disorders and administration site conditions"* (391/1291 AEs; 30.3%), *"Infections and infestations"* (193/1291 AEs; 14.9%), and *"Musculoskeletal and connective tissue disorders"* (156/1291 AEs; 12.1%).

Most patient-declared SAEs were classed under the following SOCs: "*Surgical and medical procedures"* (79/196 SAEs; 40.3%), *"General disorders and administration site conditions"* (22/196, 11.2%) and *"Musculoskeletal and connective tissue disorders"* (19/196 SAEs; 9.69%).

Action taken concerning golimumab prescription was provided for 1180/1291 AEs (91.4%) and 171/196 SAEs (87.2%). Golimumab dosage remained unchanged following most AEs (n=589, 49.9%) and SAEs (n=88, 51.5%). Overall, 111 AEs (9.41%) and 15 SAEs (8.77%) led to permanent golimumab discontinuation; 447 AEs (37.9%) and 63 SAEs (36.8%) led to temporary golimumab discontinuation.

AEs according to the physicians, among 754 patients included in the study, 352 patients (46.7%) experienced at least one AE and 79 (10.5%) patients experienced at least one SAE, in similar proportions in all disease groups. Among the 1055 physician-reported AEs in the study group, 189 (17.9%) were considered as SAEs (similar percentage of SAEs observed across all disease groups).

Two deaths were reported during the study. The first belonged to SOC *"General disorders and administration site conditions"*, (PT "death"), and the second belonged to SOC *"Psychiatric disorders"* (PT "completed suicide"), and both were reported as not related to golimumab.

Mean time to onset of AE since study inclusion was 8.68 months, with the mean time being longest for PsA patients (9.69 months), followed by AS (8.69 months) and RA patients (8.01 months).

Most declared AEs (both serious and non-serious) were affiliated to the following "*SOCs*" [most frequently reported PTs]: *"General disorders and administration site conditions"* (382/1055 AEs; 36.2%) [Treatment failure (123/382, 32.2%) and Drug effect decreased (107/382, 28.0%)], and *"Infections and infestations"* (220/1055 AEs; 20.9%) [Bronchitis (35/220, 15.9%) and Urinary tract infection (26/220, 11.8%)].

Most declared SAEs were affiliated to the following "*SOC*" [most frequently reported PTs]: *"General disorders and administration site conditions"* (55/189 SAEs; 29.1%) [Condition aggravated (14/41, 29.3%), Treatment failure (9/41, 16.4%) and Drug effect decreased (8/41, 14.5%)].

Among the 1055 AEs reported, 375 (35.5%) were considered as related to golimumab, 292 (27.7%) as not related to golimumab and 388 (36.8%) were not stated. Among the 189 SAEs reported, 61 (32.3%) were considered as related to golimumab, 82 (43.4%) as not related to golimumab and 46 (24.3%) were not stated. Overall, 174 of 754 patients (23.1%) underwent at least one AE related to golimumab and

29 patients (3.85%) experienced at least one SAE related to golimumab (similar proportions across all disease groups).
Among the 314 non-serious AEs related to golimumab, most were affiliated to the following SOCs:

1) *"General disorders and administration site conditions"* (137/314 AEs; 43.6%)
   - Drug effect decreased (45/137, 32.8%)
   - Treatment failure (42/137, 30.7%)
   - Jointly, "adverse event" and "drug ineffective" (9/137, 6.57%, for each)
2) *"Infections and infestations"* (81/314 AEs; 25.8%)
   - Bronchitis (10/81, 12.3%)
   - Tonsillitis (8/81, 9.88%)
   - Sinusitis (7/81, 8.64%)

Among the 61 SAEs identified to be related to golimumab, most belonged to the SOCs:

1) *"General disorders and administration site conditions"* (27/61 AEs; 44.3%)
   - Condition aggravated (7/27, 25.9%)
   - Drug effect decreased (7/27, 25.9%)
   - Treatment failure (6/27, 22.2%)
   - Jointly, "adverse event" and "drug ineffective" (, 6.57%, for each)
2) *"Infections and infestations"* (10/61 AEs; 16.4%)

The safety results observed in this CSR are consistent with the well-known safety profiles of golimumab with no new safety issues observed.

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