1 TITLE PAGE

CLINICAL STUDY REPORT

Sponsor Name	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. One Merck Drive, P.O. Box 100 Whitehouse Station, NJ 08889-0100, U.S.A.
Compound Name	MK-8259 (Golimumab)
Protocol Title	Achieving Minimal Disease Activity and Predictors of clinical response in Patients with Psoriatic Arthritis treated with Golimumab in clinical practice: a Multicenter Observational Study Short title: Predicting MDA in PsA
CSR Identification	039-00
Indication	Psoriasic arthritis
Trial Design	Multicentre, prospective, observational study
Phase	Observational study
Trial Initiation Date	08-May-2015
Trial Early Termination Date	Not Applicable
Trial Completion Date	29-Nov-2016
Report Date	Final Version, 27-Jun-2017
Previous CSR Identification	Draft 1, 18-May-2017
Responsible Medical Officer	Dr. Monica Mecchia, Medical Affairs Director Immunology, MSD Italia s.r.l., Via Vitorchiano 151, 00189 Rome, Italy
Investigator Name/Affiliation	PPD PPD Italy
GCP Compliance	Information regarding GCP compliance can be found in Section 5.2
Questions about the clinical study report should be directed to the individual listed on the accompanying correspondence.	

2 SYNOPSIS

SPONSOR:	MSD Italia s.r.l.	
COMPOUND NAME:	MK-8259 (Golimumab)	
INDICATION:	Psoriasic arthritis	
PROTOCOL TITLE:	Achieving Minimal Disease Activity and Predictors of clinical response in Patients with Psoriatic Arthritis treated with Golimumab in clinical practice: a Multicenter Observational Study	
TRIAL IDENTIFIERS:	Protocol Number:	039-00
	Clinical Phase:	Observational study
	EudraCT Number:	Not applicable
ETHICS:	This trial was conducted in conformance with applicable country or local requirements regarding ethical committee review, informed consent, and other statutes or regulations regarding the protection of the rights and welfare of human subjects participating in biomedical research. The signature of the primary/coordinating investigator is in Appendix 16.1.5.1 and the signatures of the principal authors of this report are in Appendix 16.1.5.2.	
TRIAL CENTERS:	This trial was conducted at 23 investigational study sites in Italy. A list of investigators and trial centers is provided in Appendix 16.1.3.1.	
DESIGN:	National (Italian), multicenter, prospective, observational study. For additional information about trial design, see the protocol in Appendix 16.1.1. Sample case report forms are in Appendix 16.1.2.	
	Planned duration of observational period	Patients were followed prospectively for 6 months with data collection at baseline (pre-treatment), 3 months and 6 months
Objectives	<u>Primary objective</u> The primary objective of the study was to develop a clinical prediction model, using a combination of baseline (pre-antiTNF treatment) clinical variables, for the achievement of 6-month minimal disease activity (MDA) in psoriatic arthritis (PsA) patients starting golimumab. <u>Secondary objectives</u> The secondary objectives of the study were: • To evaluate candidate immune-biological variables (biomarkers) for the improvement in performance of the clinical prediction model for the achievement of 6-month MDA in PsA patients starting golimumab;	

	• To develop a clinical prediction model, using a combination of baseline (pre-antiTNF treatment) clinical variables, for the achievement of 3-month MDA in PsA patients starting golimumab; • To explore clinical prediction models using a combination of baseline (pre-antiTNF treatment) clinical variables against secondary outcome measures (Disease Activity for Psoriatic Arthritis [DAPSA], Health Assessment Questionnaire [HAQ], Leeds enthesitis index [LEI] and dactilytis 0-6 month changes); • To assess changes in disease activity response evaluated by DAPSA at 3 and 6 months vs. baseline; • To assess change in functional score evaluated by HAQ at 3 and 6 months vs. baseline; • To assess change in enthesitis score evaluated by LEI at 3 and 6 months vs. baseline; • To assess change in dactilytis score evaluated by dactylitic digit count at 3 and 6 months vs. baseline.
Hypotheses	The scope of this study was to test the following hypotheses: • In patients with active PsA and inadequate response to conventional therapies, identifying predictors of MDA to golimumab can improve care in selecting patients able to achieve the target. • The a priori hypothesis to be tested was that a combination of clinical and immuno-biological variables might progressively enhance our ability to predict response to golimumab in PsA patients. The sample size was estimated based on the primary objective of the cohort study, i.e. to develop a clinical prediction model of achievement of 6-month MDA in PsA patients starting golimumab. To avoid over-fitting, the minimum number of events per variable was set to 10. Given an expected 6-month achievement of MDA by 40% of the patients, in order to develop a prediction model including up to 5 variables, 125 subjects were to be enrolled. Assuming ≈10% of lost to follow-up patients, sample size rose to 135-140 subjects. The same sample size was also sufficient to evaluate the improvement in prediction of the candidate biomarkers. Because of the higher clinical relevance of minimizing false negative responders, power calculation was performed to evaluate the improvement of the true positive rate from 60 to 70% and improvement of false negative rate from 40 to 15%, setting alpha to 5%. A number of 125 subjects with 50 responders would be sufficient to evaluate the increase in the performance of the model biomarker-enhanced prediction model with a power>80% (estimated in Stata using rocsize command).

Treatment groups	Not applicable. In agreement with the observational nature of the study, patients were treated as per routine clinical practice and entirely according to the judgment of the treating physician.	
Endpoints and definitions	<u>Primary endpoint</u> The primary endpoint of the study was the response rate to treatment, defined as proportion of patients achieving MDA at 6 months. PsA patients were classified as having MDA if they met 5 of these 7 criteria: • Tender joint count ≤1; • Swollen joint count ≤1; • Physician global assessment (PGA) for Psoriatic Activity (Clear or Almost clear); • Patient pain visual analogue scale (VAS) ≤15/100; • Patient global assessment of PsA disease activity VAS ≤20; • HAQ score ≤0.5; • Tender enthesial points ≤1. <u>Secondary endpoints</u> The secondary endpoints of the study were: • Proportion of patients achieving MDA at 3 months. • Evaluation of clinical outcomes at 3 and 6 months (change vs. baseline): - Change in LEI; - Change in dactilytis score; - Changes in functional score (by HAQ); - Change in DAPSA composite scores.	
Database lock	16-Feb-2017	Trial status: completed with 151 subjects enrolled and 149 subjects evaluable (standard population - STD - set)

RESULTS AND ANALYSIS:	The Statistical Analysis Plan is provided in Appendix 16.1.9.
Analysis description	**Primary analysis** Predictors of MDA at 6 months were individually tested by univariable logistic models and results were presented as odds ratio (OR) and 95% confidence interval (CI). A backward stepwise selection strategy (cut-off: p<0.10) was applied to multivariable logistic model in order to further select relevant variables. Statistical interactions were systematically fitted between statistically significant variables.

	Model assumptions were tested and appropriate diagnostics applied. The overall performance of the model was evaluated by the Brier score. Discriminatory ability was evaluated by estimating the C-statistics, and calibration was evaluated both statistically and graphically by the Hosmer-Lemeshow goodness-of-fit test and through a box plot. Internal validity of the prediction models was tested by bootstrap validation using 500 bootstrap repetitions on a sample with 50% size of the sample included in the model. The mean C-statistics obtained from the bootstrapping technique was presented together with its 95% CI and compared to the model C-statistics. Further logistic models for the outcome of MDA at 6 months were fitted including baseline biomarker levels (hsCRP, MMP-3, CPII) as additional candidate predictors. The improvement of the performance of the prediction models was evaluated by estimating the integrated discrimination improvement (IDI) index.
Analysis population and time point description	Analysis was performed in the STD set, defined as all enrolled subjects who received at least one dose of golimumab.
Summary	Overall, 66 patients (44.3%) achieved the MDA at 6 months, i.e. met at least 5 of the 7 pre-defined criteria, and 59 patients (39.6%) did not achieve the MDA. Results were unknown in 24 patients (16.1%). Sixty-three patients (42.3%) had a tender joint count ≤ 1, 109 (73.2%) had a swollen joint count ≤ 1, 115 (77.2%) had a clear or almost clear PGA, 54 (36.2%) had a patient assessment of pain VAS ≤ 15 mm, 56 (37.6%) had a patient's global assessment of PsA disease activity VAS ≤ 20 mm, 77 (51.7%) had a HAQ score ≤ 0.5, and 105 (70.5%) had ≤ 1 tender enthesial points. In the univariable logistic model, factors that resulted to be predictive of MDA at 6 months were male gender, lower age and lower DAPSA score, HAQ score, patient assessment of pain VAS and BASDAI score at baseline, and absence of comorbidities. In the multivariable logistic model, factors that resulted to be predictive of MDA at 6 months were lower age, higher hs-CRP value at baseline, lower DAPSA score at baseline, and longer duration of symptoms at baseline. In the biomarker-enhanced clinical prediction model, a higher hs-CRP value at baseline in the univariable logistic model, and absence of comorbidities and lower DAPSA score at baseline in the multivariable logistic model, were indicative of a higher probability to achieve MDA at 6 months.

Analysis description	**Secondary analysis** The same set of analyses as the primary ones were carried out using MDA at 3 months as dependent variable, including the development of a biomarker-enhanced prediction model (see previous point). Default summary statistics of DAPSA total score, HAQ total score, LEI Index and dactylitis score over time (screening visit, follow-up visit at 3 months and follow-up visit at 6 months) and change from screening, including the mean difference (MD) and its corresponding 95% CI, were reported. Clinical predictors of the secondary response outcomes (DAPSA, HAQ, LEI, dactylitis score 0-6 month changes) were explored using linear regression models, following the same strategy as for the primary outcome. The relationship between different disease activity measures were evaluated cross-sectionally at baseline, 3 months and 6 months by estimating linear correlation coefficients. Correlation coefficients that take into account repeated observations within the same subject were also estimated according to Bland e Altman. Default summary statistics of the hs-CRP and ESR over time and the change from screening including the MD and its corresponding 95% CI, were provided.
Analysis population and time point description	Analysis was performed in the STD set.
Summary	<u>Proportion of patients achieving MDA at 3 months</u> Overall, 54 patients (36.2%) achieved the MDA at 3 months, i.e. met at least 5 of the 7 pre-defined criteria, and 84 patients (56.4%) did not achieve the MDA. Results were unknown in 11 patients (7.4%). Sixty-one patients (40.9%) had a tender joint count ≤ 1, 106 (71.1%) had a swollen joint count ≤ 1, 123 (82.6%) had a clear or almost clear PGA, 42 (28.2%) had a patient assessment of pain VAS ≤ 15 mm, 38 (25.5%) had a patient's global assessment of PsA disease activity VAS ≤ 20 mm, 73 (49.0%) had a HAQ score ≤ 0.5, and 110 (73.8%) had ≤ 1 tender enthesial points. In the univariable logistic model, factors that resulted to be predictive of MDA at 3 months were male gender, lower age and lower DAPSA score, HAQ score, patient assessment of pain VAS and BASDAI score at baseline, and absence of comorbidities. In the multivariable logistic model, factors that resulted to be predictive of MDA at 3 months were lower age, higher hs-CRP value at baseline, lower DAPSA score and HAQ score at baseline, and longer time from diagnosis.

	In the biomarker-enhanced clinical prediction model, none of the biomarkers in the univariable logistic model, and lower age, lower BASDAI and DAPSA core at baseline, and longer time from diagnosis in the multivariable logistic model, were indicative of a higher probability to achieve MDA at 3 months. <u>hs-CRP</u> The mean and median hs-CRP decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -88.69 ± 291.661 nmol/L (median -26.67 nmol/L, range -2905.77 to 169.53 nmol/L) at Month 3 and -96.91 ± 308.537 nmol/L (median -27.62 nmol/L, range -3001.96 to 205.72 nmol/L) at Month 6. <u>ESR</u> The mean and median ESR decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -11.71 ± 17.872 mm/h (median -6.00 mm/h, range -114 to 15 mm/h) at Month 3 and was -11.83 ± 17.892 mm/h (median -7.00 mm/h, range -102 to 11 mm/h) at Month 6. <u>Tender joints count</u> The mean and median TJC decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -6.97 ± 7.288 (median -6.00, range -43 to 12) at Month 3 and was -7.72 ± 7.753 (median -6.00, range -41 to 13) at Month 6. <u>Swollen joints count</u> The mean and median SJC decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -3.33 ± 4.257 (median -2.00, range -21 to 6) at Month 3 and was -4.09 ± 4.168 (median -3.00, range -21 to 2) at Month 6. <u>Patient assessment of pain VAS</u> The mean and median patient assessment of pain VAS decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -25.50 ± 32.165 mm (median -23.50 mm, range -99 to 54 mm) at Month 3 and was -30.59 ± 33.613 mm (median -31.00 mm, range -100 to 75 mm) at Month 6. <u>Patient global assessment of PsA disease activity VAS</u> The mean and median patient global assessment of PsA disease activity VAS decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -23.39 ± 28.635 mm (median -21.00 mm, range -91 to 47 mm) at Month 3 and was -31.38 ± 30.382 mm (median -34.00 mm, range -92 to 55 mm) at Month 6.

	PGA of PsA disease activity VAS The mean and median PGA of PsA disease activity VAS decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -31.67 ± 20.139 mm (median -31.00 mm, range -83 to 15 mm) at Month 3 and was -38.82 ± 21.933 mm (median -40.00 mm, range -84 to 18 mm) at Month 6. Functional assessment (HAQ) The mean and median HAQ total score decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -0.34 ± 0.499 (median -0.31, range -1.50 to 0.75) at Month 3 and was -0.41 ± 0.518 (median -0.38, range -1.88 to 1.13) at Month 6. BASDAI The mean and median BASDAI score decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -1.91 ± 2.249 (median -1.75, range -7.70 to 3.80) at Month 3 and was -2.40 ± 2.553 (median -2.20, range -8.70 to 2.90) at Month 6. PGA for psoriatic activity Improvements from the screening visit were observed at both Month 3 and Month 6. At Month 3, the skin assessment was clear in 84 patients (56.4%), almost clear in 39 (26.2%), mild in 10 (6.7%), mild to moderate in 3 (2.0%), moderate in 1 (0.7%), and moderate to severe in 1 (0.7%). None of patients had a severe assessment. The result was unknown in 11 patients (7.4%). At Month 6, the skin assessment was clear in 84 patients (56.4%), almost clear in 31 (20.8%) and mild in 10 (6.7%). None of patients had a mild to moderate, moderate, moderate to severe, or severe assessment. The result was unknown in 24 patients (16.1%). Enthesitis index (LEI) The mean and median LEI score decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -1.07 ± 1.451 (median -1.00, range -6 to 3) at Month 3 and was -1.27 ± 1.531 (median -1.00, range -6 to 3) at Month 6. Dactylitis digit count The mean dactylitis digit count decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -0.47 ± 1.128 (median 0.00, range -6 to 2) at Month 3 and was -0.46 ± 1.118 (median 0.00, range -6 to 2) at Month 6.

	DAPSA The mean and median DAPSA total score decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -16.17 ± 12.143 (median -14.32, range -70.75 to 15.00) at Month 3 and was -19.16 ± 13.037 (median -17.12, range -67.50 to 20.19) at Month 6. Correlation tests *Pearson correlation* At Month 3, no statistically significant correlations with any diseases activity measures were observed for hs-CRP only, whereas statistically significant correlations for dactylitis digit count were observed with swollen joint count and LEI index only. Statistically significant direct correlations between all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score. At Month 6, no statistically significant correlations with any diseases activity measures were observed for hs-CRP and dactylitis digit count only. Statistically significant direct correlations between all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score. *Linear mixed model* No statistically significant correlations with any diseases activity measures were observed for hs-CRP (except with DAPSA total score). Statistically significant correlations between all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score (except between tender joint count and LEI index).

Analysis description	**Safety Analysis** All AEs recorded during the study were summarized with descriptive statistics. The incidence of AEs was summarized by SOC and maximum intensity (mild, moderate or severe), type of AE, and relationship to golimumab. All AEs were assigned to a PT and were classified by primary SOC according to the MedDRA thesaurus version 19.1.
Analysis population and time point description	Analysis was performed in the STD set.

Summary	Overall, 23 adverse events were reported in 14 patients (9.4%) and 20 treatment-related adverse events were reported in 12 patients (8.1%). Leukopenia (2 patients, 1.3%), erysipelas (2 patients, 1.3%) and ALT increased (2 patients, 1.3%) were the most common treatment-related adverse events by preferred term. The other treatment-related adverse events that were reported in one patient consisted of thrombocytopenia, bronchitis, genital candidiasis, pharyngotonsillitis, urinary tract infection, AST increased, transaminases increased, dyspnoea, alopecia, pruritus, psoriasis, pustular psoriasis, rash erythematous and rash popular. Three serious adverse events were reported in 3 patients (2.0%) and none of them was fatal or treatment-related. Six patients (4.0%) and 5 patients (3.4%) temporarily and permanently discontinued golimumab due to adverse events, respectively.

CONCLUSIONS:	• Minimal Disease Activity (MDA) after 6 months from the start of treatment with golimumab was achieved in 44.3% of evaluable patients with active PsA. • Male gender, lower age, lower DAPSA, HAQ score, patient assessment of pain VAS and BASDAI score at baseline, and absence of comorbidities, were the predictive factors of MDA at 6 months in the univariable model, while factors that were predictive of MDA at 6 months in the multivariable model were lower age, higher hs-CRP at baseline, lower DAPSA score at baseline, and longer duration of symptoms at baseline. • MDA at 3 months was achieved in 36.2% of patients, and predictive factors did not differ from those observed at 6 months. • Treatment with golimumab was associated with improvements in all disease and functional parameters measured by patient and physician, and in laboratory markers of disease activity: improvements from the screening visit were evident just after 3 months of treatment and were sustained and further increased at 6 months. • Statistically significant direct correlations were observed for all disease activity measures, except for hs-CRP and for dactylitis digit count. • Treatment with golimumab was well tolerated and the results of safety were in line with the known adverse event profile of golimumab.
PUBLICATION:	Not applicable.
REPORT DATE:	27-Jun-2017

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4 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation/Term	Definition
ACR	American College of Rheumatology
ADEPT	Adalimumab Effectiveness in Psoriatic Arthritis Trial
AE	Adverse Event
AIFA	Agenzia Italiana del Farmaco
ALT	Alanine Aminotransferase
AST	Asparate Aminotransferase
ATC	Anatomical Therapeutical Classification
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Function Index
BMI	Body Mass Index
BSA	Body Surface Area
CASPAR	Classification Criteria for Psoriatic Arthritis
CBC	Complete Blood Count
CI	Confidence Interval
COMP	Cartilage Oligomeric Matrix Protein
CPII	C-terminal Propeptides of type II procollagen
CQM	Clinical Quality Management
CRP	C-reactive Protein
CSR	Clinical Study Report
DAPSA	Disease Activity for Psoriasic Arthritis
DAREA	Disease Activity Score for Reactive Arthritis
DAS	Disease Activity Score
DD	Drug Dictionary
DIP	Distal-interphalangeal
DMARD	Disease-modifying Antirheumatic Drug
eCRF	Electronic Case Report Form
ELISA	Enzyme-linked Immunosorbent Assay
ENR	Enrolled (population)
EMR	Electronic Medical Record
ESR	Erythro-sedimentation rate
EudraCT	European Clinical Trials Database
EULAR	European League Against Rheumatism
GCP	Good Clinical Practices
GC&PVC	Global Clinical & Pharmacovigilance Compliance
GISEA	Gruppo Italiano Studio Early Arthritis
GPvP	Good Pharmacovigilance Practice

Abbreviation/Term	Definition
GRAPPA	Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
HAQ	Health Assessment Questionnaire
hs-CRP	High-specificity C-reactive Protein
ICF	Informed Consent Form
IDI	Integrated Discrimination Improvement
IEC	Independent Ethics Committee
IMPACT	Identification and Management of Psoriasis Associated Comorbidity
LEI	Leeds Enthesitis Index
MCP	Metacarpo-phalangeal
MD	Mean Difference
MDA	Minimal Disease Activity
MedDRA	Medical Dictionary for Regulatory Activities
MMP-3	Matrix Metalloproteinase-3
MSD	Merck Sharp & Dohme
NIS	Non-interventional Study
NSAID	Non-steroidal Anti-inflammatory Drug
OMERACT	Outcome Measures in Rheumatology
OR	Odds Ratio
PASI	Psoriatic Area and Severity Index
PGA	Physician Global Assessment
PIP	Proximal Inter-phalangeal
PT	Preferred Term
PROBE	Prospective Randomized Open Blinded End-point
PsA	Psoriasic Arthritis
RA	Rheumatoid Arthritis
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SD	Standard deviation
SJC	Swollen Joint Count
SmPC	Summary of Product Characteristics
SOC	System Organ Class
STD	Standard (population)
SwePsA	Swedish Early Psoriatic Arthritis
TICOPA	Tight Control Of Psoriatic Arthritis

Abbreviation/Term	Definition
TJC	Tender Joint Count
TNF	Tumour Necrosis Factor
VAS	Visual Analogue Scale
VEGF	Vascular Endothelial Growth factor
WHO-DRL	World Health Organization-Drug Reference List

5 ETHICS

5.1 Independent Ethics Committee

All Independent Ethics Committees (IECs) reviewed and approved the study protocol. A complete list of IECs, names and committee chairs can be found in Appendix 16.1.3.1.

An IEC is a review panel responsible for ensuring the protection of the rights, safety, and well-being of human subjects involved in this clinical investigation. All IECs used for this trial were adequately constituted in accordance with local regulations to provide assurance of human subject protection.

The IEC address and dates of decisions to approve the protocol and any amendments are also provided in Appendix 16.1.3.1.

5.2 Ethical Conduct of the Trial

This trial had investigator meetings at the outset to review all protocol procedures and investigator responsibilities under Good Clinical Practices (GCP). At the meeting, the conduct of the trial was explained and instructions were provided to ensure accuracy and consistency in data collection.

This trial was conducted in substantial conformance with GCP requirements and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Investigators understood that by signing the Protocol Investigator Signature Page they provided their commitment to comply with applicable GCP regulations and guidances and to conduct the trial in accordance with the protocol.

The Merck Sharp & Dohme Corp., a Subsidiary of Merck & Co., Inc., Code of Conduct for Clinical Trials is provided within the trial protocol in Appendix 16.1.1.

5.3 Subject Information and Informed Consent Form

5.3.1 Subject Informed Consent

The original, generic, sponsor-approved written informed consent form (ICF) including written subject information used in the study is provided in Appendix 16.1.3.2.

Before the start of the study, each subject was provided with a subject information leaflet giving details of the study procedures. Subjects were instructed that they were free to obtain further information from the Investigator at any time and that they were free to withdraw their consent and to discontinue their participation in the project at any time without prejudice.

Each potentially eligible subject was also informed verbally of the study's objectives and overall requirements. If the subject was willing to participate in the study, he/she was requested to give written informed consent and privacy consent after being given sufficient time to consider his/her participation and the opportunity to ask for further details. A copy of the signed ICF and of the privacy form were given to the subject. Although nursing staff could be involved in describing the trial to a subject, the investigator/sub-investigator had to participate in discussions with the subject and sign and personally date the ICF.

The initial ICF, any subsequent revised written ICF and any written information provided to the subject had to receive the IEC's approval/favourable opinion in advance of use. The subject or his/her legally acceptable representative should have been informed in a timely manner if new information became available that could be relevant to the subject's willingness to continue participation in the study. The communication of this information was provided and documented via a revised consent form or addendum to the original consent form that captured the subject's dated signature or by the subject's legally acceptable representative's dated signature.

The ICF adhered to IEC requirements, applicable laws and regulations and Sponsor requirements.

Further details on the procedures for the collection of ICF are given in Section 9.2 and 9.5.1.

A copy of the ICF including written subject information and information on subject's privacy used in the study is included in Appendix 16.1.3.2.

6 INVESTIGATORS AND TRIAL ADMINISTRATIVE STRUCTURE

This trial was conducted at 23 investigational sites in Italy.

PPD Italy, was the study coordinator.

A list of investigators including trial centres and investigator qualifications is provided in Appendix 16.1.3.1. Information for the administrative structure of the trial is provided in Appendix 16.1.4.2.

7 INTRODUCTION

Background

Psoriatic arthritis (PsA) is a chronic systemic inflammatory disorder characterized by inflammation of the joints and surrounding structures, in association with cutaneous psoriasis, can be more heterogeneous and more complex than other inflammatory arthritis such as rheumatoid arthritis (RA). Skin and nail involvement, arthritis of the peripheral and axial joints, inflammation of entheses, dactylitis, are all clinically relevant PsA manifestations and can impact PsA patients' quality of life (1, 2). The introduction of highly effective biologic agents, particularly inhibitors of tumour necrosis factor (TNF), has changed the therapeutic approach to patients with PsA and has allowed greater levels of disease control for affected patients (3-9).

To evaluate the ability to achieve the remission in PsA, several studies have utilized remission criteria used in RA which may substantially lack of content validity in a more complex disease such as PsA. With greater clinical success, there has been a growing consensus that the goal of treatment for all PsA patients should be achieving the lowest level of disease activity possible for all domains of the disease. The GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) project developed a PsA specific definition of Minimal Disease Activity (MDA) allowing for more specific evaluation of disease activity and desirable disease status (10, 11). A natural follow-on to this is the idea that PsA patients should also be treated to a target. Indeed, an international group has just informed on the treatment approaches that help achieve these states (12). Of note, a controlled study specifically addressing this, called TICOPA (Tight Control Of Psoriatic Arthritis) has been published (13-14).

A definition of MDA has been developed specifically for PsA (10). According to these criteria, a PsA patient may be classified as having MDA if they meet at least 5 of these 7 criteria: 1) tender joint count ≤ 1; 2) swollen joint count ≤ 1; 3) Psoriasis Area and Severity Index (PASI) ≤ 1 or body surface area (BSA) of psoriasis involvement $\leq 3\%$; 4) patient pain visual analogue scale (VAS) $\leq 15/100$; 5) patient global assessment of PsA disease activity VAS ≤ 20; 6) Health Assessment Questionnaire (HAQ) score ≤ 0.5; 7) tender enthesial points ≤ 1. The first application of the criteria was within the Toronto Psoriatic Arthritis Clinic, in an observational study in which patients received standard care for PsA according their clinical need and were followed for up to 5 years (15-16). In that observational cohort, 60% (208/334) of patients with PsA achieved MDA at 1 or more visits and was sustained in one-third of the population studied. This study also identified the factors associated with the achievement of MDA finding a prognostic role for the degree of inflammation and for the pattern of articular disease. The MDA criteria were subsequently validated using data from the randomized, controlled IMPACT (Identification and Management of Psoriasis Associated Comorbidity) and IMPACT2 trials in which patients received infliximab for the treatment of PsA (11). In those trials there were statistically significant differences (infliximab vs. placebo) in the percentage of patients who achieved MDA at week 24 (52% vs. 21%). In the SwePsA (Swedish Early Psoriatic Arthritis) Register, MDA was achieved in 40.1% of patients at 5 years. (17). In an Italian study on a cohort of PsA patients starting anti-TNF, at the 12 months follow-up MDA was achieved in 33 (41.8%) subject receiving infliximab, in 41 (36.9%) of those receiving etanercept and in 24 (30%) of those receiving adalimumab (18).

The recent results of a post-hoc analysis of the ADEPT (Adalimumab Effectiveness in Psoriatic Arthritis Trial) study indicated that significantly more patients treated with adalimumab achieved MDA by week 24 compared with placebo (39% vs. 7%). (19). This study also demonstrated that the modification of the MDA by replacing PASI $\leq$ 1 with Physical Global Assessment (PGA) assessments did not alter the results, improving reliability and feasibility of practical use of the index. The PASI is one of the components in the MDA, but it is somewhat complicated to calculate. While it has been used extensively in clinical trials, the PASI is not sensitive to change for small areas of involvement, and it is not often employed in clinical practice (20). The PGA of disease activity is another measure for psoriasis that has been used extensively in clinical trials and it may be employed in a static form that measures the physician impression form in which the global improvement from baseline is evaluated (20-23).

Over the last few years, different tools were used for measuring the disease activity in patients with PsA. The Disease Activity for PSoriatic Arthritis (DAPSA), which assesses 68 joints for tenderness and 66 joints for swelling, allows evaluating the disease activity specific for PsA taking into account the number and the localization of specific joints for this pathology.

TNF-alpha therapies have revolutionized the management of PsA. However, not all patients with PsA treated with a TNF-alpha achieve a good response, 20-30% of patients still fail to respond (24). Given the risk of adverse events and the considerable costs of biologics, there is a need to identify predictors of response before starting biotherapy (25).

Few studies addressed whether predictors for good clinical response to treatment with TNF-inhibitors in patients with PsA can be identified. A study on adalimumab demonstrated that lower impairment of physical function, greater pain, male sex and no systemic treatment with glucocorticoids were factors that increased the chance of achieving a good response according to EULAR criteria (26). In the SwePsA Register the most important predictors of MDA at the 5-year follow-up were: short delay between onset of symptoms and diagnosis, preserved function, and male gender (17). An Italian cohort study identified predictors of MDA in patients with PsA receiving anti-TNF. They found that age, C-reactive protein (CRP), Bath Ankylosing Spondylitis Function Index (BASFI), obesity, the presence of metabolic syndrome are negative predictors of achieving MDA (27-28).

Also biomarkers of clinical response have been evaluated in a few studies. A recent analysis of GO-REVEAL provided insight into several panels of markers that may have utility in identifying PsA patients likely to achieve American College of Rheumatology 20% improvement criteria (ACR20), Disease Activity Score 28 joints (DAS28) response, or Psoriasis Area and Severity Index with 75% improvement (PASI75) following golimumab treatment (29). Chandran et al. demonstrated that baseline as well as reduction in serum of matrix metalloproteinase-3 (MMP-3) and increase in serum cartilage oligomeric matrix protein (COMP) are independently associated with response to TNF-alpha therapy in patients with PsA (30). The GRAPPA together with the OMERACT consider high priority candidates associated with response to therapy with TNF-alpha in PsA patients the following biomarkers: high sensitivity CRP (hs-CRP), MMP-3, the C-terminal propeptides of type II procollagen (CPII) (31). Moreover, Ramonda et al. observed that MMP-3, hs-CRP and VEGF appear to be useful for the early detection of PsA and to monitor disease progression (32).

Rationale

Aim of this study was to develop a clinical prediction model for the achievement of 6-month MDA in PsA patients starting golimumab. The clinical variables collected did not alter treatment selection nor use by the physician and were collected as part of standard clinical practice. The clinical candidate predictors retrieved from the literature [gender, age, BMI, disease duration, polyarthritis, ESR/CRP, concurrent DMARD, disease activity measure (e.g. DAPSA), functional disability measure (e.g. HAQ)] were combined in a first prediction model and then soluble biomarkers (hs-CRP, MMP-3, CPII) for the improvement of the performance of the clinical prediction model were evaluated.

Identifying predictors of response to biologic therapies would improve care in selecting patients able to respond. These would also improve medical cost-effectiveness because they would decrease the number of non-responding patients.

This study responded to the need of tailoring treatment that would allow clinicians to practice a more effective and personalized medicine, optimizing the outcomes of patients with PsA as well as the treatments management.

8 OBJECTIVES AND HYPOTHESES

The scope of this study was to test the following hypotheses:

- In patients with active PsA and inadequate response to conventional therapies, identifying predictors of MDA to golimumab can improve care in selecting patients able to achieve the target.
- The a priori hypothesis to be tested was that a combination of clinical and immuno-biological variables might progressively enhance our ability to predict response to golimumab in PsA patients.

Primary objective

The primary objective of the study was to develop a clinical prediction model, using a combination of baseline (pre-antiTNF treatment) clinical variables, for the achievement of 6-month MDA in PsA patients starting golimumab.

Secondary objectives

The secondary objectives of the study were:

- To evaluate candidate immune-biological variables (biomarkers) for the improvement in performance of the clinical prediction model for the achievement of 6-month MDA in PsA patients starting golimumab;
- To develop a clinical prediction model, using a combination of baseline (pre-antiTNF treatment) clinical variables, for the achievement of 3-month MDA in PsA patients starting golimumab;
- To explore clinical prediction models using a combination of baseline (pre-antiTNF treatment) clinical variables against secondary outcome measures (DAPSA, HAQ, Leeds enthesitis index, dactilytis 0-6 month changes);
- To assess changes in disease activity response evaluated by Disease Activity for Psoriatic Arthritis (DAPSA) at 3 and 6 months vs. baseline;
- To assess change in functional score evaluated by Health Assessment Questionnaire at 3 and 6 months vs. baseline;
- To assess change in enthesitis score evaluated by Leeds Enthesitis Index (LEI) at 3 and 6 months vs. baseline;
- To assess change in dactilytis score evaluated by dactylitic digit count at 3 and 6 months vs. baseline.

9 INVESTIGATIONAL PLAN

9.1 Trial Design and Plan

This was a multicenter, prospective, observational study conducted in Italy.

PsA patients fulfilling the study inclusion and exclusion criteria outlined in Section 9.3.1 and 9.3.2, respectively, were enrolled and followed prospectively for 6 months with data collection at the approximate time points: baseline (pre-treatment), 3 months and 6 months. A time window of approximately ± 4 weeks was envisaged for follow-up visits.

The study was expected to last approximately 18 months with an inclusion period of 12 months. The maximum exposure period per patient was 6 months.

Data were collected from multiple clinics throughout Italy. Based on the protocol, an electronic case report form (eCRF) was developed for data collection where each centre was asked to enter the data. If available, socio-demographic data and disease characteristics were extracted from medical records, otherwise these data were collected at enrolment.

All data were subsequently entered into a single database stored centrally and analyzed.

All investigators were informed of final results upon completing study.

9.2 Rationale for Trial Design

The observational, prospective, multicentre study was considered an appropriate design to identify predictors of response to golimumab in PsA patients.

The definition in the European Directive 2001/20/EC non interventional studies (NIS) was used as a general principle of this study. These principles included the following regarding the enrolment and monitoring of patients:

- Patient population: PsA patients followed in normal practice, in which golimumab had been newly prescribed, were asked to participate in the study. In patients who had been prescribed these agents the moment of prescription is normally separated from the moment the agents were administered (e.g. administrative procedures, day-clinic visit to be scheduled, retrieval of the medicine at the pharmacist, etc.). For the study, the ICF was presented at the visit during which the medicine was administered. After signing the ICF, those patients agreeing to participate were followed for approximately 6 months following the initiation of the newly prescribed medicine.
- Patients who had received a prescription golimumab could be included after signing an ICF. As the decision to treat the patient with a medicine of interest in this study fell within routine practice and had to be completed prior to the decision to include the patient in the study, the ICF did not provide any information on potential benefits or risks of the drug prescribed. The patient should have been informed about drug benefits and risks as per normal practice using the patient leaflet and patient alert card, as locally applicable, prior to inclusion in the study.

9.2.1 Rationale for Endpoints

The clinical and immune-biological parameters evaluated in this study were considered as adequate for the identification of predictors of response to golimumab in patients with active PsA and inadequate response to conventional therapies.

The endpoints chosen for the evaluation of disease activity indexes consisted in domains and instruments that have in general performed well in previous studies and were chosen by GRAPPA members and established at the various OMERACT conferences, as being essential components of psoriatic disease documentation (33-34).

Appropriate prognostic biomarkers were evaluated to assess their predictive role in the clinical outcomes of the study.

9.3 Selection of Trial Population

The study population included all patients referred to participating clinics and diagnosed with PsA that fulfilled the study inclusion and exclusion criteria outlined in Section 9.3.1 and 9.3.2, respectively. Patients were enrolled after the decision to treat with golimumab was made, but before the initiation of the newly prescribed medicine, i.e. patients had not to have initiated treatment prior to the baseline data collection (enrolment).

This study planned to enrol 140 patients newly prescribed treatment with golimumab according to regular clinical practice. For an efficient conduction of the study, about 20 key Italian university and hospital centres for rheumatic diseases care were to be involved in the study. These were centres of excellence including GISEA (Gruppo Italiano Studio Early Arthritis) centres expert in PsA and managing about 10 patients/month treated with biologic drugs for PsA. For this study, each centre was planned to recruit about 7 patients during the recruitment period of 12 months.

An eligibility run was performed in about 20 sites in order to ensure the final number of sites with the proper criteria such as: hospitals with specialized physicians for rheumatic disease care, interest in participation and appropriate qualifications of principal investigator as well as designee involved, complying with protocol procedures and ICF, cooperative within the context of review of study documents (eCRF, ICF), available hospital procedures, laboratory and personnel within the context of the study, appropriate study population and ability to enrol the required number of patients within a short time frame period, as defined within the study.

The sites selected to participate in this study should have fulfilled the following criteria:

- Physicians should have had experience in the biologic treatment of patients with PsA;
- Physicians should have maintained their patients' records regularly.

9.3.1 Inclusion Criteria

A subject had to meet all the criteria listed below to participate in the study.

1. Adult ≥ 18 years of age with PsA predominantly characterized by peripheral synovitis (as per CASPAR [Classification Criteria for Psoriatic Arthritis] criteria);
2. Subject non-responder or insufficient responder to the conventional therapies according to physician’s decision;
3. Subject newly prescribed golimumab as indicated by the treating physician according to usual clinical practice;
4. Patient was informed of the potential benefits and risks of golimumab as per normal practice using the patient alert card and the product leaflet;

5. Concomitant treatment with traditional DMARDs was allowed according to investigators' decision.
6. Naive to anti-TNFs or other biologic agents prior to initiation of golimumab as indicated by the patient's medical records. In addition, this was evaluated by the investigator and patient interview during screening.
7. Data on the following parameters (a set of core variables) had to be available at enrolment (prior to the first injection of golimumab): age, gender, BMI, diagnosis duration (duration since date of diagnosis), information on presence/absence of polyarthritis, ESR/CRP, concurrent DMARD, functional disability measure (e.g. HAQ), disease activity measure (DAPSA). The associated timeframe for the acute phase reactants as well as clinical and functional outcome measures availability were ± 4 weeks of golimumab prescribed;
8. Signed informed consent form. The informed consent included a section relating to the request for consent for evaluation of biomarkers in serum from blood sample as per the Italian Ministry of Health regulation (AIFA Determination of March 2008).
9. Each female subject had to agree to use a medically accepted method of contraception while participating in the study.

9.3.2 Exclusion Criteria

A subject meeting any of the exclusion criteria listed below had to be excluded from participating in the study:

1. Prior or current use of an anti-TNF or other biologic agents for any disease;
2. Patient who had already started treatment with golimumab at the time of the enrolment;
3. Current MDA;
4. Any contraindication to treatment with golimumab as per Summary of Product Characteristics (SmPC).

9.3.3 Subjects Withdrawal/Discontinuation Criteria

Not applicable for this study. No subject withdrawal/discontinuation criteria were pre-defined in the study protocol.

9.4 Treatments

9.4.1 Treatments Administered

In agreement with the observational nature of the study, patients were treated as per routine clinical practice and entirely according to the judgment of the physician.

There was no study-related intervention on the medical or drug management of the patient.

9.4.2 Identity of Investigational Product

Due to the observational nature of this study, no study medication was dispensed to participating patients.

Treatment with golimumab was accessed as per routine customary practice at each site/clinic. More specifically, the sponsor did not supply or reimburse any treatment used by the patients in the study.

9.4.3 Dose Selection and Timing of Dose Administration

Not applicable. The posology and method of administration of golimumab were according the SmPC.

9.4.4 Trial Blinding/Masking

Not applicable.

9.4.5 Randomization or Treatment Allocation

No randomisation or treatment allocation procedures were used in this study.

Each patient who signed an ICF was defined as participating in the study. At the screening visit the subject was given a sequential patient number, assigned in the format XX-YYY, where XX was the site number and YYY was a sequential number beginning with 001. E.g. the patient enrolled first at site 2 had patient No. 02-001, while the second patient in that site had No. 02-002.

9.4.6 Concomitant Medications

No pre-determined criteria for permitted and non-permitted medications taken at entry and during the study were defined.

The investigator or qualified designee recorded all medication, if any, taken by the subject at baseline and during the study.

9.5 Clinical Procedures/Assessments

9.5.1 Measurements Assessed and Timing of Assessment

The study procedures to be performed at each visit are shown in the Study Flow Chart (Figure 9.5.1-1). Individual study procedures are described in detail below. It could be necessary to perform these procedures at unscheduled time points if deemed clinically necessary by the investigator. Furthermore, additional evaluations/testing could be deemed necessary by the Sponsor for reasons related to subject safety.

Data were collected from multiple centres. Based on the protocol, an Electronic Medical Record (EMR) was developed for data collection. Each local centre was asked to enter the data into the EMR. All the data entered in the EMR were entered into a single database stored centrally and analyzed.

Figure 9.5.1-1. Study Flow Chart

Study Period:	**Enrolment**	**Observation/Follow-up**[b]	
Visit:	*Screening/ Baseline*[a]	*3-month follow-up*	*6-month follow up = study end*
Study month	*0*	*3*	*6*
Informed Consent	X		
Inclusion/Exclusion Criteria	X		
Socio-demographic data	X		
Age	X		
Gender	X		
Body Mass Index	X		
Metabolic syndrome	X		
Smoking	X		
Comorbidities	X		
Symptom duration	X		
Time from diagnosis	X		
Physical examination (1)	X	X	X
Joint counts (66 SJC, 68 TJC)	X	X	X
Patient global assessment of pain (VAS)	X	X	X
Patient global assessment of PsA disease activity (VAS)	X	X	X
Physician Global Assessment of disease activity (VAS)	X	X	X
Health Assessment Questionnaire (HAQ)	X	X	X
BASDAI score	X	X	X
DAPSA score	X	X	X
PGA for psoriatic activity	X	X	X
LEI Index	X	X	X
Dactylitic digit count	X	X	X
Laboratory test (2)	X	X	X
MDA	X	X	X
Serum Sample (3)	X		X
Medications (4)	X	X	X

Abbreviations: SJC = Swollen Joint Count; TJC = Tender Joint Count; VAS = Visual Analogue Scale; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; DAPSA= Disease Activity for Psoriatic Arthritis; LEI = Leeds Enthesitis Index; PGA = Physician global assessment; MDA = Minimal Disease Activity

[a] Enrolment could be any time after the treating physician had made the decision to prescribe golimumab but before the patient received the treatment. It was not mandatory for all procedures to occur on the same day. Baseline data could be obtained on the day of or prior to the first dose of golimumab.
[b] A time window of approximately ± 4 weeks was envisaged for follow-up visits.

(1) Complete physical examination for screening visit, including height and weight.
(2) To include routinary chemistry and haematology, ESR, CRP.
(3) Serum samples were collected at baseline and at 6 months and were then sent to the central laboratory for the retrospective assessment of biomarkers [high sensitivity C-reactive protein (hs-CRP), matrix metalloproteinase-

3 (MMP-3), C-terminal propeptides of type II procollagen (CPII)].
(4) Data were captured on medication given for the treatment of PsA and comorbidities. The categories of medications, and the number of days on each category of treatments were recorded.

Patient characteristics

The following parameters were recorded at baseline:

- Age (years);
- Gender (male/female);
- Weight (kg);
- Height (cm);
- Body mass index (kg/m^2);
- Metabolic syndrome;
- Smoking history;
- Comorbidities: uveitis, inflammatory bowel disease, hypertension, stroke, ischemic heart disease, thyroid disease, liver disease, lung disease, renal disease;
- Symptom duration;
- Time from diagnosis.

The following parameters were recorded at baseline, and at 3 and 6 months:

Parameters for MDA assessment:

- Swollen joint count;
- Tender joint count;
- Physician global assessment (PGA) for Psoriatic Activity (Clear or Almost clear);
- Patient global assessment of pain (Visual Analogue Scale, VAS);
- Patient global assessment of PsA disease activity (VAS);
- Physician global assessment of disease activity (VAS);
- Functional status (HAQ);
- Leeds Enthesitis Index (LEI).

Other parameters:

- Dactylitis score;
- Laboratory tests;
- Level of disease activity (DAPSA);
- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);
- Medications for PsA and comorbidities manifestations.

Biomarkers evaluation at baseline and 6 months:

- High sensitivity C-reactive protein (hs-CRP);
- Matrix metalloproteinase-3 (MMP-3);
- C-terminal pro-peptides of type II procollagen (CPII).

The serum samples were collected and were sent to the central laboratory for the retrospective assessment.

Study procedures

The following procedures/evaluations were performed in the study:

Administrative procedures

General informed consent

Consent had to be documented by the subject's dated signature or by the subject's legally acceptable representative's dated signature on a consent form along with the dated signature of the person conducting the consent discussion.

The informed consent included a section relating to the request for consent for evaluation of biomarkers in serum from blood sample as per the Italian Ministry of Health regulation (AIFA Determination of March 2008).

A copy of the signed and dated consent form should have been given to the subject before participation in the study.

The initial informed consent form, any subsequent revised written informed consent form and any written information provided to the subject had to receive the IEC's approval/favourable opinion in advance of use. The subject or his/her legally acceptable representative should have been informed in a timely manner if new information became available that could be relevant to the subject's willingness to continue participation in the study. The communication of this information was provided and documented via revised consent form or addendum to the original consent form that captured the subject's dated signature or by the subject's legally acceptable representative's dated signature.

Specific about a study and the study population was added to the consent form template at the protocol level.

The informed consent adhered to IECs requirements, applicable laws and regulations and Sponsor requirements.

Medical history

A medical history was obtained by the investigator or qualified designee, including a detailed history of psoriatic arthritis and any other significant medical history.

Medications

Data were captured on medication given for the treatment of PsA: prior to study entry, at baseline and during the study (at the time points as indicated in the study flow chart).

These medications included: non-steroidal anti-inflammatory drugs (NSAIDs); type and number of previous DMARDs, corticosteroids, analgesics, medications for PsA

manifestations and comorbidities. For medications, the categories of medications and the number of days on each category of treatments were recorded.

Data on golimumab usage as well as reasons for discontinuation of treatment were collected at baseline, 3 months and 6 months.

Clinical assessments

Review of Inclusion/Exclusion Criteria

The inclusion and exclusion criteria were reviewed by the investigator or qualified designee to ensure that the subject qualified for the trial.

General Physical Examination

A complete physical examination was performed. If the subject was discontinued for any reason during the treatment phase, every attempt should have been made to perform a final physical examination.

Disease Activity Indexes and Instruments for PsA clinical evaluation

The evaluations of PsA included the following domains:

- 68-tender and 66-swollen joints count (68-TJC and 66-SJC), including the temporomandibular, sternoclavicular, acromioclavicular, shoulder, elbow, wrist (including the carpometacarpal and intercarpal joints as one unit), metacarpo-phalangeal (MCP), Proximal inter-phalangeal (PIP), distal-interphalangeal (DIP), hip, knee, talotibial, midtarsal (including subtalar), metatarsophalangeal, and interphalangeal joints of the toes (proximal and distal joints of each toe counted as one unit);
- Patient's assessment of pain (Visual Analogue Scale - VAS);
- Patient's global assessment of disease activity (VAS);
- Physician's global assessment (PGA) of disease activity (VAS);
- Patient's assessment (VAS) of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);
- Disease Activity for PSoriatic Arthritis (DAPSA);
- Patient's assessment of physical function using the Health Assessment Questionnaire (HAQ) and the C-reactive protein (CRP) level;
- Assessment of dactylitis;
- Assessment of Leeds Enthesitis Index (LEI).

The BASDAI consisted of 10 cm VAS used to answer 6 questions pertaining to the 5 major symptoms of Ankylosing Spondylitis: fatigue, spinal pain, joint pain/swelling, areas of localized tenderness, morning stiffness. To give each symptom equal weighting, the mean of the two scores relating to morning stiffness (intensity and duration) was taken. The resulting 0 to 50 score was divided by 5 to give a final 0–10 BASDAI score.

The DAPSA was adapted from the DAREA (disease activity score for reactive arthritis), a score validated for reactive arthritis (35). It was developed from a clinical cohort and validated using clinical trial data (36). It is composed of five untransformed, unweighted

variables, including two patient-centred items (PGA and pain on an 11-point numeric rating scale [NRS]), one physician centred item (66-SJC), one item dependent on patient and physician (68-TJC) and a laboratory variable (CRP in mg/dl). The composite score is a simple sum of the five single scores.

For dactylitis, a simple dactylitic digit count was applied. The tender dactylitis count is a simple count based on the presence or absence of tender joints. Twenty digits are assessed as entire digits, looking for signs of tender dactylitis. Dactylitis index ranges from 0 to 20.

The Leeds Enthesitis Index (LEI) was used for the measurement of enthesitis. The LEI is the only measure developed specifically for PsA (37) and includes an assessment of 6 sites: bilateral Achilles tendon insertions, medial femoral condyles and lateral epicondyles of the humerus. Tenderness at each site was quantified on a dichotomous criteria (0 = not tender; 1= tender). LEI score ranges from 0 to 6 and is the sum of each of the 6 single scores.

The Physician Global Assessment (PGA) scale is an assessment of psoriasis on a 7-point scale (0 = clear, 1 = almost clear, 2 = mild, 3 = mild to moderate, 4 = moderate, 5 = moderate to severe, and 6 = severe) (20-23). For modification of the MDA, PASI $\leq$ 1 was substituted with PGA “Clear” or “Almost clear” (19).

Functional assessments

The Health Assessment Questionnaire (HAQ) was used. It was originally developed to assess disability in rheumatoid arthritis, by focusing on physical disability and pain and has been used widely in inflammatory arthritis clinical trials, including PsA (38). HAQ is a self-administered questionnaire using the patient's functional ability during the last week. It consists of 20 items converging to 8 scales measuring dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. The patients rated each activity as 0 = without any difficulty, 1 = some difficulty, 2 = much difficulty and 3 = unable. The final score was calculated as the average of the maximum score of each subscale, and it ranged from 0 to 3 with higher scores indicating more disability. At each of the scheduled visits, physician asked patients to complete the questionnaire.

Visual analogue scale

A Visual Analogue Scale (VAS) was used for the assessment of the following measures: patient’s assessment of pain, patient’s global assessment of disease activity, PGA of disease activity. It is a testing technique for measuring subjective phenomena (as pain or global disease assessment) in which a patient selects from a gradient of alternatives (as from “no pain” to “worst imaginable pain” or from “every day” to “never”) arranged in linear fashion. VAS is usually measured with metric rule. The line on the eCRF was exactly 10 cm long. Scores were recorded in millimetre format (from 0 to 100).

Laboratory tests

High-specificity C-reactive protein (hs-CRP) was recorded in nmol/L and Erythrocyte sedimentation rate (ESR) was recorded in mm/h at baseline (prior to the administration of golimumab). The association time frame for hs-CRP/ESR availability was ± 4 weeks of golimumab prescribed. At approximately 3 months and approximately 6 months following the administration of golimumab, provided that hs-CRP and ESR were collected as part of the normal clinical follow up, these results were obtained as well. The date of hs-CRP and/or ESR was recorded in the eCRF.

Complete blood count (CBC) and serum biochemistry tests could be done locally as per routine practice.

Serum biomarkers

According to Italian Minister of Health regulation on observational studies, "Guidelines for the classification and management of observational studies on drugs" (AIFA Determination of March 2008), blood tests, the use of which is justified by the rationale of the study, are to be considered current clinical practice procedures. Therefore, the evaluation of serum biomarkers fell in current clinical practice. The centres collected serum samples for biomarker evaluation of patients enrolled in the study after asking the Informed Consent to the patients for this evaluation.

The evaluation of prognostic biomarkers is not used in the clinical management of the patient but for the evaluation of their potential usefulness on improving the prediction of clinical outcomes. The assessment of biomarkers was a parallel study in the clinical study and was done according to the PROBE (Prospective randomized open blinded end-point) design, in which serum samples were collected prospectively from the study population. At baseline the serum samples were collected and were then sent to the central laboratory for the retrospective assessment (39).

Based on the evidence from previous studies and GRAPPA Group (29-32), the following biomarkers were selected and assayed using commercial ELISA kits according to manufacturers' instructions: hs-CRP, MMP-3 and cartilage biomarkers CPII.

Blood samples were drawn at baseline and 6-months, were processed immediately, and serum aliquots were frozen at -20 °C or -80 °C at the site before the shipment to the central laboratory (Quintiles Ltd, TheAlba Campus, Rosebank, Livingston, EH54 7EG United Kingdom) for biomarkers analysis. Samples were centrally tested and results were sent to the statistical analysis unit.

Study parameters and measurements

Primary endpoint

The primary endpoint of the study was the response rate to treatment, defined as proportion of patients achieving MDA at 6 months.

PsA patients were classified as having MDA if they met at least 5 of these 7 criteria (11):

- Tender joint count ≤ 1;
- Swollen joint count ≤ 1;
- Physician global assessment (PGA) for Psoriatic Activity (Clear or Almost clear);
- Patient pain visual analogue scale (VAS) ≤ 15/100;
- Patient global assessment of PsA disease activity VAS ≤ 20;
- Health Assessment Questionnaire (HAQ) score ≤ 0.5;
- Tender enthesial points ≤ 1.

Secondary endpoints

The secondary endpoints of the study were:

- Proportion of patients achieving MDA at 3 months;
- Evaluation of clinical outcomes at 3 and 6 months (change vs. baseline:
  - Change in Leeds Enthesitis Index (LEI);
  - Change in dactilytis score;
  - Changes in functional score (by HAQ);
  - Change in Disease Activity in Psoriatic Arthritis (DAPSA) composite scores.

Adverse events

Adverse event

An adverse event (AE) was defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product or who undergoes a protocol-specified procedure and which does not necessarily have to have a causal relationship with this treatment or procedure. An AE could therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition that was temporally associated with the use of the Sponsor's product, was also an AE.

Changes resulting from normal growth and development that did not vary significantly in frequency or severity from expected levels were not to be considered AEs. Examples of this may include, but are not limited to, teething, typical crying in infants and children and onset of menses or menopause occurring at a physiologically appropriate time.

Sponsor's product included any pharmaceutical product, biological product, device, diagnostic agent or protocol-specified procedure, whether investigational (including placebo or active comparator product) or marketed, manufactured by, licensed by, provided by or distributed by the Sponsor for human use.

AEs could occur during the course of the use of the Sponsor's product in studies or within the follow-up period specified by the protocol, or prescribed in clinical practice, from overdose (whether accidental or intentional), from abuse and from withdrawal.

Serious adverse event

A serious adverse event (SAE) was defined as an AE which was fatal or life threatening, resulted in persistent or significant disability/incapacity, required inpatient hospitalization, prolongation of existing inpatient hospitalization, or was a congenital anomaly/birth defect, cancer, the result of an overdose or was another important medical event.

Other important medical events that might not result in death, might not be life-threatening, or might not require hospitalization could be considered a SAE when, based upon appropriate

medical judgment, they could jeopardize the patient or subject and could require medical or surgical intervention to prevent one of the other outcomes listed previously.

Other relevant safety information

The following events were considered important safety information and should have been collected/reported using the same timeframes and reporting methods as SAEs:

- Exposure of product during pregnancy or lactation;
- Lack of effect.

Causality assessment

A causality assessment (attribution) had to be performed and recorded for each SAE/non-serious AE in relationship to a Sponsor's product. During studies with direct patient contact (visits), the assessment of causality was determined by an investigator who was a qualified physician according to his/her best clinical judgment. The following criteria were used as guidance (not all criteria had to be present to be indicative of attribution to a Sponsor's product: there was evidence of exposure to the Sponsor's product; the temporal sequence of the AE onset relative to the administration of the Sponsor's product was reasonable; and the AE was more likely explained by the Sponsor's product than by another cause. In studies without direct patient contact, the assessment of causality was to be determined by a notation of attribution in medical records. Attribution could be assigned by the investigator or the Sponsor. Examples included a drug-induced rash that an investigator attributed to a specific product, or a clinical notation that a product was discontinued because it caused insomnia.

9.5.2 Appropriateness of Measurements

As anticipated in Section 9.2.1, the clinical and immune-biological parameters evaluated in this study were considered as adequate for the identification of predictors of response to golimumab in patients with active PsA and inadequate response to conventional therapies.

9.5.3 Drug Concentration Measurements

Not applicable.

9.6 Data Quality Assurance

Clinical studies conducted worldwide by the sponsor are subject to Quality Control (QC) and Quality Assurance (QA) oversight, including independent audits, as prescribed by company and departmental Standard Operating Procedures.

Quality Control & Quality Assurance activities are intrinsic to all clinical trial-related activities. Such activities include, but are not limited to, on-site monitoring inclusive of source data verification, medical monitoring of clinical trial data and resultant databases and quality reviews of regulatory submission documents.

The Clinical Quality Management (CQM) group implemented Quality Control Plans to assess the state of compliance (real-time measurements) and to identify any potential process gaps (risk-based selection of processes). CQM analyzed the data from these Quality Control Plans together with the data from internal compliance audits and Health Authority inspections. The goal was to identify any emerging risks/trends of non-compliance to support

continuous process improvement as well as to prevent the recurrence of any identified quality issues.

An independent compliance oversight function also exists within the organization. The Global Clinical & Pharmacovigilance Compliance (GC&PVC) group is part of Merck Compliance. This group independently assessed compliance through a comprehensive, risk-based audit program to ensure compliance with applicable Good Clinical Practice (GCP), Good Pharmacovigilance Practices (GPvP) regulations and applicable company policies and procedures.

The Merck Code of Conduct within the protocol describes how the trial was monitored to ensure compliance with GCP (Appendix 16.1.1.1).

All authors reviewed this clinical study report (CSR) for accuracy of scientific content. Signatures of the authors of this CSR authors are in Appendix 16.1.5.2. The coordinating investigator's signature is in Appendix 16.1.5.1.

9.7 Changes in the Conduct of the Trial

No protocol amendments were generated at any time during the study.

9.8 Statistical Analysis Plan

A Statistical Analysis Plan (SAP) was issued on 09 Feb 2017 before the database lock and contained full details of all planned summaries, listings and analyses. The final SAP is included in Appendix 16.1.9.

Sample size

The sample size was estimated based on the primary objective of the cohort study, i.e. to develop a clinical prediction model of achievement of 6-month MDA in PsA patients starting golimumab.

To avoid over-fitting, the minimum number of events per variable was set to 10.

Given an expected 6-month achievement of MDA by 40% of the patients, in order to develop a prediction model including up to 5 variables, 125 subjects were to be enrolled. Assuming ≈10% of lost to follow-up patients, sample size rose to 135-140 subjects.

The same sample size was also sufficient to evaluate the improvement in prediction of the candidate biomarkers. Because of the higher clinical relevance of minimizing false negative responders, power calculation was performed to evaluate the improvement of the true positive rate from 60 to 70% and improvement of false negative rate from 40 to 15%, setting alpha to 5% (40). A number of 125 subjects with 50 responders would be sufficient to evaluate the increase in the performance of the model biomarker-enhanced prediction model with a power>80% (estimated in Stata using rocsize command).

General methodology

All data summaries and listings were performed using the SAS System version 9.4 under Windows 10 PRO operating system. The statistical analysis was performed by SPARC Consulting (Milan, Italy) on behalf of LB Research.

Analyses were descriptive in nature; no formal hypothesis was tested in this retrospective chart review. All enrolled subjects were included in the analysis using data collected within the subjects' observation period.

In general, continuous variables were summarized using number of patients, mean, standard deviation (SD), median, minimum, first quartile, third quartile and maximum. For categorical variables, data were summarized by the number and percentage of subjects in each category.

Two-sided 95% confidence intervals (CI) for proportions and means were also produced, where clinically appropriate.

The statistical testing was conducted at the α level of 0.05.

Adjustments for covariates

Not applicable for this study.

Multicenter studies

Site related differences were not evaluated.

Multiple comparisons/multiplicity

Not applicable. No multiple comparisons/multiplicity analyses were planned or performed.

Examination of subgroups

Not applicable. No study subgroups were pre-defined.

Handling of data, dropouts and missing values

Missing values in predictors (including items of composite scores) were systematically evaluated and multiple imputation (>10 datasets) was carried out along with appropriate diagnostics. No imputation of outcome was done.

Other missing data were not supposed to be replaced.

The number of patients with missing data was presented under the "*unknown"* category.

Missing values were included in the denominator count when computing percentages.

When continuous data are being summarized, only the non-missing values were evaluated for computing summary statistics.

Analysis population

The following populations were considered in the statistical analysis:

- The enrolled subjects set (ENR), defined as all subjects who signed the informed consent form.
- The standard population (STD) set, defined as all subjects in the ENR set who received at least one dose of golimumab.

The analysis of the primary and secondary endpoints, and of safety parameters, and the exploratory analysis, were performed in the STD population.

Replacement policy

No patient prematurely discontinued from the study for any reason was replaced.

Interim analysis

No interim analyses were scheduled or performed.

Protocol deviations

Inclusion and exclusion criteria not met were not considered as reasons for exclusion from statistical analysis. Therefore, all patients included in the study database were evaluated.

An individual data listing of patients who did not satisfy the eligibility criteria was performed.

Study limitations

The major limitation of this study is related to the generalizability of the results.

A prediction model developed in a population of PsA treated with golimumab is not directly applicable to other drugs. The selection of PsA patients in a single-country study might not reflect the general population treated with golimumab worldwide, in terms of genetic background, disease duration, previous exposure of non-biologic and biologic DMARDs. The absence of subjects exposed to other drugs might lead to describe responders to any effective drug rather than to a specific drug (golimumab).

The results from this study might not be conclusive and might need an external validation in order to be eventually applicable in the selection of high-probability responders to be treated with golimumab.

Disposition of patients

Tables and data listings were presented for the ENR population.

The number of patients enrolled by site, the summary of analysis populations, an individual data listing of the patients excluded from the STD population, the summary of reasons for premature withdrawal of patients from the treatment/study, an individual data listing of the patients who did not satisfy the eligibility criteria and an individual data listing of the patients who prematurely interrupted the treatment were presented.

Demographics and other characteristics at entry

Demographic and other baseline data were summarized descriptively for STD population.

Categorical data were presented as absolute and relative frequencies. For continuous data, mean, standard deviation, median, 25^{th} and 75^{th} percentiles, minimum and maximum were presented.

Disease characteristics

Data was summarized for STD population with descriptive statistics.

Default frequency tabulations were presented for PsA characteristics (presence of polyarthritis, previous PsA therapy and assumption of concomitant DMARDs).

Time from initial diagnosis (in months) and time from symptoms onset (in months) were calculated as the difference between the date of informed consent and the start date and presented with default summary statistics.

Medical history and comorbidities

Data was summarized for STD population with descriptive statistics.

Previous diseases are those reported as "*Not on-going*" whereas the Concomitant Diseases are those reported as "*on-going*" at study start in eCRF.

All verbatim terms were assigned to a Preferred Term (PT) and were classified by primary System Organ Class (SOC) according to the MedDRA thesaurus version 19.1.

The following data were presented:

1. A default frequency tabulation of patients who exhibited at least one previous disease;
2. a frequency table showing the previous diseases by primary SOC and PT;
3. A default frequency tabulation of patients who exhibited at least one concomitant disease;
4. A frequency table showing the concomitant diseases by primary SOC and PT.

Concomitant medications

Concomitant medications were summarized for STD population with descriptive statistics.

Medications were coded using the World Health Organization-Drug Reference List (WHO-DRL) Drug Dictionary (DD) version 2015 and classified according to 3rd level ATC subgroup (Primary therapeutic subgroup) and generic name.

A frequency table of concomitant treatments by primary therapeutic subgroup and generic name was presented.

Study drug

Data was summarized for STD population with descriptive statistics.

Descriptive analyses were presented for the number of injections of golimumab, the duration of treatment administration and the assumed dose.

Physical examination

Abnormalities reported at Screening visit or at Follow-up Visit at 3 months or at Follow-up visit at 6 months in the eCRF "*Physical Exam*" form were summarized for STD population with descriptive statistics.

All verbatim terms were assigned to a PT and were classified by primary SOC according to the MedDRA thesaurus version 19.1.

The following data were presented by visit:

1. A default frequency tabulation of patients who exhibited at least one abnormality;
2. A frequency table showing the abnormalities by primary SOC and PT.

Disease Activity Indexes for PsA clinical evaluation and functional and disability assessment

Data was summarized for STD population with descriptive statistics.

Peripheral Joint assessment

Default summary statistics of TJC and SJC over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Visual Analogue Scale (VAS)

A VAS was used for the assessment of the following measures: patient's global assessment of pain; patient's global assessment of PsA disease activity; and physician's global assessment of PsA disease activity.

Default summary statistics of the variables over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Functional assessment: Health Assessment Questionnaire (HAQ)

Default summary statistics (count and percentage) of each of the 8 scale subscores over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) were reported.

Default summary statistics of the total HAQ score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI

Default summary statistics of the BASDAI score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Disease Activity for Psoriatic Arthritis (DAPSA)

Default summary statistics of DAPSA total score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Physician Global Assessment (PGA) for Psoriatic Activity

Default summary statistics (frequency count and percentage) of PGA score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) were reported.

Leeds Enthesitis Index (LEI)

Default summary statistics of LEI total score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Dactylitis score

Default summary statistics of Dactylitis total score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening were reported.

Minimal Disease Activity (MDA)

PsA patients were classified as having MDA if they met 5 of the 7 criteria reported in the above definition of the primary endpoint (Section 9.5.1).

Default summary statistics of each of the 7 criteria (as categorical variables) and of MDA were reported over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months).

Analysis of efficacy

Primary endpoint

The primary efficacy endpoint was the response rate to treatment, defined as proportion of patients achieving MDA at 6 months.

The following steps have been followed to develop the clinical prediction model of MDA at 6 months. The category "MDA at 6 months = YES" was modelled.

The list of candidate predictors retrieved from the literature was restricted based on the a priori relevance (consistency across studies), distribution and by combining similar predictors and were the following: gender (male/female), age (continuous variable), BMI (continuous variable), smoking history (no/current/past), time from diagnosis, symptoms duration before diagnosis, polyarthritis (absent/present), hs-CRP at baseline (continuous variable), concurrent DMARDs and glucocorticoids (Yes/No), DAPSA score at baseline (continuous variable), HAQ score at baseline (continuous variable), VAS PGA of pain at baseline (continuous variable), BASDAI at baseline (continuous variable), comorbidities (absent/present), psoriasis/nail psoriasis at baseline (Yes/No) where PGA "Clear" or "Almost Clear" meant "no psoriasis".

Predictors were coded and transformed as appropriate based on the type and distribution. Missing values in predictors (including items of composite scores) were systematically evaluated and multiple imputation (>10 datasets) was carried out along with appropriate diagnostics. No imputation of outcome was done.

Baseline predictors were individually tested by univariable logistic models and results were presented as odds ratio (OR) and 95% CI.

A backward stepwise selection strategy (cut-off: $p<0.10$) was applied to multivariable logistic model in order to further select relevant variables.

Statistical interactions were systematically fitted between statistically significant variables.

Model assumptions were tested and appropriate diagnostics applied. The overall performance of the model was evaluated by the Brier score. Discriminatory ability was evaluated by estimating the C-statistics, and calibration evaluated both statistically and graphically by the Hosmer-Lemeshow goodness-of-fit test and through a box plot.

Internal validity of the prediction models was tested by bootstrap validation using 500 bootstrap repetitions on a sample with 50% size of the sample included in the model. The mean C-statistics obtained from the bootstrapping technique was presented together with its 95% CI and compared to the model C-statistics.

Secondary endpoints

The following analyses were performed for secondary endpoints:

1. Further logistic models for the outcome of MDA at 6 months were fitted including baseline biomarker levels (hs-CRP, MMP-3, CPII) as additional candidate predictors. The improvement of the performance of the prediction models was evaluated by estimating the integrated discrimination improvement (IDI) index.
2. The same set of analyses as the primary ones were carried out using MDA at 3 months as dependent variable, including the development of a biomarker-enhanced prediction model (see previous point).
3. Clinical predictors of the secondary response outcomes (DAPSA, HAQ, LEI, dactylitis score 0-6 month changes) were explored using linear regression models, following the same strategy as for the primary outcome (a priori selection, univariable analysis,

backward stepwise selection with cut-off $p<0.10$ and performance evaluation via R^2 calculation, and biomarker-enhanced prediction models). A prediction model and a biomarker-enhanced prediction model for each of the 4 secondary outcomes were presented.

4. Default summary statistics of DAPSA total score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening, including the mean difference (MD) and its corresponding 95% CI, were reported.
5. Default summary statistics of HAQ total score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening, including the MD and its corresponding 95% CI, were reported.
6. Default summary statistics of LEI Index over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening, including the MD and its corresponding 95% CI) were reported.
7. Default summary statistics of dactylitis score over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and change from screening, including the MD and its corresponding 95% CI, were reported.

Exploratory analyses

The exploratory analyses were performed in the STD population.

The relationship between different disease activity measures (68-TJC, 66-SJC, VAS, HAQ score, hs-CRP level, BASDAI, PGA, LEI, Dactylitis score, DAPSA score) were evaluated cross-sectionally at baseline, 3 months and 6 months by estimating linear correlation coefficients. Correlation coefficients that take into account repeated observations within the same subject were also estimated according to Bland e Altman.

Laboratory tests

Laboratory evaluation included hs-CRP and ESR at Screening Visit, Follow-up Visit at 3 months and Follow-up Visit at 6 months.

Default summary statistics of the values over time (Screening Visit, Follow-up visit at 3 months and Follow-up visit at 6 months) and the change from screening were provided.

Analysis of safety

Adverse events

All AEs recorded during the study were summarized with descriptive statistics for the STD population.

The incidence of AEs was summarized by SOC and maximum intensity (mild, moderate or severe), type of AE, relationship to golimumab.

Deaths reportable as SAEs and non-fatal SAEs were listed by patient and tabulated by type of AE.

All AEs were assigned to a PT and were classified by primary SOC according to the MedDRA thesaurus version 19.1.

The following listing and tables were presented:

1. An overview of AEs with the number of patients who exhibited at least one AE, number of AEs, number of related AEs, number of SAEs, number of related SAEs, number of patients reported at least one SAE, number of patients who died, number of patients who temporarily discontinued golimumab due to an AE, number of patients with premature withdrawal due to an AE;
2. Summary of all AEs, SAEs and related AEs by primary SOC and PT.
3. List of AEs, SAEs and related AEs by patient;
4. List of patients with AEs leading to withdrawal from golimumab;
5. List of patients with AEs leading to temporary discontinuation of golimumab.

9.9 Changes in Planned Analyses

The statistical analysis of the results of the study was based on the study protocol version 1.1 dated 12 Nov 2014 (Appendix 16.1.1.1) and on the analyses planned in the final SAP (Appendix 16.1.9). This document describes the statistical analyses to be conducted for the final assessment of the study data.

10 TRIAL SUBJECTS AND DATA SETS ANALYZED

10.1 Subject Disposition

The distribution of subjects enrolled by centre is presented in Section 14, Table 1.

Overall, 151 patients were enrolled in 23 sites in Italy.

The summary of end of study visit is presented in Section 14, Table 5.

Overall, 125 patients (82.8%) completed the study and 26 patients (17.2%) prematurely discontinued the study.

The primary reason for study discontinuation was withdrawal of consent in 3 patients (11.5% of discontinued), subject lost to follow-up in 9 (34.6%) and other reasons in 14 (53.8%). Data listing of patients that prematurely discontinued the study is presented in Section 14, Table 6.

Treatment at the end of study was ongoing in 120 patients (96.0% of those that completed the study).

10.2 Protocol Deviations

No violations of inclusion and exclusion criteria were reported during the study (Section 14, Table 4).

10.3 Subjects Whose Treatment Was Prematurely Unblinded

Not applicable.

10.4 Subject Populations Analyzed

The summary of analysis samples is presented in Section 14, Table 2.

Of the 151 enrolled patients, 2 patients (1.3%) were excluded from the STD set and 149 (98.7%) patients were evaluable.

The patients excluded from the STD set were patient number PPD and patient number PPD who withdrew the consent (Section 14, Table 3).

10.5 Demographic and Other Subject Characteristics

Demographic data and other patient characteristics at screening

The summary of demographic data and other patients' characteristics at screening in the STD set is presented in Table 10.5-1.

Table 10.5-1. Summary of demographic data and other patients' characteristics at screening (STD set)

Number of subjects in STD set	149
Gender, N (%)	
Male	80 (53.7%)
Female	69 (46.3%)
Age (years)	
Mean ± SD	49.16 ± 11.25
Median (range)	50.0 (21 to 75)
Ethnicity, N (%)	
Caucasian	146 (98.0%)
Non-Caucasian	3 (2.0%)
Civil status, N (%)	
Married	119 (79.9%)
Not married	30 (20.1%)
Education, N (%)	
Compulsory education	57 (38.3%)
High school	70 (47.0%)
University	22 (14.8%)
Employment, N (%)	
No	34 (22.8%)
Yes	99 (66.4%)
Other	16 (10.7%)

N = number of patients
Source: Section 14, Table 7

The STD set included 80 (53.7%) males and 69 (46.3%) females.

The mean (± SD) age was 49.16 ± 11.25 years (median 50.0 years, range 21 to 75 years).

The vast majority of patients were of Caucasian ethnicity (146 patients, 98.0%). Most of patients were married (119 patients, 79.9%) and had an employment (99 patients, 66.4%).

Vital signs at screening

The summary of vital signs at screening in the STD set is presented in Section 14, Table 8.

The mean (± SD) weight was 77.99 ± 15.50 kg (median 78.0 kg, range 47 to 127 kg). The mean (± SD) height was 1.70 ± 0.10 m (median 1.70 m, range 1.50 to 1.90 m). The mean (± SD) BMI was 26.87 ± 4.25 kg/m^2 (median 27.00 kg/m^2, range 18.0 to 39.0 kg/m^2).

Smoking habits at screening

The summary of smoking habits at screening in the STD set is presented in Section 14, Table 9.

Twenty-eight patients (18.8%) were current smokers, 96 (64.4%) were no smokers and 25 (16.8%) were former smokers. The mean (± SD) numbers of smoked cigarettes/day in current smokers was 12.11 ± 5.77 (median 10.0, range 3 to 30). The mean (± SD) time from quit smoking in former smokers was 13.30 ± 9.69 years (median 14.50 years, range 1 to 31 years).

Psoriatic arthritis at screening

The summary of psoriatic arthritis characteristics at screening in the STD set is presented in Table 10.5-2.

Table 10.5-2. Summary of psoriatic arthritis characteristics at screening (STD set)

Number of subjects in STD set	149
Time from first diagnosis (months)	(n=149)
Mean ± SD	45.49 ± 70.58
Median (range)	21.47 (0.03 to 554.47)
Time from onset of symptoms (months)	(n=139)
Mean ± SD	84.60 ± 95.30
Median (range)	53.43 (2.17 to 554.47)
Polyarthritis, N (%)	
Absent	14 (9.4%)
Present	135 (90.6%)
Previous PsA therapy, N (%)	
No	0 (0.0%)
Yes	149 (100.0%)
Concomitant DMARDs, N (%)	
No	43 (28.9%)
Yes	106 (71.1%)

N=number of patients
n=Number of observations
Source: Section 14, Table 10

The mean (± SD) time from first diagnosis was 45.49 ± 70.58 months (median 21.47 months, range 0.03 to 554.47 months).

The mean (± SD) time from onset of symptoms was 84.60 ± 95.30 months (median 53.43 months, range 2.17 to 554.47 months). Therefore, the onset of symptoms preceded the first diagnosis of an average of about 3.25 years.

The vast majority of patients had polyarthritis (135 patients, 90.6%) and most of patients were had received concomitant DMARDs (106 patients, 71.1%). All 149 patients had received a previous PsA therapy.

Previous and concomitant diseases

Previous diseases

The summary of previous diseases in the STD set is presented in Section 14, Table 11.

Overall, 29 patients (19.5%) had at least one previous disease.

Surgical and medical procedures (20 procedures performed in 13 patients, 8.7%) were the most commonly reported SOC.

Concomitant diseases

The summary of concomitant diseases in the STD set is presented in Section 14, Table 12.

Overall, 101 patients (67.8%) had at least one concomitant disease.

Metabolism and nutrition disorders (56 diseases reported in 40 patients, 26.8%), vascular disorders (35 diseases reported in 35 patients, 23.5%), gastrointestinal disorders (23 diseases reported in 20 patients, 13.4%), and endocrine disorders (19 diseases reported in 19 patients, 12.8%) were the most commonly reported SOC.

Hypertension (33 patients, 22.1%), thyroid disorder (18 patients, 12.1%), liver disorder (11 patients, 7.4%), hypercholesterolemia (11 patients, 7.4%) and psoriasis (11 patients, 7.4%) were the most commonly reported diseases by preferred term.

Physical examination

The summary of physical examination at screening in the STD set is presented in Section 14, Table 13.

Overall, 97 patients (65.1%) had at least one abnormality in the physical examination.

Musculoskeletal and connective tissue disorders (181 abnormal findings in 65 patients, 43.6%), and skin and subcutaneous tissue disorders (131 abnormal findings in 65 patients, 43.6%) were the most commonly involved SOCs.

Psoriasis (49 patients, 32.9%), arthralgia (46 patients, 30.9%) and joint swelling (40 patients, 26.8%) were the most commonly reported abnormalities by preferred term.

Concomitant treatments

The summary of concomitant treatments in the STD set is presented in Section 14, Table 57.

Overall, 141 patients (94.6%) were receiving at least one concomitant medication.

Antipsoriatics for systemic use (87 patients, 58.4%), vitamin B 12 and folic acid (72 patients, 48.3%), non-steroidal anti-inflammatory and anti-rheumatic products (59 patients, 39.6%) and corticosteroids for systemic use (55 patients, 36.9%) were the most commonly taken drug classes.

Methotrexate (87 patients, 58.4%), folic acid (71 patients, 47.7%), cholecalciferol (37 patients, 24.8%) and etoricoxib (35 patients, 23.5%) were the most commonly taken drugs by generic name.

Laboratory tests

The summary of laboratory tests at screening in the STD set is presented in Section 14, Table 14.

The mean (± SD) hs-CRP was 136.261 ± 316.560 nmol/L (median 51.430 nmol/L, range 0.000 to 3047.680 nmol/L). The mean (± SD) ESR was 23.349 ± 19.633 mm/h (median 19.0 mm/h, range 2 to 120 mm/h).

Peripheral joint assessment

The summary of peripheral joint assessment at screening in the STD set is presented in Section 14, Table 15.

The mean (± SD) tender joints count (68 joints) was 11.8 ± 9.5 (median 10.0, range 1 to 55). The mean (± SD) swollen joints count (66 joints) was 4.7 ± 4.7 (median 4.0, range 0 to 22).

VAS

The summary of VAS assessment at screening in the STD set is presented in Section 14, Table 16.

The mean (± SD) patient's global assessment of pain was 61.2 ± 24.4 mm (median 64.0 mm, range 3 to 100 mm). The mean (± SD) patient's global assessment of PsA disease activity was 63.2 ± 19.4 mm (median 65.0 mm, range 11 to 100 mm). The mean (± SD) PGA of PsA disease activity was 54.8 ± 19.3 mm (median 55.0 mm, range 10 to 98 mm).

Functional assessment (HAQ)

The summary of functional assessment (HAQ) at screening in the STD set is presented in Section 14, Table 17 (subscales score) and Table 18 (calculated HAQ score).

The mean (± SD) calculated HAQ score was 0.95 ± 0.60 (median 0.88, range 0.00 to 2.75).

Apart from the scale grip, in which 46.3% of patients reported a score of 0 (without any difficulty), a score of 1 (some difficulty) was the most frequently reported score for the other scales, ranging from 37.6% of patients for eating to 59.7% of patients for reach. A score of 3 (unable) was reported in a minority of patients in all scales, with the highest rate reported for hygiene (8.1% of patients).

BASDAI

The summary of BASDAI at screening in the STD set is presented in Section 14, Table 19.

The mean (± SD) calculated BASDAI score was 5.87 ± 1.94 (median 6.20, range 0.50 to 9.80).

Joint pain/swelling was the symptom with the highest mean VAS (6.5 ± 2.5 mm) and morning stiffness duration was the symptom with the lowest mean VAS (3.4 ± 2.8 mm).

Physician Global Assessment (PGA) of psoriatic activity

The summary of PGA of psoriatic activity (skin assessment) at screening in the STD set is presented in Section 14, Table 20.

The skin assessment was clear in 57 patients (38.3%), almost clear in 37 (24.8%), mild in 31 (20.8%), mild to moderate in 16 (10.7%), moderate in 5 (3.4%), moderate to severe in 2 (1.3%) and severe in 1 (0.7%).

Enthesitis index (LEI)

The summary of LEI score at screening in the STD set is presented in Section 14, Table 21.

The mean (± SD) LEI score was 1.9 ± 1.6 (median 2.0, range 0.0 to 6.0).

Dactylitis

The summary of dactylitis digit count at screening in the STD set is presented in Section 14, Table 22.

The mean (± SD) dactylitis digit count was 0.6 ± 1.4 (median 0.0, range 0 to 10).

DAPSA

The summary of DAPSA score at screening in the STD set is presented in Section 14, Table 23.

The mean (± SD) DAPSA score was 30.37 ± 14.51 (median 27.20, range 7.75 to 82.35).

Minimal disease activity (MDA)

The summary of MDA at screening in the STD set is presented in Section 14, Table 24.

None of the 149 patients (0.0%) had achieved the MDA at baseline, i.e. did not meet at least 5 of the 7 pre-defined criteria.

Four patients (2.7%) had a tender joint count ≤ 1, 31 (20.8%) had a swollen joint count ≤ 1, 94 (63.1%) had a clear or almost clear PGA, 7 (4.7%) had a patient assessment of pain VAS ≤ 15 mm, 2 (1.3%) had a patient's global assessment of PsA disease activity VAS ≤ 20 mm, 43 (28.9%) had a HAQ score ≤ 0.5, and 66 (44.3%) had ≤ 1 tender enthesial points.

Correlation tests

The summary of correlation tests (Pearson) between diseases activity measures at screening in the STD set is presented in Section 14, Table 55.1.

No statistically significant correlations with any diseases activity measures were observed for hs-CRP only, whereas statistically significant correlations for dactylitis digit count were observed with swollen joint count only.

Statistically significant direct correlations with all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index (except with swollen joint count) and DAPSA total score.

The strongest levels of correlations (i.e. those with an r Pearson's correlation coefficient ≥ 0.7) were observed between tender joint count and DAPSA total score (r = 0.8902), and between swollen joint count and DAPSA total score (r = 0.7444).

10.6 Measurements of Treatment Compliance

Not applicable.

11 PHARMACODYNAMIC, PHARMACOKINETIC, BIOAVAILABILITY, IMMUNOGENICITY, AND/OR EFFICACY EVALUATION AND RESULTS

11.1 Efficacy Summary

Primary endpoint: response rate to treatment, defined as proportion of patients achieving MDA at 6 months

The summary of the proportion of patients achieving MDA at 6 months in the STD set is presented in Table 11.1-1.

Table 11.1-1. Summary of the proportion of patients achieving MDA at 6 months (STD set)

Number of subjects in STD set	149
Tender joints count, N (%)	
> 1	62 (41.6%)
≤ 1	63 (42.3%)
Unknown	24 (16.1%)
Swollen joints count, N (%)	
> 1	16 (10.7%)
≤ 1	109 (73.2%)
Unknown	24 (16.1%)
PGA for psoriatic activity, N (%)	
Other	10 (6.7%)
Clear or almost clear	115 (77.2%)
Unknown	24 (16.1%)
Patient assessment of pain VAS, N (%)	
> 15 mm	71 (47.7%)
≤ 15 mm	54 (36.2%)
Unknown	24 (16.1%)
Patient global assessment of PsA disease activity VAS, N (%)	
> 20 mm	69 (46.3%)
≤ 20 mm	56 (37.6%)
Unknown	24 (16.1%)
HAQ score, N (%)	
> 0.5	48 (32.2%)
≤ 0.5	77 (51.7%)
Unknown	24 (16.1%)
Tender enthesial points, N (%)	
> 1	20 (13.4%)
≤ 1	105 (70.5%)
Unknown	24 (16.1%)
MDA achieved, N (%)	
No	59 (39.6%)
Yes	66 (44.3%)
Unknown	24 (16.1%)

N=Number of patients
Source: Section 14, Table 42

Overall, 66 patients (44.3%) achieved the MDA at 6 months, i.e. met at least 5 of the 7 pre-defined criteria, and 59 patients (39.6%) did not achieve the MDA. Results were unknown in 24 patients (16.1%).

Sixty-three patients (42.3%) had a tender joint count ≤ 1, 109 (73.2%) had a swollen joint count ≤ 1, 115 (77.2%) had a clear or almost clear PGA, 54 (36.2%) had a patient assessment of pain VAS ≤ 15 mm, 56 (37.6%) had a patient's global assessment of PsA disease activity VAS ≤ 20 mm, 77 (51.7%) had a HAQ score ≤ 0.5, and 105 (70.5%) had ≤ 1 tender enthesial points.

Clinical prediction model of MDA at 6 months

The summary of the evaluation of the clinical prediction model of MDA at 6 months in the STD set is presented in Section 14, Table 43.

- Univariable logistic model

In the univariable logistic model, factors that resulted to be predictive of MDA at 6 months were:

- Gender (female: OR, 0.3197; 95% CI, 0.1531 to 0.6677, p = 0.0024), i.e. males had a higher probability to achieve MDA at 6 months;
- Age (OR, 0.957; 95% CI, 0.9252 to 0.9899, p = 0.0109), i.e. younger patients had a higher probability to achieve MDA at 6 months;
- DAPSA score at baseline (OR, 0.9287; 95% CI, 0.8967 to 0.9618, p<0.0001), i.e. a lower DAPSA score at baseline was indicative of a higher probability to achieve MDA at 6 months;
- HAQ score at baseline (OR, 0.2937; 95% CI, 0.1423 to 0.6063, p = 0.0009), i.e. a lower HAQ score at baseline was indicative of a higher probability to achieve MDA at 6 months;
- Patient assessment of pain VAS at baseline (OR, 0.9833; 95% CI, 0.9684 to 0.9984, p = 0.0299), i.e. a lower pain VAS at baseline was indicative of a higher probability to achieve MDA at 6 months;
- BASDAI score at baseline (OR, 0.7036; 95% CI, 0.5733 to 0.8635, p = 0.0008), i.e. a lower BASDAI score at baseline was indicative of a higher probability to achieve MDA at 6 months;
- Presence of comorbidities (yes: OR, 0.3258; 95% CI, 0.1465 to 0.7241, p = 0.0059), i.e. patients without comorbidities had a higher probability to achieve MDA at 6 months.

- Multivariable logistic model

Following the backward stepwise selection in the multivariable logistic model, in which five factors remained in the model, factors that resulted to be predictive of MDA at 6 months were:

- Age (OR, 0.9542; 95% CI, 0.9112 to 0.9993, p = 0.0465), i.e. younger patients had a higher probability to achieve MDA at 6 months;

- hs-CRP at baseline (OR, 1.0015; 95% CI, 1.0002 to 1.0028, p = 0.0241), i.e. a higher hs-CRP value at baseline was indicative of a higher probability to achieve MDA at 6 months;
- DAPSA score at baseline (OR, 0.9255; 95% CI, 0.8879 to 0.9647, p = 0.0003), i.e. a lower DAPSA score at baseline was indicative of a higher probability to achieve MDA at 6 months;
- Duration of symptoms before diagnosis (OR, 1.0057; 95% CI, 1.0007 to 1.0107, p = 0.0260), i.e. a longer duration of symptoms at baseline was indicative of a higher probability to achieve MDA at 6 months.

Biomarker-enhanced clinical prediction model of MDA at 6 months

The summary of the evaluation of the biomarker-enhanced clinical prediction model of MDA at 6 months in the STD set is presented in Section 14, Table 44.

- Univariable logistic model

In the univariable logistic model, the following biomarker resulted to be predictive of MDA at 6 months:

- hs-CRP at baseline (OR, 1.0688; 95% CI, 1.008 to 1.1334, p = 0.0261), i.e. a higher hs-CRP value at baseline was indicative of a higher probability to achieve MDA at 6 months.

- Multivariable logistic model

Following the backward stepwise selection in the multivariable logistic model, in which four factors remained in the model, factors that resulted to be predictive of MDA at 6 months were:

- Presence of comorbidities (yes: OR, 0.2645; 95% CI, 0.0881 to 0.7941, p = 0.0177), i.e. patients without comorbidities had a higher probability to achieve MDA at 6 months;
- DAPSA score at baseline (OR, 0.9231; 95% CI, 0.885 to 0.9628, p = 0.0002), i.e. a lower DAPSA score at baseline was indicative of a higher probability to achieve MDA at 6 months.

Secondary endpoints

Proportion of patients achieving MDA at 3 months

The summary of the proportion of patients achieving MDA at 3 months in the STD set is presented in Table 11.1-2.

Table 11.1-2. Summary of the proportion of patients achieving MDA at 3 months (STD set)

Number of subjects in STD set	149
Tender joints count, N (%)	
> 1	77 (51.7%)
≤ 1	61 (40.9%)
Unknown	11 (7.4%)
Swollen joints count, N (%)	
> 1	32 (21.5%)
≤ 1	106 (71.1%)
Unknown	11 (7.4%)
PGA for psoriatic activity, N (%)	
Other	15 (10.1%)
Clear or almost clear	123 (82.6%)
Unknown	11 (7.4%)
Patient assessment of pain VAS, N (%)	
> 15 mm	96 (64.4%)
≤ 15 mm	42 (28.2%)
Unknown	11 (7.4%)
Patient global assessment of PsA disease activity VAS, N (%)	
> 20 mm	100 (67.1%)
≤ 20 mm	38 (25.5%)
Unknown	11 (7.4%)
HAQ score, N (%)	
> 0.5	65 (43.6%)
≤ 0.5	73 (49.0%)
Unknown	11 (7.4%)
Tender enthesial points, N (%)	
> 1	28 (18.8%)
≤ 1	110 (73.8%)
Unknown	11 (7.4%)
MDA achieved, N (%)	
No	84 (56.4%)
Yes	54 (36.2%)
Unknown	11 (7.4%)

N=Number of patients
Source: Section 14, Table 41

Overall, 54 patients (36.2%) achieved the MDA at 3 months, i.e. met at least 5 of the 7 pre-defined criteria, and 84 patients (56.4%) did not achieve the MDA. Results were unknown in 11 patients (7.4%).

Sixty-one patients (40.9%) had a tender joint count ≤ 1, 106 (71.1%) had a swollen joint count ≤ 1, 123 (82.6%) had a clear or almost clear PGA, 42 (28.2%) had a patient assessment of pain VAS ≤ 15 mm, 38 (25.5%) had a patient's global assessment of PsA disease activity VAS ≤ 20 mm, 73 (49.0%) had a HAQ score ≤ 0.5, and 110 (73.8%) had ≤ 1 tender enthesial points.

Clinical prediction model of MDA at 3 months

The summary of the evaluation of the clinical prediction model of MDA at 3 months in the STD set is presented in Section 14, Table 45.

- Univariable logistic model

In the univariable logistic model, factors that resulted to be predictive of MDA at 3 months were:

- Gender (female: OR, 0.3028; 95% CI, 0.1452 to 0.6314, p = 0.0014), i.e. males had a higher probability to achieve MDA at 3 months;
- Age (OR, 0.946; 95% CI, 0.9147 to 0.9785, p = 0.0013), i.e. younger patients had a higher probability to achieve MDA at 3 months;
- DAPSA score at baseline (OR, 0.9328; 95% CI, 0.8999 to 0.967, p = 0.0001), i.e. a lower DAPSA score at baseline was indicative of a higher probability to achieve MDA at 3 months;
- HAQ score at baseline (OR, 0.1809; 95% CI, 0.0816 to 0.401, p<0.0001), i.e. a lower HAQ score at baseline was indicative of a higher probability to achieve MDA at 3 months;
- Patient assessment of pain VAS at baseline (OR, 0.9849; 95% CI, 0.9711 to 0.9989, p = 0.0345), i.e. a lower pain VAS at baseline was indicative of a higher probability to achieve MDA at 3 months;
- BASDAI score at baseline (OR, 0.652; 95% CI, 0.5318 to 0.7993, p<0.0001), i.e. a lower BASDAI score at baseline was indicative of a higher probability to achieve MDA at 3 months;
- Presence of comorbidities (yes: OR, 0.2942; 95% CI, 0.1369 to 0.6319, p = 0.0017), i.e. patients without comorbidities had a higher probability to achieve MDA at 3 months.

- Multivariable logistic model

Following the backward stepwise selection in the multivariable logistic model, in which five factors remained in the model, factors that resulted to be predictive of MDA at 3 months were:

- Age (OR, 0.9438; 95% CI, 0.906 to 0.9831; p = 0.0055), i.e. younger patients had a higher probability to achieve MDA at 3 months;
- hs-CRP at baseline (OR, 1.0019; 95% CI, 1.0005 to 1.0033, p = 0.0072), i.e. a higher hs-CRP value at baseline was indicative of a higher probability to achieve MDA at 3 months;
- DAPSA score at baseline (OR, 0.9352; 95% CI, 0.8908 to 0.9818, p = 0.0069), i.e. a lower DAPSA score at baseline was indicative of a higher probability to achieve MDA at 3 months;
- HAQ score at baseline (OR, 0.373; 95% CI, 0.1413 to 0.9844, p = 0.0464), i.e. a lower HAQ score at baseline was indicative of a higher probability to achieve MDA at 3 months;

- Time from diagnosis (OR, 1.0085; 95% CI, 1.0021 to 1.0149, p = 0.0088), i.e. a longer time from diagnosis was indicative of a higher probability to achieve MDA at 3 months.

Biomarker-enhanced clinical prediction model of MDA at 3 months

The summary of the evaluation of the biomarker-enhanced clinical prediction model of MDA at 6 months in the STD set is presented in Section 14, Table 46.

- Univariable logistic model

In the univariable logistic model, none of the biomarkers resulted to be predictive of MDA at 3 months.

- Multivariable logistic model

Following the backward stepwise selection in the multivariable logistic model, in which four factors remained in the model, factors that resulted to be predictive of MDA at 3 months were:

- Age (OR, 0.932; 95% CI, 0.8902 to 0.9758; p = 0.0027), i.e. younger patients had a higher probability to achieve MDA at 3 months;
- BASDAI score at baseline (OR, 0.757; 95% CI, 0.5782 to 0.9912, p = 0.0430), i.e. a lower BASDAI score at baseline was indicative of a higher probability to achieve MDA at 3 months;
- DAPSA score at baseline (OR, 0.9406; 95% CI, 0.8942 to 0.9893, p = 0.0175), i.e. a lower DAPSA score at baseline was indicative of a higher probability to achieve MDA at 3 months;
- Time from diagnosis (OR, 1.0088; 95% CI, 1.0022 to 1.0154, p = 0.0085), i.e. a longer time from diagnosis was indicative of a higher probability to achieve MDA at 3 months.

<u>hs-CRP</u>

The summary of changes in hs-CRP from the screening visit in the STD set is presented in Table 11.1-3.

Table 11.1-3. Summary of changes in hs-CRP (nmol/L) from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	136.25 ± 316.560
Median (range)	51.43 (0.00 to 3047.68)
Change from screening to Month 3	(n=131)
Mean ± SD	-88.69 ± 291.661
Median (range)	-26.67 (-2905.77 to 169.53)
Change from screening to Month 6	(n=120)
Mean ± SD	-96.61 ± 308.537
Median (range)	-27.62 (-3001.96 to 205.72)

n=Number of observations
Source: Section 14, Table 25

The mean and median hs-CRP decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -88.69 ± 291.661 nmol/L (median -26.67 nmol/L, range -2905.77 to 169.53 nmol/L) at Month 3 and -96.91 ± 308.537 nmol/L (median -27.62 nmol/L, range -3001.96 to 205.72 nmol/L) at Month 6.

ESR

The summary of changes in ESR from the screening visit in the STD set is presented in Table 11.1-4.

Table 11.1-4. Summary of changes in ESR (mm/h) from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	23.35 ± 19.633
Median (range)	19.00 (2 to 120)
Change from screening to Month 3	(n=130)
Mean ± SD	-11.71 ± 17.872
Median (range)	-6.00 (-114 to 15)
Change from screening to Month 6	(n=119)
Mean ± SD	-11.83 ± 17.892
Median (range)	-7.00 (-102 to 11)

n=Number of observations
Source: Section 14, Table 26

The mean and median ESR decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -11.71 ± 17.872 mm/h (median -6.00 mm/h, range -114 to 15 mm/h) at Month 3 and was -11.83 ± 17.892 mm/h (median -7.00 mm/h, range -102 to 11 mm/h) at Month 6.

Tender joints count

The summary of changes in tender joints count (68 joints) from the screening visit in the STD set is presented in Table 11.1-5.

Table 11.1-5. Summary of changes in tender joints count from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	11.77 ± 9.523
Median (range)	10.00 (1 to 55)
Change from screening to Month 3	(n=138)
Mean ± SD	-6.97 ± 7.288
Median (range)	-6.00 (-43 to 12)
Change from screening to Month 6	(n=125)
Mean ± SD	-7.72 ± 7.753
Median (range)	-6.00 (-41 to 13)

n=Number of observations
Source: Section 14, Table 27

The mean and median tender joints count decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -6.97 ± 7.288 (median -6.00, range -43 to 12) at Month 3 and was -7.72 ± 7.753 (median -6.00, range -41 to 13) at Month 6.

Swollen joints count

The summary of changes in swollen joints count (66 joints) from the screening visit in the STD set is presented in Table 11.1-6.

Table 11.1-6. Summary of changes in swollen joints count from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	4.73 ± 4.687
Median (range)	4.00 (0 to 22)
Change from screening to Month 3	(n=138)
Mean ± SD	-3.33 ± 4.257
Median (range)	-2.00 (-21 to 6)
Change from screening to Month 6	(n=125)
Mean ± SD	-4.09 ± 4.168
Median (range)	-3.00 (-21 to 2)

n=Number of observations
Source: Section 14, Table 28

The mean and median swollen joints count decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -3.33 ± 4.257 (median -2.00, range -21 to 6) at Month 3 and was -4.09 ± 4.168 (median -3.00, range -21 to 2) at Month 6.

Patient assessment of pain VAS

The summary of changes in patient assessment of pain VAS from the screening visit in the STD set is presented in Table 11.1-7.

Table 11.1-7. Summary of changes in patient assessment of pain VAS (mm) from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	61.18 ± 24.367
Median (range)	64.00 (3 to 100)
Change from screening to Month 3	(n=138)
Mean ± SD	-25.50 ± 32.165
Median (range)	-23.50 (-99 to 54)
Change from screening to Month 6	(n=125)
Mean ± SD	-30.59 ± 33.613
Median (range)	-31.00 (-100 to 75)

n=Number of observations
Source: Section 14, Table 29

The mean and median patient assessment of pain VAS decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -25.50 ± 32.165 mm (median -23.50 mm, range -99 to 54 mm) at Month 3 and was -30.59 ± 33.613 mm (median -31.00 mm, range -100 to 75 mm) at Month 6.

Patient global assessment of PsA disease activity VAS

The summary of changes in patient global assessment of PsA disease activity VAS from the screening visit in the STD set is presented in Table 11.1-8.

Table 11.1-8. Summary of changes in patient global assessment of PsA disease activity VAS (mm) from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	63.25 ± 19.450
Median (range)	65.00 (11 to 100)
Change from screening to Month 3	(n=138)
Mean ± SD	-23.39 ± 28.635
Median (range)	-21.00 (-91 to 47)
Change from screening to Month 6	(n=125)
Mean ± SD	-31.38 ± 30.382
Median (range)	-34.00 (-92 to 55)

n=Number of observations
Source: Section 14, Table 30

The mean and median patient global assessment of PsA disease activity VAS decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -23.39 ± 28.635 mm (median -21.00 mm, range -91 to 47 mm) at Month 3 and was -31.38 ± 30.382 mm (median -34.00 mm, range -92 to 55 mm) at Month 6.

PGA of PsA disease activity VAS

The summary of changes in PGA of PsA disease activity VAS from the screening visit in the STD set is presented in Table 11.1-9.

Table 11.1-9. Summary of changes in PGA global assessment of PsA disease activity VAS (mm) from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	54.80 ± 19.274
Median (range)	55.00 (10 to 98)
Change from screening to Month 3	(n=138)
Mean ± SD	-31.67 ± 20.139
Median (range)	-31.00 (-83 to 15)
Change from screening to Month 6	(n=125)
Mean ± SD	-38.82 ± 21.933
Median (range)	-40.00 (-84 to 18)

n=Number of observations
Source: Section 14, Table 31

The mean and median PGA of PsA disease activity VAS decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -31.67 ± 20.139 mm (median -31.00 mm, range -83 to 15 mm) at Month 3 and was -38.82 ± 21.933 mm (median -40.00 mm, range -84 to 18 mm) at Month 6.

Functional assessment (HAQ)

The summary of changes in HAQ total score from the screening visit in the STD set is presented in Table 11.1-10.

Table 11.1-10. Summary of changes in HAQ total score from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	0.95 ± 0.601
Median (range)	0.88 (0.00 to 2.75)
Change from screening to Month 3	(n=138)
Mean ± SD	-0.34 ± 0.499
Median (range)	-0.31 (-1.50 to 0.75)
Change from screening to Month 6	(n=125)
Mean ± SD	-0.41 ± 0.518
Median (range)	-0.38 (-1.88 to 1.13)

n=Number of observations
Source: Section 14, Table 34

The mean and median HAQ total score decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -0.34 ± 0.499 (median -0.31, range -1.50 to 0.75) at Month 3 and was -0.41 ± 0.518 (median -0.38, range -1.88 to 1.13) at Month 6.

The summary of changes in HAQ subscales from the screening visit in the STD set is presented in Section 14, Table 32 (changes at Month 3) and Table 33 (changes at Month 6).

At Month 3, apart from the scale reach, in which 46.3% of patients reported a score of 1 (some difficulty), a score of 0 (without any difficulty) was the most frequently reported score for the other scales, ranging from 39.6% of patients for common daily activities to 61.7% of patients for grip. A score of 3 (unable) was reported in a minority of patients in all scales, with the highest rate reported for hygiene (4.7% of patients).

At Month 6, as evidence of further improvements of results observed at Month 3, a score of 0 (without any difficulty) was the most frequently reported score for all scales, ranging from 40.3% of patients for common daily activities to 63.8% of patients for grip. A score of 3 (unable) was reported in a minority of patients in all scales, with the highest rate reported for hygiene (4.0% of patients).

Clinical prediction model of change in HAQ score from baseline to 6 months

The summary of the evaluation of the clinical prediction model of change in HAQ score from baseline to 6 months in the STD set is presented in Section 14, Table 49.

- Univariable linear regression model

In the univariable linear regression model, factors that resulted to be predictive of decrease in HAQ score from baseline to 6 months were HAQ score at baseline ($p<0.0001$) and BASDAI at baseline ($p = 0.0046$).

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which four factors remained in the model, factors that resulted to be predictive of decrease in HAQ score from baseline to 6 months were age ($p = 0.0130$), DAPSA score at baseline ($p = 0.0021$), HAQ score at baseline ($p<0.0001$), and presence of psoriasis/nail psoriasis at baseline ($p = 0.0493$).

Biomarker-enhanced prediction model of change in HAQ score from baseline to 6 months

The summary of the evaluation of the biomarker-enhanced clinical prediction model of change in HAQ score from baseline to 6 months in the STD set is presented in Section 14, Table 50.

- Univariable linear regression model

In the univariable linear regression model, none of the biomarkers resulted to be predictive of decrease in HAQ score from baseline to 6 months.

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which six factors remained in the model, factors that resulted to be predictive of decrease in HAQ score from baseline to 6 months were age ($p = 0.0316$), DAPSA score at baseline ($p = 0.0367$), HAQ score at baseline ($p<0.0001$), and MMP-3 ($p = 0.0413$).

BASDAI

The summary of changes in BASDAI score from the screening visit in the STD set is presented in Table 11.1-11.

Table 11.1-11. Summary of changes in BASDAI score from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	5.87 ± 1.944
Median (range)	6.20 (0.50 to 9.80)
Change from screening to Month 3	(n=136)
Mean ± SD	-1.91 ± 2.249
Median (range)	-1.75 (-7.70 to 3.80)
Change from screening to Month 6	(n=125)
Mean ± SD	-2.40 ± 2.553
Median (range)	-2.20 (-8.70 to 2.90)

n=Number of observations
Source: Section 14, Table 35

The mean and median BASDAI score decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -1.91 ± 2.249 (median -1.75, range -7.70 to 3.80) at Month 3 and was -2.40 ± 2.553 (median -2.20, range -8.70 to 2.90) at Month 6.

PGA for psoriatic activity

The summary of PGA for psoriatic activity (skin assessments) in the STD set is presented in Section 14, Table 36 (Month 3) and Table 37 (Month 6).

Improvements from the screening visit were observed at both Month 3 and Month 6.

At Month 3, the skin assessment was clear in 84 patients (56.4%), almost clear in 39 (26.2%), mild in 10 (6.7%), mild to moderate in 3 (2.0%), moderate in 1 (0.7%), and moderate to severe in 1 (0.7%). None of patients had a severe assessment. The result was unknown in 11 patients (7.4%).

At Month 6, the skin assessment was clear in 84 patients (56.4%), almost clear in 31 (20.8%) and mild in 10 (6.7%). None of patients had a mild to moderate, moderate, moderate to severe, or severe assessment. The result was unknown in 24 patients (16.1%).

Enthesitis index (LEI)

The summary of changes in LEI score from the screening visit in the STD set is presented in Table 11.1-12.

Table 11.1-12. Summary of changes in LEI score from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	1.91 ± 1.649
Median (range)	2.00 (0 to 6)
Change from screening to Month 3	(n=138)
Mean ± SD	-1.07 ± 1.451
Median (range)	-1.00 (-6 to 3)
Change from screening to Month 6	(n=125)
Mean ± SD	-1.27 ± 1.531
Median (range)	-1.00 (-6 to 3)

n=Number of observations
Source: Section 14, Table 38

The mean and median LEI score decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -1.07 ± 1.451 (median -1.00, range -6 to 3) at Month 3 and was -1.27 ± 1.531 (median -1.00, range -6 to 3) at Month 6.

Clinical prediction model of change in LEI score from baseline to 6 months

The summary of the evaluation of the clinical prediction model of change in LEI score from baseline to 6 months in the STD set is presented in Section 14, Table 51.

- Univariable linear regression model

In the univariable linear regression model, factors that resulted to be predictive of decrease in LEI score from baseline to 6 months were DAPSA score at baseline (p = 0.0040), HAQ score

at baseline (p = 0.0150), patient assessment of pain VAS at baseline (p = 0.0035) and BASDAI at baseline (p = 0.0209).

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which two factors remained in the model, none of factors resulted to be predictive of decrease in LEI score from baseline to 6 months.

Biomarker-enhanced prediction model of change in LEI score from baseline to 6 months

The summary of the evaluation of the biomarker-enhanced clinical prediction model of change in LEI score from baseline to 6 months in the STD set is presented in Section 14, Table 52.

- Univariable linear regression model

In the univariable linear regression model, none of the biomarkers resulted to be predictive of decrease in LEI score from baseline to 6 months.

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which one factor (DAPSA score at baseline) remained in the model, it resulted to be predictive of decrease in LEI score from baseline to 6 months (p = 0.0037).

Dactylitis digit count

The summary of changes in dactylitis digit count from the screening visit in the STD set is presented in Table 11.1-13.

Table 11.1-13. Summary of changes in dactylitis digit count from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	0.60 ± 1.399
Median (range)	0.00 (0 to 10)
Change from screening to Month 3	(n=138)
Mean ± SD	-0.47 ± 1.128
Median (range)	0.00 (-6 to 2)
Change from screening to Month 6	(n=125)
Mean ± SD	-0.46 ± 1.118
Median (range)	0.00 (-6 to 2)

n=Number of observations
Source: Section 14, Table 39

The mean dactylitis digit count decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -0.47 ± 1.128 (median 0.00, range -6 to 2) at Month 3 and was -0.46 ± 1.118 (median 0.00, range -6 to 2) at Month 6.

Clinical prediction model of change in dactylitis digit count from baseline to 6 months

The summary of the evaluation of the clinical prediction model of change in dactylitis digit count from baseline to 6 months in the STD set is presented in Section 14, Table 53.

- Univariable linear regression model

In the univariable linear regression model, none of factors resulted to be predictive of decrease in dactylitis digit count from baseline to 6 months.

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which one factor (HAQ score at baseline) remained in the model, it resulted to be predictive of decrease in dactylitis digit count from baseline to 6 months (p = 0.0118).

Biomarker-enhanced prediction model of change in dactylitis digit count from baseline to 6 months

The summary of the evaluation of the biomarker-enhanced clinical prediction model of change in dactylitis digit count from baseline to 6 months in the STD set is presented in Section 14, Table 54.

- Univariable linear regression model

In the univariable linear regression model, none of the biomarkers resulted to be predictive of decrease in dactylitis digit count from baseline to 6 months.

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which two factors remained in the model, the factor that resulted to be predictive of decrease in dactylitis digit count from baseline to 6 months was HAQ score at baseline (p = 0.0061).

DAPSA

The summary of DAPSA total score from the screening visit in the STD set is presented in Table 11.1-14.

Table 11.1-14. Summary of changes in DAPSA total score from the screening visit (STD set)

Number of subjects in STD set	149
Screening visit	(n=149)
Mean ± SD	30.27 ± 14.509
Median (range)	27.20 (7.75 to 82.35)
Change from screening to Month 3	(n=131)
Mean ± SD	-16.17 ± 12.143
Median (range)	-14.32 (-70.75 to 15.00)
Change from screening to Month 6	(n=120)
Mean ± SD	-19.16 ± 13.037
Median (range)	-17.12 (-67.50 to 20.19)

n=Number of observations
Source: Section 14, Table 40

The mean and median DAPSA total score decreased from the screening visit to Month 3 and Month 6.

The mean (± SD) change from the screening visit was -16.17 ± 12.143 (median -14.32, range -70.75 to 15.00) at Month 3 and was -19.16 ± 13.037 (median -17.12, range -67.50 to 20.19) at Month 6.

Clinical prediction model of change in DAPSA score from baseline to 6 months

The summary of the evaluation of the clinical prediction model of change in DAPSA score from baseline to 6 months in the STD set is presented in Section 14, Table 47.

- Univariable linear regression model

In the univariable linear regression model, factors that resulted to be predictive of decrease in DAPSA score from baseline to 6 months were BMI ($p = 0.0424$), time from diagnosis ($p = 0.0454$), hs-CRP at baseline ($p = 0.0407$), DAPSA score at baseline ($p<0.0001$), HAQ score at baseline ($p = 0.0032$), patient assessment of pain VAS at baseline ($p<0.0001$), and BASDAI at baseline ($p = 0.0403$).

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which five factors remained in the model, factors that resulted to be predictive of decrease in DAPSA score from baseline to 6 months were gender ($p = 0.0277$), BMI ($p = 0.0029$), DAPSA score at baseline ($p<0.0001$), and patient assessment of pain VAS at baseline ($p = 0.0201$).

Biomarker-enhanced prediction model of change in DAPSA score from baseline to 6 months

The summary of the evaluation of the biomarker-enhanced clinical prediction model of change in DAPSA score from baseline to 6 months in the STD set is presented in Section 14, Table 48.

- Univariable linear regression model

In the univariable linear regression model, none of the biomarkers resulted to be predictive of decrease in DAPSA score from baseline to 6 months.

- Multivariable linear regression model

Following the backward stepwise selection in the multivariable linear regression model, in which five factors remained in the model, factors that resulted to be predictive of decrease in DAPSA score from baseline to 6 months were gender ($p = 0.0376$), BMI ($p = 0.0251$), time from diagnosis ($p = 0.0186$), DAPSA score at baseline ($p<0.0001$), and patient assessment of pain VAS at baseline ($p = 0.0077$).

<u>Correlation tests</u>

Month 3

The summary of correlation tests (Pearson) between diseases activity measures at Month 3 in the STD set is presented in Section 14, Table 55.2.

No statistically significant correlations with any diseases activity measures were observed for hs-CRP only, whereas statistically significant correlations for dactylitis digit count were observed with swollen joint count and LEI index only.

Statistically significant direct correlations between all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score.

The strongest levels of correlations (i.e. those with an r Pearson's correlation coefficient ≥ 0.7) were observed between: tender joint count and DAPSA total score (r = 0.9309); patient's global assessment of pain VAS and HAQ total score (r = 0.7204), BASDAI (r = 0.8060) and DAPSA total score (r = 0.8154); HAQ total score and BASDAI (r = 0.7720); and DAPSA total score (r = 0.7288); BASDAI and DAPSA total score (r = 0.7315).

Month 6

The summary of correlation tests (Pearson) between diseases activity measures at Month 3 in the STD set is presented in Section 14, Table 55.3.

No statistically significant correlations with any diseases activity measures were observed for hs-CRP and dactylitis digit count only.

Statistically significant direct correlations between all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score.

The strongest levels of correlations (i.e. those with an r Pearson's correlation coefficient ≥ 0.7) were observed between: tender joint count and swollen joint count (r = 0.7209) and DAPSA total score (r = 0.9194); swollen joint count and DAPSA total score (r = 0.7390); patient's global assessment of pain VAS and BASDAI (r = 0.8483) and DAPSA total score (r = 0.8015); HAQ total score and BASDAI (r = 0.7217); and BASDAI and DAPSA total score (r = 0.7380).

Linear mixed model

The summary of correlation tests by linear mixed model (Bland and Altman) between diseases activity measures in the STD set is presented in Section 14, Table 56.

No statistically significant correlations with any diseases activity measures were observed for hs-CRP (except with DAPSA total score).

Statistically significant correlations with all the other diseases activity measures were observed for tender joint count, swollen joint count, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score (except between tender joint count and LEI index).

12 SAFETY EVALUATION

12.1 Extent of Exposure

The summary of study drug administration in the STD set is presented in Section 14, Table 58.

The mean (± SD) number of injections of golimumab was 6.04 ± 1.41 (median 6.00, range 1-8). The mean (± SD) duration of treatment administration was 5.17 ± 1.33 months (median 5.13 months, range 0.03-7.23 months). The mean (± SD) total administered dose was 307.75 ± 83.75 mg (median 300.0 mg, range 50-700 mg).

12.2 Adverse Events

12.2.1 Brief Summary of Adverse Events

The overview of incidence of adverse events in the STD set is presented in Table 12.2-1.

Table 12.2-1. Overview of incidence of adverse events (STD set)

Number of subjects in STD set	149
Number of adverse events	23
Number (%) of patients with at least one adverse event	14 (9.4%)
Number of treatment-related adverse events	20
Number (%) of patients with at least one treatment-related adverse event	12 (8.1%)
Number of serious adverse events	3
Number (%) of patients with at least one serious adverse event	3 (2.0%)
Number of treatment-related serious adverse events	0
Number of fatal adverse event	0
Number of adverse events leading to temporary discontinuation of golimumab	9
Number (%) of patients who temporarily discontinued golimumab due to adverse events	6 (4.0%)
Number of adverse events leading to permanent discontinuation of golimumab	6
Number (%) of patients who permanently discontinued golimumab due to adverse events	5 (3.4%)

N=Number of patients
Source: Section 14, Table 59

Overall, 23 adverse events were reported in 14 patients (9.4%) and 20 treatment-related adverse events were reported in 12 patients (8.1%).

Three serious adverse events were reported in 3 patients (2.0%) and none of them was fatal or treatment-related.

Six patients (4.0%) temporarily discontinued golimumab due to adverse events (9 events) and 5 patients (3.4%) permanently discontinued golimumab due to adverse events (6 events).

12.2.2 Display and Analysis of Overall Adverse Events

<u>All adverse events</u>

The summary of all adverse events by SOC and PT in the STD set is presented in Section 14, Table 60.

Overall, 23 adverse events were reported in 14 patients (9.4%).

Infections and infestations, and skin and subcutaneous tissue disorders (both with 6 events reported in 5 patients, 3.4%), were the most commonly reported SOC.

Leukopenia (2 patients, 1.3%), erysipelas (2 patients, 1.3%) and ALT increased (2 patients, 1.3%) were the most common adverse events by preferred term. None of the other adverse events was reported in more than one patient.

Adverse events by maximum intensity

The summary of all adverse events by SOC, PT and maximum intensity in the STD set is presented in Section 14, Table 61.

All adverse events were of mild or moderate intensity, and there were no adverse events of severe intensity.

Of the 23 reported adverse events, 11 were of mild intensity and 12 were of moderate intensity.

12.2.3 Display and Analysis of Drug-Related Adverse Events

The summary of all treatment-related adverse events by SOC and PT in the STD set is presented in Section 14, Table 63.

Overall, 20 treatment-related adverse events were reported in 12 patients (8.1%).

Infections and infestations, and skin and subcutaneous tissue disorders (both with 6 events reported in 5 patients, 3.4%), were the most commonly reported SOC.

Leukopenia (2 patients, 1.3%), erysipelas (2 patients, 1.3%) and ALT increased (2 patients, 1.3%) were the most common treatment-related adverse events by preferred term. The other treatment-related adverse events that were reported in one patient consisted of thrombocytopenia, bronchitis, genital candidiasis, pahryngotonsillitis, urinary tract infection, AST increased, transaminases increased, dyspnoea, alopecia, pruritus, psoriasis, pustular psoriasis, rash eryrthematous and rash popular.

12.2.4 Display and Analysis of Serious Adverse Events

12.2.4.1 Serious Adverse Events

The summary of all serious adverse events by SOC and PT in the STD set is presented in Section 14, Table 62.

Three serious adverse events were reported in 3 patients (2.0%) and none of them was treatment-related (Section 14, Table 64).

Listing of these patients is presented in Section 14, Table 66.

The 3 serious adverse events consisted of (preferred term);

- Basal cell carcinoma in patient No. PPD
- Drug-induced liver injury (reported term: methotrexate toxic hepatitis) in patient No. PPD
- Lympadenopathy in patient No. PPD

12.2.4.2 Deaths

No fatal adverse events occurred in any patient.

12.2.5 Display and Analysis of Other Significant Adverse Events

Adverse events leading to permanent discontinuation of golimumab

Five patients (3.4%) permanently discontinued golimumab due to adverse events (6 events).

Listing of these patients is presented in Section 14, Table 68.

Adverse events leading to permanent discontinuation of golimumab consisted of (preferred term):

- Pustular psoriasis in patient No. PPD
- Alopecia in patient No. PPD
- Pruritus in patient No. PPD
- Transaminases increased in patient No. PPD
- AST and ALT increased in patient No. PPD

All these adverse events were related to golimumab.

Adverse events leading to temporary discontinuation of golimumab

Six patients (4.0%) temporarily discontinued golimumab due to adverse events (9 events).

Listing of these patients is presented in Section 14, Table 69.

Adverse events leading to temporary discontinuation of golimumab consisted of (preferred term):

- Basal cell carcinoma (not related to golimumab), dyspnoea (related to golimumab) and bronchitis (related to golimumab) in patient No. PPD
- Rash erythematous (related to golimumab) and rash popular (related to golimumab) in patient No. PPD
- Drug-induced liver injury (reported term: methotrexate toxic hepatitis) (not related to golimumab) in patient No. PPD
- Erysipelas (related to golimumab) in patient No. PPD
- Urinary tract infection (related to golimumab) in patient No. PPD
- Pharyngotonsillitis (related to golimumab) in patient No. PPD

12.2.6 Adverse Events of Special Interest

No cases of pregnancy or lactation were reported during the study. No other adverse events of special interest were pre-defined in the study protocol.

12.2.7 Listing of All Adverse Events by Subject

Listing of all adverse events by subject (with specification of age and gender), reported term, PT, SOC, seriousness, date of start and date of end, intensity, correlation with golimumab,

action taken, outcome and progress at end of study, is presented in Section 14, Table 65. The same listing is presented in Section 14, Tables 66, 68 and 69 for serious adverse events, adverse events leading to permanent discontinuation of golimumab, and adverse events leading to temporary discontinuation of golimumab, respectively.

12.3 Clinical Evaluation of Laboratory Safety Tests

12.3.1 Listing of Specific Laboratory Tests by Subject

Not applicable.

12.3.2 Evaluation of Each Laboratory Test

12.3.2.1 Laboratory Values Over Time

Not applicable.

12.3.2.2 Individual Subject Changes

Not applicable.

12.3.2.3 Specific Abnormal Laboratory Values of Clinical Relevance

Not applicable.

12.4 Vital Signs, Other Physical Observations, and Special Examinations Related to Safety

Not applicable.

12.5 Subjects at Increased Risk, Pregnant Women, and Other Potentially Vulnerable Subjects

Not applicable.

12.6 Safety Summary

The results of safety of this study were in line with the known safety profile of golimumab.

Treatment-related adverse events were reported in 12 patients overall (8.1%): leucopenia, erysipelas and ALT increased were reported in 2 patients (1.3%), whereas the other treatment-related adverse events that were reported in no more than one patient. None of the three serious adverse events was fatal and none of them was considered as related to treatment. Six patients (4.0%) and 5 patients (3.4%) temporarily and permanently discontinued golimumab due to adverse events, respectively.

13 DISCUSSION AND CONCLUSIONS

The primary objective of this multicenter, prospective, observational study conducted in Italy was to identify predictors of Minimal Disease Activity (MDA) following treatment for 6 months with golimumab in patients with active PsA, and hence to evaluate if the identification of these predictors can improve care in selecting patients able to achieve the target.

The MDA was defined as the achievement of at least 5 of the following 7 criteria: TJC ≤ 1, SJC ≤ 1, PGA for psoriatic activity as clear or almost clear, patient pain VAS ≤ 15 mm, patient global assessment of PsA disease activity VAS ≤ 20 mm, HAQ score ≤ 0.5, and tender enthesial points ≤ 1.

Other objectives of the study were to assess changes from baseline to 3 and 6 months in disease activity response (DAPSA), functional state (HAQ), enthesitis score and dactylitic digit count.

The study population included adult patients with PsA predominantly characterized by peripheral synovitis (as per CASPAR criteria), who had unsatisfactory response to conventional therapies, were naive to anti-TNFs or other biologic agents and were prescribed golimumab according to usual clinical practice. To be eligible for study participation, patients were also required to have availability of a set of core variables prior to the first injection of golimumab, including age, gender, BMI, duration of PsA since date of diagnosis, information on presence/absence of polyarthritis, ESR/CRP, concurrent DMARD, HAQ and DAPSA score.

According to estimations formulated in the sample size calculation, 151 patients overall were enrolled in 23 sites in Italy and 149 of them were evaluable (2 patients withdrew the consent).

More than 80% of patients completed the study and 120 patients (96.0% of those that completed the study) were still receiving golimumab at the end of study.

The evaluable population included 80 (53.7%) males and 69 (46.3%) females, and the mean (± SD) age was 49.16 ± 11.25 years (median 50.0 years, range 21 to 75 years). The mean (± SD) time from first diagnosis was 45.49 ± 70.58 months (median 21.47 months, range 0.03 to 554.47 months) and this time frame followed the time from onset of symptoms for an average of about 3.25 years. The majority of patients had polyarthritis (135 patients, 90.6%), and had received concomitant DMARDs (106 patients, 71.1%). All 149 patients had received a previous PsA therapy.

The results of the primary variable of the study showed that 66 patients (44.3% of evaluable) achieved the MDA at 6 months, while 59 patients (39.6%) did not achieve the MDA and results were unknown in 24 (16.1%). The proportions of patients who achieved the 7 pre-defined criteria at Month 6 ranged from 36.2% for patient assessment of pain VAS ≤ 15 mm to 77.2% for clear or almost clear PGA for psoriatic activity. Therefore, the proportion of patients achieving MDA at 6 months was in line with the hypothesis used in the sample size estimation.

The analysis of the predictive factors showed that factors that resulted to be predictive of MDA at 6 months in the univariable predictive model were male gender, lower age and lower DAPSA score, HAQ score, patient assessment of pain VAS and BASDAI score at baseline,

and absence of comorbidities, while factors that resulted to be predictive of MDA at 6 months in the multivariable predictive model were lower age, higher hs-CRP value at baseline, lower DAPSA score at baseline, and longer duration of symptoms at baseline. In the biomarker-enhanced clinical prediction model, a higher hs-CRP value at baseline in the univariable logistic model, and absence of comorbidities and lower DAPSA score at baseline were indicative of a higher probability to achieve MDA at 6 months in the multivariable logistic model.

The results of the secondary endpoints showed that 54 patients (36.2%) achieved the MDA at 3 months, while 84 patients (56.4%) did not achieve the MDA and results were unknown in 11 (7.4%). The proportions of patients who achieved the 7 pre-defined criteria at Month 3 ranged from 25.5% for patient's global assessment of PsA disease activity VAS ≤ 20 mm to 82.6% for clear or almost clear PGA for psoriatic activity.

In the univariable logistic model, factors that resulted to be predictive of MDA at 3 months were the same that were reported at 6 months, whereas, in the multivariable logistic model, factors that resulted to be predictive of MDA at 3 months were lower age, higher hs-CRP value at baseline, lower DAPSA score and HAQ score at baseline, and longer time from diagnosis. In the biomarker-enhanced clinical prediction model, none of the biomarkers in the univariable logistic model, and lower age, lower BASDAI and DAPSA core at baseline, and longer time from diagnosis were predictive for the achievement of MDA at 3 months in the multivariable logistic model.

Treatment with golimumab was associated with improvements in all disease and functional parameters. Improvements from the screening visit were evident after just 3 months of treatment and were sustained and further increased at 6 months.

Mean and median HAQ total score decreased from the screening visit to Month 3 and Month 6: the mean (± SD) change from the screening visit was -0.34 ± 0.499 (median -0.31, range -1.50 to 0.75) at Month 3 and was -0.41 ± 0.518 (median -0.38, range -1.88 to 1.13) at Month 6. At Month 6, a score of 0 (without any difficulty) was the most frequently reported score for all subscales, ranging from 40.3% of patients for common daily activities to 63.8% of patients for grip, whereas a score of 3 (unable) was reported in a minority of patients in all subscales.

The evaluation of enthesitis showed that the mean and median LEI score decreased from the screening visit to Month 3 and Month 6: the mean (± SD) change from the screening visit was -1.07 ± 1.451 (median -1.00, range -6 to 3) at Month 3 and was -1.27 ± 1.531 (median -1.00, range -6 to 3) at Month 6.

Similarly, the mean dactylitis digit count decreased from the screening visit to Month 3 and Month 6; the mean (± SD) change from the screening visit was -0.47 ± 1.128 (median 0.00, range -6 to 2) at Month 3 and was -0.46 ± 1.118 (median 0.00, range -6 to 2) at Month 6.

The results of DAPSA composite score, which includes five untransformed and unweighted variables measured by patient and physician, further confirmed the effectiveness of golimumab after 3 and 6 months from the start of treatment. The mean and median DAPSA total score decreased from the screening visit to Month 3 and Month 6. The mean (± SD) change from the screening visit was -16.17 ± 12.143 (median -14.32, range -70.75 to 15.00) at Month 3 and was -19.16 ± 13.037 (median -17.12, range -67.50 to 20.19) at Month 6.

The evaluation of all the other efficacy variables, which included laboratory parameters (hs-CRP and ESR), TJC and SJC, patient assessment of pain VAS, patient global assessment of PsA disease activity VAS, PGA of PsA disease activity VAS and skin assessment, and VAS for symptoms of ankylosing spondylitis (BASDAI total score) also showed improvements from the screening visit to both Month 3 and Month 6.

In the correlation tests performed with Pearson correlation, statistically significant direct correlations with all the other diseases activity measures were observed for TJC, SJC, patient's global assessment of pain VAS, HAQ total score, BASDAI, LEI index and DAPSA total score. No statistically significant correlations with any diseases activity measures were observed for hs-CRP and for dactylitis digit count at both Month 3 and Month 6, except between dactylitis digit count and SJC and LEI index at Month 3.

In the correlation tests performed with a linear mixed model, statistically significant direct correlations were observed with all diseases activity measures, except for hs-CRP (which correlated with DAPSA total score only) and between tender joint count and LEI index.

The results of safety of this study were in line with the known safety profile of golimumab. Overall, treatment with golimumab was well tolerated.

Adverse events were reported in 14 patients (9.4%) and were considered as related with treatment in 12 patients (8.1%). Treatment-related leucopenia, erysipelas and ALT increased were reported in 2 patients (1.3%), whereas the other treatment-related adverse events that were reported in one patient. None of the three serious adverse events was fatal and none of them was considered as related to treatment. Six patients (4.0%) and 5 patients (3.4%) temporarily and permanently discontinued golimumab due to adverse events, respectively.

In conclusion, the results of the study have shown that:

- Minimal Disease Activity (MDA) after 6 months from the start of treatment with golimumab was achieved in 44.3% of evaluable patients with active PsA.
- Male gender, lower age, lower DAPSA, HAQ score, patient assessment of pain VAS and BASDAI score at baseline, and absence of comorbidities, were the predictive factors of MDA at 6 months in the univariable model, while factors that were predictive of MDA at 6 months in the multivariable model were lower age, higher hs-CRP at baseline, lower DAPSA score at baseline, and longer duration of symptoms at baseline.
- MDA at 3 months was achieved in 36.2% of patients, and predictive factors did not differ from those observed at 6 months.
- Treatment with golimumab was associated with improvements in all disease and functional parameters measured by patient and physician, and in laboratory markers of disease activity: improvements from the screening visit were evident just after 3 months of treatment and were sustained and further increased at 6 months.
- Statistically significant direct correlations were observed for all disease activity measures, except for hs-CRP and for dactylitis digit count.
- Treatment with golimumab was well tolerated and the results of safety were in line with the known adverse event profile of golimumab.

14 NARRATIVES, SUPPLEMENTAL TABLES AND/OR FIGURES

14.1 Demographic Data

Please refer to the following tables:

Table 7. Demographic data

14.2 Efficacy Data

Please refer to the following tables:

Table 25. CRP (nmol/L) during the study and change from Screening Visit

Table 26. ESR (mm/h) during the study and change from Screening Visit

Table 27. Peripheral Joint assessment (Tenderness) during the study and change from Screening Visit

Table 28. Peripheral Joint assessment (Swelling) during the study and change from Screening Visit

Table 29. Patient Global Assessment of pain (VAS in mm) during the study and change from Screening Visit

Table 30. Patient global assessment of PsA disease activity (VAS in mm) during the study and change from Screening Visit

Table 31. Physician Global assessment of disease activity (VAS in mm) during the study and change from Screening Visit

Table 32. Summary of Functional Assessment at Follow-up Visit at 3 months (HAQ - Subscale scores)

Table 33. Summary of Functional Assessment at Follow-up Visit at 6 months (HAQ – Subscale scores)

Table 34. HAQ total score during the study and change from Screening Visit (calculated)

Table 35. BASDAI score during the study and change from Screening Visit (calculated)

Table 36. Summary of 3-month FU PGA (Physician Global Assessment for Psoriatic activity) - Skin Assessments

Table 37. Summary of 6-month FU PGA (Physician Global Assessment for Psoriatic activity) - Skin Assessments

Table 38. LEI score during the study and change from Screening Visit

Table 39. Dactylitis score during the study and change from Screening Visit

Table 40. DAPSA total score during the study and change from Screening Visit

Table 41. Summary of Minimal Disease Activity (MDA) at Follow-up Visit at 3 months

Table 42. Summary of Minimal Disease Activity (MDA) at Follow-up Visit at 6 months

Table 43. Clinical prediction model of MDA at 6 months

Table 44. Biomarker-enhanced clinical prediction model of MDA at 6 months

Table 45. Clinical prediction model of MDA at 3 months

Table 46. Biomarker-enhanced clinical prediction model of MDA at 3 months

Table 47. Clinical prediction model of change in DAPSA score from baseline to Follow-up Visit at 6 months

Table 48. Biomarker-enhanced clinical prediction model of change in DAPSA score from baseline to Follow-up Visit at 6 months

Table 49. Clinical prediction model of change in HAQ score from baseline to Follow-up Visit at 6 months

Table 50. Biomarker-enhanced clinical prediction model of change in HAQ score from baseline to Follow-up Visit at 6 months

Table 51. Clinical prediction model of change in LEI index from baseline to Follow-up Visit at 6 months

Table 52. Biomarker-enhanced clinical prediction model of change in LEI index from baseline to Follow-up Visit at 6 months

Table 53. Clinical prediction model of change in dactylitis score from baseline to Follow-up Visit at 6 months

Table 54. Biomarker-enhanced clinical prediction model of change in dactylitis score from baseline to Follow-up Visit at 6 months

Table 55.1. Correlation between disease activity measures at baseline(Pearson)

Table 55.2. Correlation between disease activity measures at 3 months (Pearson)

Table 55.3. Correlation between disease activity measures at 6 months (Pearson)

Table 56. Correlation between disease activity measures (Bland and Altman)

14.3 Safety Data

14.3.1 Listings of Deaths, Other Serious and Significant Adverse Events

Listing of serious adverse events, adverse events leading to permanent discontinuation of golimumab, and adverse events leading to temporary discontinuation of golimumab by subject (with specification of age and gender), reported term, PT, SOC, seriousness, date of start and date of end, intensity, correlation with golimumab, action taken, outcome and progress at end of study, is presented in Tables 66, 68 and 69, respectively.

14.3.2 Narratives of Deaths, Other Serious and Significant Adverse Events

As no treatment-related serious adverse events were reported in any patient, a short narrative of the 3 patients with serious adverse events is provided below (for details, refer to Table 69):

- Patient No. PPD the patient had a diagnosis of basal cell carcinoma (reported term: basal cell carcinoma), which was mild in intensity and was considered as not related with golimumab. The event required the temporary discontinuation of golimumab, was not recovered and was ongoing at the end of the study;

- Patient No. PPD the patient had a drug-induced liver injury (reported term: methotrexate toxic hepatitis), which was moderate in intensity and was considered as not related with golimumab. The event required the temporary discontinuation of golimumab and a specific concomitant treatment. The event recovered and was not ongoing at the end of the study;
- Patient No. PPD the patient had lympadenopathy (preferred term: bilateral cervical lympadenopathies), which was moderate in intensity and was considered as not related with golimumab. The event did not require any treatment, recovered and was not ongoing at the end of the study.

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Table 1 - Patients enrolled by site

Population: ENR

Site	Statistic	N = 151
PPD	n (%)	12 (7.9%)
	n (%)	13 (8.6%)
	n (%)	6 (4.0%)
	n (%)	6 (4.0%)
	n (%)	3 (2.0%)
	n (%)	1 (0.7%)
	n (%)	4 (2.6%)
	n (%)	5 (3.3%)
	n (%)	11 (7.3%)
	n (%)	7 (4.6%)
	n (%)	9 (6.0%)
	n (%)	4 (2.6%)
	n (%)	3 (2.0%)
	n (%)	9 (6.0%)
	n (%)	2 (1.3%)
	n (%)	5 (3.3%)
	n (%)	5 (3.3%)
	n (%)	8 (5.3%)
	n (%)	8 (5.3%)
	n (%)	4 (2.6%)
	n (%)	4 (2.6%)
	n (%)	7 (4.6%)
	n (%)	15 (9.9%)

Note: Percentages are based on all enrolled patients.

Source: Disposition.sas, SPARC Consulting. Run on 17MAY2017

Table 2 - Analysis Samples

	Statistics		
Number of enrolled patients	n (%)		151
Number of patients in the STD set	n (%)	149	(98.7%)
Number of patients excluded from STD set	n (%)	2	(1.3%)

Note: Percentages are based on all enrolled patients (N).
The Standard population (STD) includes all subjects who signed the informed consent form and received at least one dose of Golimumab.

Source: Samples.sas, SPARC Consulting. Run on 17MAY2017

Table 3 - Data listing of patients excluded from the STD population

Table 4 - Data listing of inclusion or exclusion criteria violation

NO CRITERIA VIOLATION WERE REPORTED IN THE STUDY

Source: ViolationCriteria.sas. Run 17MAY17 11:56

Table 5 - Summary of End of Study visit

Popolazione: ENR

		Statistics	N=151
Study completed?	No	n (%)	26 (17.2%)
	Yes	n (%)	125 (82.8%)
	Total	n	151
Primary reason for premature treatment discontinuation°	Withdrawal of consent	n (%)	3 (11.5%)
	Subject lost to follow-up	n (%)	9 (34.6%)
	Other	n (%)	14 (53.8%)
	Total	n	26
Ongoing treatment at the end of the study? #	No	n (%)	5 (4.0%)
	Yes	n (%)	120 (96.0%)
	Total	n	125

Notes:
1) Percentages are calculated on the total number of patients in the ENR population.
2) ° includes only those patients who did not complete the study.
3) # includes only those patients who completed the study.

Source: Eos_summary.sas, run on 17MAY2017

Table 6 - Data listing of patients who prematurely discontinued the treatment

Table 7 - Demographic data

Popolazione: STD

		Statistics	N=149
Gender	Male	n (%)	80 (53.7%)
	Female	n (%)	69 (46.3%)
	Total	n	149
Age (years)		n	149
		Mean	49.16
		SD	11.25
		Median	50.00
		Q1,Q3	41.00,57.00
		Min,Max	21.00,75.00
Ethnicity	Caucasian	n (%)	146 (98.0%)
	Non-Caucasian	n (%)	3 (2.0%)
	Total	n	149
Civil Status	Married	n (%)	119 (79.9%)
	Non-Married	n (%)	30 (20.1%)
	Total	n	149
Education	Compulsory education	n (%)	57 (38.3%)
	High School	n (%)	70 (47.0%)
	University	n (%)	22 (14.8%)
	Total	n	149
Employment	No	n (%)	34 (22.8%)
	Yes	n (%)	99 (66.4%)
	Other	n (%)	16 (10.7%)
	Total	n	149

Note:
Percentages are calculated on the total number of patients in the STD population.

Source: Demo.sas, run on 17MAY2017

Table 8 - Summary of vital signs at Screening Visit

Popolazione: STD

	Statistics	N=149
Weight (kg)	n	149
	Mean	77.99
	SD	15.50
	Median	78.00
	Q1,Q3	67.00,85.00
	Min,Max	47.00,127.00
Height (m)	n	149
	Mean	1.70
	SD	0.10
	Median	1.70
	Q1,Q3	1.63,1.77
	Min,Max	1.50,1.90
BMI(kg/m2)	n	149
	Mean	26.87
	SD	4.25
	Median	27.00
	Q1,Q3	24.00,29.00
	Min,Max	18.00,39.00

Source: VitalSign.sas, run on 17MAY2017

Table 9 - Summary of smoking habits

Popolazione: STD		Statistics	N=149
Smoker	No	n (%)	96 (64.4%)
	Current	n (%)	28 (18.8%)
	Past	n (%)	25 (16.8%)
	Total	n	149
No. of cigarettes/day °		n	27
		Mean	12.11
		SD	5.77
		Median	10.00
		Q1,Q3	10.00,15.00
		Min,Max	3.00,30.00
Time from last cigarette (years) #		n	20
		Mean	13.30
		SD	9.69
		Median	14.50
		Q1,Q3	2.00,20.00
		Min,Max	1.00,31.00

Notes:
° No. of cigarettes/day was reported only for current smokers.
Time from last cigarette was calculated only for past smokers as the difference between the year of informed consent and the end year of smoking.

Source: Smoke.sas, run on 17MAY2017

Table 10 - Summary of Psoriatic Arthritis (PsA) characteristics

Popolazione: STD

		Statistics	N=149
Time from initial diagnosis (months)°		n	149
		Mean	45.49
		SD	70.58
		Median	21.47
		Q1,Q3	7.57,53.43
		Min,Max	0.03,554.47
Time from symptoms onset (months)#		n	139
		Mean	84.60
		SD	95.30
		Median	53.43
		Q1,Q3	21.77,113.57
		Min,Max	2.17,554.47
Polyarthritis	Absence	n (%)	14 (9.4%)
	Presence	n (%)	135 (90.6%)
	Total	n	149
Previous PsA therapy	Yes	n (%)	149 (100.0%)
	Total	n	149
Concomitant DMARDs	No	n (%)	43 (28.9%)
	Yes	n (%)	106 (71.1%)
	Total	n	149

Notes:
° Time from initial diagnosis was calculated as follows: (Informed consent date - Initial diagnosis date +1)/30.
Time from symptoms onset was calculated as follows: (Informed consent date - Symptoms onset date +1)/30.
If 'Initial diagnosis date' and 'Symptoms onset date' day was 'na' we specify '01' for the calculation
If 'Initial diagnosis date' and 'Symptoms onset date' month was 'na' we specify '07' for the calculation

Source: psa.sas, run on 17MAY2017

Table 11 - Summary of previous diseases

Population: STD

Primary SOC/PT	Statistics		N=149
No. of patients with at least one previous disease	n (%)		29 (19.5%)
Cardiac Disorders	n (%)	E	2 (1.3%) 2
Atrial Fibrillation	n (%)	E	1 (0.7%) 1
Pericarditis	n (%)	E	1 (0.7%) 1
Endocrine Disorders	n (%)	E	2 (1.3%) 2
Thyroid Disorder	n (%)	E	2 (1.3%) 2
Eye Disorders	n (%)	E	1 (0.7%) 1
Cataract	n (%)	E	1 (0.7%) 1
Gastrointestinal Disorders	n (%)	E	2 (1.3%) 2
Diverticulum	n (%)	E	1 (0.7%) 1
Gastric Polyps	n (%)	E	1 (0.7%) 1
Hepatobiliary Disorders	n (%)	E	1 (0.7%) 1
Cholelithiasis	n (%)	E	1 (0.7%) 1
Infections And Infestations	n (%)	E	1 (0.7%) 1
Subcutaneous Abscess	n (%)	E	1 (0.7%) 1
Injury, Poisoning And Procedural Complications	n (%)	E	4 (2.7%) 4
Femur Fracture	n (%)	E	1 (0.7%) 1
Foot Fracture	n (%)	E	1 (0.7%) 1
Hip Fracture	n (%)	E	1 (0.7%) 1
Incisional Hernia	n (%)	E	1 (0.7%) 1
Metabolism And Nutrition Disorders	n (%)	E	1 (0.7%) 1
Diabetes Mellitus	n (%)	E	1 (0.7%) 1
Musculoskeletal And Connective Tissue Disorders	n (%)	E	2 (1.3%) 5
Intervertebral Disc Degeneration	n (%)	E	1 (0.7%) 1
Intervertebral Disc Protrusion	n (%)	E	1 (0.7%) 2

Notes:
Percentages are calculated on the total number of patients in the STD population.
Previous Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'not ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 11 - Summary of previous diseases

Population: STD

Primary SOC/PT	Statistics	N=149
Periarthritis	n (%) E	1 (0.7%) 1
Spondylolisthesis	n (%) E	1 (0.7%) 1
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	n (%) E	3 (2.0%) 3
Neoplasm Malignant	n (%) E	2 (1.3%) 2
Prostatic Adenoma	n (%) E	1 (0.7%) 1
Nervous System Disorders	n (%) E	2 (1.3%) 2
Carpal Tunnel Syndrome	n (%) E	1 (0.7%) 1
Morton's Neuralgia	n (%) E	1 (0.7%) 1
Renal And Urinary Disorders	n (%) E	1 (0.7%) 1
Nephropathy	n (%) E	1 (0.7%) 1
Reproductive System And Breast Disorders	n (%) E	2 (1.3%) 2
Uterine Disorder	n (%) E	1 (0.7%) 1
Varicocele	n (%) E	1 (0.7%) 1
Respiratory, Thoracic And Mediastinal Disorders	n (%) E	1 (0.7%) 1
Lung Disorder	n (%) E	1 (0.7%) 1
Surgical And Medical Procedures	n (%) E	13 (8.7%) 20
Appendicectomy	n (%) E	4 (2.7%) 4
Tonsillectomy	n (%) E	3 (2.0%) 3
Carpal Tunnel Decompression	n (%) E	2 (1.3%) 2
Bunion Operation	n (%) E	1 (0.7%) 1
Colectomy	n (%) E	1 (0.7%) 1
Hernia Repair	n (%) E	1 (0.7%) 1
Hysterosalpingo-Oophorectomy	n (%) E	1 (0.7%) 1
Meniscus Removal	n (%) E	1 (0.7%) 1
Nasal Septal Operation	n (%) E	1 (0.7%) 1
Polypectomy	n (%) E	1 (0.7%) 1
Rhinoplasty	n (%) E	1 (0.7%) 1

Notes:
Percentages are calculated on the total number of patients in the STD population.
Previous Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'not ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 11 - Summary of previous diseases

Population: STD

Primary SOC/PT	Statistics	N=149
Rotator Cuff Repair	n (%) E	1 (0.7%) 1
Spinal Fusion Surgery	n (%) E	1 (0.7%) 1
Synovectomy	n (%) E	1 (0.7%) 1
Vascular Disorders	n (%) E	2 (1.3%) 2
Hypertension	n (%) E	1 (0.7%) 1
Thrombophlebitis Superficial	n (%) E	1 (0.7%) 1

Notes:
Percentages are calculated on the total number of patients in the STD population.
Previous Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'not ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 12 - Summary of concomitant diseases

Population: STD

Primary SOC/PT	Statistics	N=149
No. of patients with at least one concomitant disease	n (%)	101 (67.8%)
Blood And Lymphatic System Disorders	n (%) E	2 (1.3%) 2
Anaemia	n (%) E	1 (0.7%) 1
Thrombocytopenia	n (%) E	1 (0.7%) 1
Cardiac Disorders	n (%) E	2 (1.3%) 2
Atrioventricular Block First Degree	n (%) E	1 (0.7%) 1
Myocardial Ischaemia	n (%) E	1 (0.7%) 1
Congenital, Familial And Genetic Disorders	n (%) E	1 (0.7%) 1
Methylenetetrahydrofolate Reductase Gene Mutation	n (%) E	1 (0.7%) 1
Endocrine Disorders	n (%) E	19 (12.8%) 19
Thyroid Disorder	n (%) E	18 (12.1%) 18
Autoimmune Thyroiditis	n (%) E	1 (0.7%) 1
Eye Disorders	n (%) E	6 (4.0%) 6
Glaucoma	n (%) E	2 (1.3%) 2
Cataract	n (%) E	1 (0.7%) 1
Chorioretinal Disorder	n (%) E	1 (0.7%) 1
Uveitis	n (%) E	1 (0.7%) 1
Xerophthalmia	n (%) E	1 (0.7%) 1
Gastrointestinal Disorders	n (%) E	20 (13.4%) 23
Gastrooesophageal Reflux Disease	n (%) E	6 (4.0%) 6
Chronic Gastritis	n (%) E	4 (2.7%) 4
Inflammatory Bowel Disease	n (%) E	3 (2.0%) 3
Diverticulum	n (%) E	2 (1.3%) 2
Anal Fistula	n (%) E	1 (0.7%) 1
Diarrhoea	n (%) E	1 (0.7%) 1
Dry Mouth	n (%) E	1 (0.7%) 1

Notes:
Percentages are calculated on the total number of patients in the STD population.
Concomitant Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 12 - Summary of concomitant diseases

Population: STD

Primary SOC/PT	Statistics	N=149
Duodenitis	n (%) E	1 (0.7%) 1
Gastric Ulcer	n (%) E	1 (0.7%) 1
Gastritis	n (%) E	1 (0.7%) 1
Malabsorption	n (%) E	1 (0.7%) 1
Periodontal Disease	n (%) E	1 (0.7%) 1
Hepatobiliary Disorders	n (%) E	13 (8.7%) 14
Liver Disorder	n (%) E	11 (7.4%) 12
Cholestasis	n (%) E	1 (0.7%) 1
Hepatic Haematoma	n (%) E	1 (0.7%) 1
Immune System Disorders	n (%) E	3 (2.0%) 4
Drug Hypersensitivity	n (%) E	2 (1.3%) 2
Multiple Allergies	n (%) E	1 (0.7%) 1
Seasonal Allergy	n (%) E	1 (0.7%) 1
Infections And Infestations	n (%) E	8 (5.4%) 10
Latent Tuberculosis	n (%) E	5 (3.4%) 5
Viral Hepatitis Carrier	n (%) E	3 (2.0%) 3
Helicobacter Gastritis	n (%) E	1 (0.7%) 1
Oral Candidiasis	n (%) E	1 (0.7%) 1
Metabolism And Nutrition Disorders	n (%) E	40 (26.8%) 56
Hypercholesterolaemia	n (%) E	11 (7.4%) 11
Obesity	n (%) E	9 (6.0%) 9
Hyperuricaemia	n (%) E	8 (5.4%) 8
Diabetes Mellitus	n (%) E	7 (4.7%) 7
Dyslipidaemia	n (%) E	6 (4.0%) 6
Vitamin D Deficiency	n (%) E	6 (4.0%) 6
Metabolic Syndrome	n (%) E	4 (2.7%) 4
Hypovitaminosis	n (%) E	2 (1.3%) 2
Gout	n (%) E	1 (0.7%) 1
Hyperglycaemia	n (%) E	1 (0.7%) 1
Hyperhomocysteinaemia	n (%) E	1 (0.7%) 1

Notes:
Percentages are calculated on the total number of patients in the STD population.
Concomitant Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 12 - Summary of concomitant diseases

Population: STD

Primary SOC/PT	Statistics	N=149
Musculoskeletal And Connective Tissue Disorders	n (%) E	14 (9.4%) 17
Fibromyalgia	n (%) E	4 (2.7%) 4
Osteoporosis	n (%) E	3 (2.0%) 3
Osteoarthritis	n (%) E	2 (1.3%) 2
Osteopenia	n (%) E	2 (1.3%) 2
Axial Spondyloarthritis	n (%) E	1 (0.7%) 1
Back Pain	n (%) E	1 (0.7%) 1
Intervertebral Disc Disorder	n (%) E	1 (0.7%) 1
Intervertebral Disc Protrusion	n (%) E	1 (0.7%) 1
Morphoea	n (%) E	1 (0.7%) 1
Pain In Extremity	n (%) E	1 (0.7%) 1
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	n (%) E	1 (0.7%) 1
Haemangioma Of Liver	n (%) E	1 (0.7%) 1
Nervous System Disorders	n (%) E	9 (6.0%) 9
Epilepsy	n (%) E	2 (1.3%) 2
Carotid Artery Disease	n (%) E	1 (0.7%) 1
Cerebrovascular Disorder	n (%) E	1 (0.7%) 1
Headache	n (%) E	1 (0.7%) 1
Neuropathy Peripheral	n (%) E	1 (0.7%) 1
Paraesthesia	n (%) E	1 (0.7%) 1
Parkinson's Disease	n (%) E	1 (0.7%) 1
Parkinsonian Rest Tremor	n (%) E	1 (0.7%) 1
Psychiatric Disorders	n (%) E	5 (3.4%) 6
Depression	n (%) E	4 (2.7%) 4
Anxiety	n (%) E	1 (0.7%) 1
Panic Attack	n (%) E	1 (0.7%) 1
Renal And Urinary Disorders	n (%) E	5 (3.4%) 5
Nephropathy	n (%) E	3 (2.0%) 3
Renal Atrophy	n (%) E	1 (0.7%) 1

Notes:
Percentages are calculated on the total number of patients in the STD population.
Concomitant Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 12 - Summary of concomitant diseases

Population: STD

Primary SOC/PT	Statistics	N=149
Renal Cyst	n (%) E	1 (0.7%) 1
Reproductive System And Breast Disorders	n (%) E	6 (4.0%) 6
Benign Prostatic Hyperplasia	n (%) E	2 (1.3%) 2
Ovarian Cyst	n (%) E	2 (1.3%) 2
Endometriosis	n (%) E	1 (0.7%) 1
Premature Menopause	n (%) E	1 (0.7%) 1
Respiratory, Thoracic And Mediastinal Disorders	n (%) E	7 (4.7%) 7
Lung Disorder	n (%) E	6 (4.0%) 6
Rhinitis Allergic	n (%) E	1 (0.7%) 1
Skin And Subcutaneous Tissue Disorders	n (%) E	13 (8.7%) 14
Psoriasis	n (%) E	11 (7.4%) 11
Dermal Cyst	n (%) E	1 (0.7%) 1
Hidradenitis	n (%) E	1 (0.7%) 1
Vitiligo	n (%) E	1 (0.7%) 1
Surgical And Medical Procedures	n (%) E	1 (0.7%) 1
Hysterectomy	n (%) E	1 (0.7%) 1
Vascular Disorders	n (%) E	35 (23.5%) 35
Hypertension	n (%) E	33 (22.1%) 33
Peripheral Venous Disease	n (%) E	1 (0.7%) 1
Raynaud's Phenomenon	n (%) E	1 (0.7%) 1

Notes:
Percentages are calculated on the total number of patients in the STD population.
Concomitant Diseases are those reported in the 'Medical History/Comorbidities' form in the study CRF and reported as 'ongoing' at study start.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 Dictionary.
Each patient is counted at most once within each SOC and PT.

Source: Concomitant_dis_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 13 - Summary of physical examination

Population: STD

Primary SOC/PT	Statistics		N=149
No. of patients with at least one abnormality	n (%)		97 (65.1%)
Blood And Lymphatic System Disorders	n (%)	E	2 (1.3%) 2
Lymphadenopathy	n (%)	E	2 (1.3%) 2
Cardiac Disorders	n (%)	E	2 (1.3%) 2
Cyanosis	n (%)	E	1 (0.7%) 1
Tachyarrhythmia	n (%)	E	1 (0.7%) 1
Ear And Labyrinth Disorders	n (%)	E	1 (0.7%) 1
Deafness Neurosensory	n (%)	E	1 (0.7%) 1
Endocrine Disorders	n (%)	E	1 (0.7%) 1
Cushingoid	n (%)	E	1 (0.7%) 1
Gastrointestinal Disorders	n (%)	E	8 (5.4%) 9
Abdominal Pain	n (%)	E	3 (2.0%) 4
Abdominal Distension	n (%)	E	1 (0.7%) 1
Abdominal Pain Lower	n (%)	E	1 (0.7%) 1
Abdominal Pain Upper	n (%)	E	1 (0.7%) 1
Abdominal Tenderness	n (%)	E	1 (0.7%) 1
Tongue Exfoliation	n (%)	E	1 (0.7%) 1
Hepatobiliary Disorders	n (%)	E	4 (2.7%) 5
Hepatomegaly	n (%)	E	4 (2.7%) 5
Infections And Infestations	n (%)	E	2 (1.3%) 2
Erysipelas	n (%)	E	1 (0.7%) 1
Latent Tuberculosis	n (%)	E	1 (0.7%) 1
Injury, Poisoning And Procedural Complications	n (%)	E	2 (1.3%) 2
Epicondylitis	n (%)	E	2 (1.3%) 2
Investigations	n (%)	E	7 (4.7%) 12

Notes:
Percentages are calculated on the total number of patients in the STD population.
Physical examination abnormalities are those reported in the CRF Physical Exam form at the Screening Visit, at Follow-up Visit at 3 months or at Follow-up Visit at 6 months.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 dictionary.
Each patient is counted at most once within each SOC and PT.

Source: phyEx_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 13 - Summary of physical examination

Population: STD

Primary SOC/PT	Statistics	N=149
Breath Sounds Abnormal	n (%) E	5 (3.4%) 7
Cardiac Murmur	n (%) E	2 (1.3%) 4
Cardiac Murmur Functional	n (%) E	1 (0.7%) 1
Metabolism And Nutrition Disorders	n (%) E	1 (0.7%) 3
Obesity	n (%) E	1 (0.7%) 3
Musculoskeletal And Connective Tissue Disorders	n (%) E	65 (43.6%) 181
Arthralgia	n (%) E	46 (30.9%) 82
Joint Swelling	n (%) E	40 (26.8%) 47
Arthritis	n (%) E	7 (4.7%) 12
Tendon Pain	n (%) E	7 (4.7%) 8
Pain In Extremity	n (%) E	6 (4.0%) 10
Dactylitis	n (%) E	4 (2.7%) 6
Musculoskeletal Pain	n (%) E	4 (2.7%) 5
Back Pain	n (%) E	1 (0.7%) 1
Bursitis	n (%) E	1 (0.7%) 1
Foot Deformity	n (%) E	1 (0.7%) 1
Intervertebral Disc Protrusion	n (%) E	1 (0.7%) 1
Mobility Decreased	n (%) E	1 (0.7%) 1
Morphoea	n (%) E	1 (0.7%) 2
Muscle Contracture	n (%) E	1 (0.7%) 1
Neck Pain	n (%) E	1 (0.7%) 1
Osteoarthritis	n (%) E	1 (0.7%) 1
Plantar Fasciitis	n (%) E	1 (0.7%) 1
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	n (%) E	1 (0.7%) 1
Haemangioma	n (%) E	1 (0.7%) 1
Nervous System Disorders	n (%) E	2 (1.3%) 2
Hypoaesthesia	n (%) E	1 (0.7%) 1
Tremor	n (%) E	1 (0.7%) 1
Respiratory, Thoracic And Mediastinal Disorders	n (%) E	2 (1.3%) 3

Notes:
Percentages are calculated on the total number of patients in the STD population.
Physical examination abnormalities are those reported in the CRF Physical Exam form at the Screening Visit, at Follow-up Visit at 3 months or at Follow-up Visit at 6 months.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 dictionary.
Each patient is counted at most once within each SOC and PT.

Source: phyEx_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 13 - Summary of physical examination

Population: STD

Primary SOC/PT	Statistics	N=149
Cough	n (%) E	1 (0.7%) 1
Pharyngeal Disorder	n (%) E	1 (0.7%) 1
Pleural Rub	n (%) E	1 (0.7%) 1
Skin And Subcutaneous Tissue Disorders	n (%) E	65 (43.6%) 131
Psoriasis	n (%) E	49 (32.9%) 76
Skin Exfoliation	n (%) E	10 (6.7%) 12
Erythema	n (%) E	8 (5.4%) 9
Nail Dystrophy	n (%) E	6 (4.0%) 7
Hyperkeratosis	n (%) E	5 (3.4%) 5
Nail Disorder	n (%) E	4 (2.7%) 4
Nail Psoriasis	n (%) E	4 (2.7%) 6
Alopecia	n (%) E	2 (1.3%) 2
Rash	n (%) E	2 (1.3%) 2
Vitiligo	n (%) E	2 (1.3%) 3
Eczema	n (%) E	1 (0.7%) 1
Livedo Reticularis	n (%) E	1 (0.7%) 1
Onycholysis	n (%) E	1 (0.7%) 1
Pustular Psoriasis	n (%) E	1 (0.7%) 1
Skin Discolouration	n (%) E	1 (0.7%) 1
Vascular Disorders	n (%) E	3 (2.0%) 3
Hypertension	n (%) E	3 (2.0%) 3

Notes:
Percentages are calculated on the total number of patients in the STD population.
Physical examination abnormalities are those reported in the CRF Physical Exam form at the Screening Visit, at Follow-up Visit at 3 months or at Follow-up Visit at 6 months.
N = number of patients, % = percentage of patients, E = number of events.
Diseases were coded using MedDRA version 18.1 dictionary.
Each patient is counted at most once within each SOC and PT.

Source: phyEx_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 14 - Summary of Baseline Laboratory tests

Popolazione: STD

	Statistics	N=149
Reactant Protein (CRP) (nmol/L)	n	149
	Mean	136.251
	SD	316.560
	Median	51.430
	Q1,Q3	27.620,133.336
	Min,Max	0.000,3047.680
Erythrocyte Sedimentation Rate (ESR) (mm/h)	n	149
	Mean	23.349
	SD	19.633
	Median	19.000
	Q1,Q3	10.000,32.000
	Min,Max	2.000,120.000

Source: Lab_base.sas, run on 17MAY2017

Table 15 - Summary of Baseline Peripheral Joint Assessment

Popolazione: STD

	Statistics	N=149
Tenderness (68 joint count)	n	149
	Mean	11.8
	SD	9.5
	Median	10.0
	Q1,Q3	5.0,15.0
	Min,Max	1.0,55.0
Swelling (66 joint count)	n	149
	Mean	4.7
	SD	4.7
	Median	4.0
	Q1,Q3	2.0,7.0
	Min,Max	0.0,22.0

Source: JC_base.sas, run on 17MAY2017

Table 16 - Summary of Baseline VAS

Popolazione: STD

	Statistics	N=149
Patient Global assessment of pain (mm)	n	149
	Mean	61.2
	SD	24.4
	Median	64.0
	Q1,Q3	47.0,80.0
	Min,Max	3.0,100.0
Patient Global assessment of PsA disease activity (mm)	n	149
	Mean	63.2
	SD	19.4
	Median	65.0
	Q1,Q3	50.0,76.0
	Min,Max	11.0,100.0
Physician Global assessment of PsA disease activity (mm)	n	149
	Mean	54.8
	SD	19.3
	Median	55.0
	Q1,Q3	41.0,70.0
	Min,Max	10.0,98.0

Source: VAS_base.sas, run on 17MAY2017

Table 17 - Summary of Baseline Functional Assessment (HAQ - Subscale scores)

Popolazione: STD

		Statistics	N=149
Dressing and Grooming	Without any difficulty	n (%)	47 (31.5%)
	Some difficulty	n (%)	74 (49.7%)
	Much difficulty	n (%)	25 (16.8%)
	Unable	n (%)	3 (2.0%)
	Total	n	149
Arising	Without any difficulty	n (%)	48 (32.2%)
	Some difficulty	n (%)	78 (52.3%)
	Much difficulty	n (%)	19 (12.8%)
	Unable	n (%)	4 (2.7%)
	Total	n	149
Eating	Without any difficulty	n (%)	55 (36.9%)
	Some difficulty	n (%)	56 (37.6%)
	Much difficulty	n (%)	30 (20.1%)
	Unable	n (%)	8 (5.4%)
	Total	n	149
Walking	Without any difficulty	n (%)	51 (34.2%)
	Some difficulty	n (%)	67 (45.0%)
	Much difficulty	n (%)	30 (20.1%)
	Unable	n (%)	1 (0.7%)
	Total	n	149
Hygiene	Without any difficulty	n (%)	54 (36.2%)
	Some difficulty	n (%)	65 (43.6%)
	Much difficulty	n (%)	18 (12.1%)
	Unable	n (%)	12 (8.1%)
	Total	n	149
Reach	Without any difficulty	n (%)	23 (15.4%)
	Some difficulty	n (%)	89 (59.7%)
	Much difficulty	n (%)	30 (20.1%)
	Unable	n (%)	7 (4.7%)
	Total	n	149
Grip	Without any difficulty	n (%)	69 (46.3%)
	Some difficulty	n (%)	58 (38.9%)
	Much difficulty	n (%)	18 (12.1%)
	Unable	n (%)	4 (2.7%)
	Total	n	149
Common daily activities	Without any difficulty	n (%)	24 (16.1%)
	Some difficulty	n (%)	65 (43.6%)
	Much difficulty	n (%)	52 (34.9%)
	Unable	n (%)	8 (5.4%)
	Total	n	149

Source: HAQ_base.sas, run on 17MAY2017

Table 18 - Summary of Baseline Functional Assessment (HAQ - total score)

Popolazione: STD

	Statistics	N=149
HAQ score (calculated)	n	149
	Mean	0.95
	SD	0.60
	Median	0.88
	Q1,Q3	0.50,1.25
	Min,Max	0.00,2.75

Source: HAQ_tot_base.sas, run on 17MAY2017

Table 19 - Summary of Baseline BASDAI (single items and total BASDAI score)

Popolazione: STD	Statistics	N=149
Fatigue (VAS - cm)	n	149
	Mean	6.1
	SD	2.4
	Median	7.0
	Q1,Q3	5.0,8.0
	Min,Max	0.0,10.0
Spinal pain (VAS - cm)	n	149
	Mean	5.7
	SD	2.9
	Median	6.0
	Q1,Q3	3.0,8.0
	Min,Max	0.0,10.0
Joint pain / swelling (VAS - cm)	n	149
	Mean	6.5
	SD	2.5
	Median	7.0
	Q1,Q3	5.0,8.0
	Min,Max	0.0,10.0
Areas of localized tenderness (VAS - cm)	n	149
	Mean	6.2
	SD	2.6
	Median	7.0
	Q1,Q3	5.0,8.0
	Min,Max	0.0,10.0
Morning stiffness (intensity) (VAS - cm)	n	149
	Mean	6.2
	SD	2.7
	Median	7.0
	Q1,Q3	4.0,8.0
	Min,Max	0.0,10.0
Morning stiffness (duration) (VAS - cm)	n	149
	Mean	3.4
	SD	2.8
	Median	3.0
	Q1,Q3	1.0,5.0
	Min,Max	0.0,10.0
BASDAI score (calculated)	n	149
	Mean	5.87
	SD	1.94
	Median	6.20
	Q1,Q3	4.50,7.30
	Min,Max	0.50,9.80

Source: BASDAI_base.sas, run on 17MAY2017

Table 20 - Summary of Baseline PGA (Physician Global Assessment for Psoriatic activity) - Skin Assessments

Popolazione: STD

		Statistics	N=149
Skin assessments	Clear	n (%)	57 (38.3%)
	Almost Clear	n (%)	37 (24.8%)
	Mild	n (%)	31 (20.8%)
	Mild to Moderate	n (%)	16 (10.7%)
	Moderate	n (%)	5 (3.4%)
	Moderate to Severe	n (%)	2 (1.3%)
	Severe	n (%)	1 (0.7%)
	Total	n	149

Source: PGA_base.sas, run on 17MAY2017

Table 21 - Summary of Baseline Enthesitis Index (LEI score)

Popolazione: STD

	Statistics	N=149
LEI score	n	149
	Mean	1.9
	SD	1.6
	Median	2.0
	Q1,Q3	1.0,2.0
	Min,Max	0.0,6.0

Source: LEI_base.sas, run on 17MAY2017

Table 22 - Summary of Baseline Dactylitis score

Popolazione: STD

	Statistics	N=149
Dactylitis score	n	149
	Mean	0.6
	SD	1.4
	Median	0.0
	Q1,Q3	0.0,1.0
	Min,Max	0.0,10.0

Source: Dactyl_base.sas, run on 17MAY2017

Table 23 - Summary of Baseline DAPSA score

Popolazione: STD

	Statistics	N=149
DAPSA score	n	149
	Mean	30.37
	SD	14.51
	Median	27.20
	Q1,Q3	20.05,36.70
	Min,Max	7.75,82.35

Source: Dapsa_base.sas, run on 17MAY2017

Table 24 - Summary of Baseline Minimal Disease Activity (MDA)

Popolazione: STD

		Statistics	N=149
Tender Joint count	>1	n (%)	145 (97.3%)
	<=1	n (%)	4 (2.7%)
	Total	n	149
Swollen Joint count	>1	n (%)	118 (79.2%)
	<=1	n (%)	31 (20.8%)
	Total	n	149
PGA for Psoriatic activity	Other	n (%)	55 (36.9%)
	Clear or Almost clear	n (%)	94 (63.1%)
	Total	n	149
Patient pain VAS	>15 mm	n (%)	142 (95.3%)
	<=15 mm	n (%)	7 (4.7%)
	Total	n	149
Patient global assessment of PsA disease activity VAS	>20 mm	n (%)	147 (98.7%)
	<=20 mm	n (%)	2 (1.3%)
	Total	n	149
HAQ score	>0.5	n (%)	106 (71.1%)
	<=0.5	n (%)	43 (28.9%)
	Total	n	149
Tender entheseal points	>1	n (%)	83 (55.7%)
	<=1	n (%)	66 (44.3%)
	Total	n	149
Has the patient achieved the MDA?	No	n (%)	149 (100.0%)
	Total	n	149

Source: MDA_base.sas, run on 17MAY2017

Table 25 - CRP (nmol/L) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	136.25 (316.560)	
	Median	51.43	
	Min/Max	0.00/3047.68	
Follow-up Visit at 3 months	n	131	131
	Mean (SD)	37.57 (47.678)	-88.69 (291.661)
	Median	22.86	-26.67
	Min/Max	0.00/272.39	-2905.77/169.53
Follow-up Visit at 6 months	n	120	120
	Mean (SD)	34.70 (48.402)	-96.61 (308.537)
	Median	18.67	-27.62
	Min/Max	0.00/306.67	-3001.96/205.72

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: CRP_FUP.sas, run on 17MAY2017

Table 26 - ESR (mm/h) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	23.35 (19.633)	
	Median	19.00	
	Min/Max	2.00/120.00	
Follow-up Visit at 3 months	n	130	130
	Mean (SD)	11.11 (9.420)	-11.71 (17.872)
	Median	8.00	-6.00
	Min/Max	0.00/43.00	-114.00/15.00
Follow-up Visit at 6 months	n	119	119
	Mean (SD)	11.38 (9.420)	-11.83 (17.892)
	Median	8.00	-7.00
	Min/Max	0.00/41.00	-102.00/11.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: ESR_FUP.sas, run on 17MAY2017

Table 27 - Peripheral Joint assessment (Tenderness) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	11.77 (9.523)	
	Median	10.00	
	Min/Max	1.00/55.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	4.83 (6.773)	-6.97 (7.288)
	Median	2.00	-6.00
	Min/Max	0.00/34.00	-43.00/12.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	3.99 (6.700)	-7.72 (7.753)
	Median	1.00	-6.00
	Min/Max	0.00/44.00	-41.00/13.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: tenderness_FUP.sas, run on 17MAY2017

Table 28 - Peripheral Joint assessment (Swelling) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	4.73 (4.687)	
	Median	4.00	
	Min/Max	0.00/22.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	1.24 (2.530)	-3.33 (4.257)
	Median	0.00	-2.00
	Min/Max	0.00/16.00	-21.00/6.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	0.61 (1.650)	-4.09 (4.168)
	Median	0.00	-3.00
	Min/Max	0.00/10.00	-21.00/2.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: Swelling_FUP.sas, run on 17MAY2017

Table 29 - Patient Global Assessment of pain (VAS in mm) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	61.18 (24.367)	
	Median	64.00	
	Min/Max	3.00/100.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	35.15 (27.528)	-25.50 (32.165)
	Median	32.00	-23.50
	Min/Max	0.00/98.00	-99.00/54.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	28.67 (27.074)	-30.59 (33.613)
	Median	22.00	-31.00
	Min/Max	0.00/98.00	-100.00/75.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: VAS_FUP.sas, run on 17MAY2017

Table 30 - Patient global assessment of PsA disease activity (VAS in mm) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	63.25 (19.450)	
	Median	65.00	
	Min/Max	11.00/100.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	39.59 (25.984)	-23.39 (28.635)
	Median	39.00	-21.00
	Min/Max	0.00/100.00	-91.00/47.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	30.92 (25.598)	-31.38 (30.382)
	Median	25.00	-34.00
	Min/Max	0.00/93.00	-92.00/55.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: VAS_FUP.sas, run on 17MAY2017

Table 31 - Physician Global assessment of disease activity (VAS in mm) during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	54.80 (19.274)	
	Median	55.00	
	Min/Max	10.00/98.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	23.14 (18.635)	-31.67 (20.139)
	Median	20.00	-31.00
	Min/Max	0.00/72.00	-83.00/15.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	15.62 (17.441)	-38.82 (21.933)
	Median	10.00	-40.00
	Min/Max	0.00/83.00	-84.00/18.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: VAS_FUP.sas, run on 17MAY2017

Table 32 - Summary of Functional Assessment at Follow-up Visit at 3 months (HAQ - Subscale scores)

Popolazione: STD		Statistics	N=149
Dressing and Grooming	Without any difficulty	n (%)	74 (49.7%)
	Some difficulty	n (%)	52 (34.9%)
	Much difficulty	n (%)	11 (7.4%)
	Unable	n (%)	1 (0.7%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Arising	Without any difficulty	n (%)	74 (49.7%)
	Some difficulty	n (%)	52 (34.9%)
	Much difficulty	n (%)	10 (6.7%)
	Unable	n (%)	2 (1.3%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Eating	Without any difficulty	n (%)	76 (51.0%)
	Some difficulty	n (%)	46 (30.9%)
	Much difficulty	n (%)	15 (10.1%)
	Unable	n (%)	1 (0.7%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Walking	Without any difficulty	n (%)	79 (53.0%)
	Some difficulty	n (%)	48 (32.2%)
	Much difficulty	n (%)	10 (6.7%)
	Unknown	n (%)	12 (8.1%)
	Total	n	149
Hygiene	Without any difficulty	n (%)	76 (51.0%)
	Some difficulty	n (%)	43 (28.9%)
	Much difficulty	n (%)	12 (8.1%)
	Unable	n (%)	7 (4.7%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Reach	Without any difficulty	n (%)	46 (30.9%)
	Some difficulty	n (%)	69 (46.3%)
	Much difficulty	n (%)	18 (12.1%)
	Unable	n (%)	4 (2.7%)
	Unknown	n (%)	12 (8.1%)
	Total	n	149
Grip	Without any difficulty	n (%)	92 (61.7%)
	Some difficulty	n (%)	37 (24.8%)
	Much difficulty	n (%)	7 (4.7%)
	Unable	n (%)	2 (1.3%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149

Source: HAQ_FUP.sas, run on 17MAY2017

Table 32 - Summary of Functional Assessment at Follow-up Visit at 3 months (HAQ - Subscale scores)

Popolazione: STD

		Statistics	N=149
Common daily activities	Without any difficulty	n (%)	59 (39.6%)
	Some difficulty	n (%)	56 (37.6%)
	Much difficulty	n (%)	20 (13.4%)
	Unable	n (%)	3 (2.0%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149

Source: HAQ_FUP.sas, run on 17MAY2017

Table 33 - Summary of Functional Assessment at Follow-up Visit at 6 months (HAQ - Subscale scores)

Popolazione: STD

		Statistics	N=149
Dressing and Grooming	Without any difficulty	n (%)	80 (53.7%)
	Some difficulty	n (%)	34 (22.8%)
	Much difficulty	n (%)	10 (6.7%)
	Unable	n (%)	1 (0.7%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Arising	Without any difficulty	n (%)	78 (52.3%)
	Some difficulty	n (%)	41 (27.5%)
	Much difficulty	n (%)	6 (4.0%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Eating	Without any difficulty	n (%)	80 (53.7%)
	Some difficulty	n (%)	36 (24.2%)
	Much difficulty	n (%)	8 (5.4%)
	Unable	n (%)	1 (0.7%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Walking	Without any difficulty	n (%)	77 (51.7%)
	Some difficulty	n (%)	42 (28.2%)
	Much difficulty	n (%)	6 (4.0%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Hygiene	Without any difficulty	n (%)	79 (53.0%)
	Some difficulty	n (%)	29 (19.5%)
	Much difficulty	n (%)	11 (7.4%)
	Unable	n (%)	6 (4.0%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Reach	Without any difficulty	n (%)	61 (40.9%)
	Some difficulty	n (%)	45 (30.2%)
	Much difficulty	n (%)	17 (11.4%)
	Unable	n (%)	2 (1.3%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Grip	Without any difficulty	n (%)	95 (63.8%)
	Some difficulty	n (%)	26 (17.4%)
	Much difficulty	n (%)	4 (2.7%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149

Table 33 - Summary of Functional Assessment at Follow-up Visit at 6 months (HAQ – Subscale scores)

Popolazione: STD

		Statistics	N=149
Common daily activities	Without any difficulty	n (%)	60 (40.3%)
	Some difficulty	n (%)	51 (34.2%)
	Much difficulty	n (%)	13 (8.7%)
	Unable	n (%)	1 (0.7%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149

Source: HAQ_FUP.sas, run on 17MAY2017

Table 34 - HAQ total score during the study and change from Screening Visit (calculated)

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	0.95 (0.601)	
	Median	0.88	
	Min/Max	0.00/2.75	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	0.61 (0.593)	-0.34 (0.499)
	Median	0.50	-0.31
	Min/Max	0.00/2.50	-1.50/0.75
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	0.49 (0.547)	-0.41 (0.518)
	Median	0.25	-0.38
	Min/Max	0.00/2.25	-1.88/1.13

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: HAQ_tot_FUP.sas, run on 17MAY2017

Table 35 - BASDAI score during the study and change from Screening Visit (calculated)

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	5.87 (1.944)	
	Median	6.20	
	Min/Max	0.50/9.80	
Follow-up Visit at 3 months	n	136	136
	Mean (SD)	3.93 (2.569)	-1.91 (2.249)
	Median	3.60	-1.75
	Min/Max	0.00/9.20	-7.70/3.80
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	3.36 (2.539)	-2.40 (2.553)
	Median	2.80	-2.20
	Min/Max	0.00/8.80	-8.70/2.90

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: BASDAI_FUP.sas, run on 17MAY2017

Table 36 - Summary of 3-month FU PGA (Physician Global Assessment for Psoriatic activity) - Skin Assessments

Popolazione: STD

		Statistics	N=149
Skin assessments	Clear	n (%)	84 (56.4%)
	Almost Clear	n (%)	39 (26.2%)
	Mild	n (%)	10 (6.7%)
	Mild to Moderate	n (%)	3 (2.0%)
	Moderate	n (%)	1 (0.7%)
	Moderate to Severe	n (%)	1 (0.7%)
	Total	n	149
	Unknown	n (%)	11 (7.4%)

Source: PGA_FUP.sas, run on 17MAY2017

Table 37 - Summary of 6-month FU PGA (Physician Global Assessment for Psoriatic activity) - Skin Assessments

Popolazione: STD

		Statistics	N=149
Skin assessments	Clear	n (%)	84 (56.4%)
	Almost Clear	n (%)	31 (20.8%)
	Mild	n (%)	10 (6.7%)
	Total	n	149
	Unknown	n (%)	24 (16.1%)

Source: PGA_FUP.sas, run on 17MAY2017

Table 38 - LEI score during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	1.91 (1.649)	
	Median	2.00	
	Min/Max	0.00/6.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	0.84 (1.384)	-1.07 (1.451)
	Median	0.00	-1.00
	Min/Max	0.00/6.00	-6.00/3.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	0.60 (1.100)	-1.27 (1.531)
	Median	0.00	-1.00
	Min/Max	0.00/5.00	-6.00/3.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: LEI_FUP.sas, run on 17MAY2017

Table 39 - Dactylitis score during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	0.60 (1.399)	
	Median	0.00	
	Min/Max	0.00/10.00	
Follow-up Visit at 3 months	n	138	138
	Mean (SD)	0.15 (0.845)	-0.47 (1.128)
	Median	0.00	0.00
	Min/Max	0.00/9.00	-6.00/2.00
Follow-up Visit at 6 months	n	125	125
	Mean (SD)	0.15 (0.899)	-0.46 (1.118)
	Median	0.00	0.00
	Min/Max	0.00/9.00	-6.00/2.00

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: Dactyl_FUP.sas, run on 17MAY2017

Table 40 - DAPSA total score during the study and change from Screening Visit

Population: STD N=149

	Statistic	Value	Change from Screening
Screening Visit	n	149	
	Mean (SD)	30.37 (14.509)	
	Median	27.20	
	Min/Max	7.75/82.35	
Follow-up Visit at 3 months	n	131	131
	Mean (SD)	13.69 (12.138)	-16.17 (12.143)
	Median	10.58	-14.32
	Min/Max	0.00/65.99	-70.75/15.00
Follow-up Visit at 6 months	n	120	120
	Mean (SD)	11.25 (11.713)	-19.16 (13.037)
	Median	8.37	-17.12
	Min/Max	0.01/69.05	-67.50/20.19

Notes:
Change from Screening values include only those patients with both a Screening value and a value for summarized time period.
n represents the number of patients contributing to summary statistics.

Source: Dapsa_FUP.sas, run on 17MAY2017

Table 41 - Summary of Minimal Disease Activity (MDA) at Follow-up Visit at 3 months

Popolazione: STD

		Statistics	N=149
Tender Joint count	>1	n (%)	77 (51.7%)
	<=1	n (%)	61 (40.9%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Swollen Joint count	>1	n (%)	32 (21.5%)
	<=1	n (%)	106 (71.1%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
PGA for Psoriatic activity	Other	n (%)	15 (10.1%)
	Clear or Almost clear	n (%)	123 (82.6%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Patient pain VAS	>15 mm	n (%)	96 (64.4%)
	<=15 mm	n (%)	42 (28.2%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Patient global assessment of PsA disease activity VAS	>20 mm	n (%)	100 (67.1%)
	<=20 mm	n (%)	38 (25.5%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
HAQ score	>0.5	n (%)	65 (43.6%)
	<=0.5	n (%)	73 (49.0%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Tender entheseal points	>1	n (%)	28 (18.8%)
	<=1	n (%)	110 (73.8%)
	Unknown	n (%)	11 (7.4%)
	Total	n	149
Has the patient achieved the MDA?	No	n (%)	84 (56.4%)
	Yes	n (%)	54 (36.2%)
	Total	n	149
	Unknown	n (%)	11 (7.4%)

Source: MDA_FUP.sas, run on 17MAY2017

Table 42 - Summary of Minimal Disease Activity (MDA) at Follow-up Visit at 6 months

Popolazione: STD

		Statistics	N=149
Tender Joint count	>1	n (%)	62 (41.6%)
	<=1	n (%)	63 (42.3%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Swollen Joint count	>1	n (%)	16 (10.7%)
	<=1	n (%)	109 (73.2%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
PGA for Psoriatic activity	Other	n (%)	10 (6.7%)
	Clear or Almost clear	n (%)	115 (77.2%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Patient pain VAS	>15 mm	n (%)	71 (47.7%)
	<=15 mm	n (%)	54 (36.2%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Patient global assessment of PsA disease activity VAS	>20 mm	n (%)	69 (46.3%)
	<=20 mm	n (%)	56 (37.6%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
HAQ score	>0.5	n (%)	48 (32.2%)
	<=0.5	n (%)	77 (51.7%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Tender entheseal points	>1	n (%)	20 (13.4%)
	<=1	n (%)	105 (70.5%)
	Unknown	n (%)	24 (16.1%)
	Total	n	149
Has the patient achieved the MDA?	No	n (%)	59 (39.6%)
	Yes	n (%)	66 (44.3%)
	Total	n	149
	Unknown	n (%)	24 (16.1%)

Source: MDA_FUP.sas, run on 17MAY2017

Table 43 - Clinical prediction model of MDA at 6 months

Population: STD

		Considered	OR (95% CI)	p-value	read	used
Univariable Logistic models	Gender	Female	0.3197 (0.1531- 0.6677)	0.0024	149	125
	Age		0.957 (0.9252- 0.9899)	0.0109	149	125
	BMI		0.9884 (0.909- 1.0747)	0.7841	149	125
	Smoking history	Current	1.374 (0.528- 3.5752)	0.5448	149	125
		Past	1.0377 (0.4102- 2.6253)	0.8010		
	Time from diagnosis		1.0024 (0.9973- 1.0075)	0.3576	149	125
	Symptoms duration before diagnosis		1.0018 (0.9979- 1.0056)	0.3680	149	117
	CRP at baseline		1.0003 (0.9991- 1.0015)	0.6371	149	125
	Concurrent DMARD and Glucocorticoids	Yes	1.372 (0.6227- 3.0228)	0.4327	149	125
	DAPSA score at baseline		0.9287 (0.8967- 0.9618)	<.0001	149	125
	HAQ score at baseline		0.2937 (0.1423- 0.6063)	0.0009	149	125
	Patient global assessment of pain (VAS) at baseline		0.9833 (0.9684- 0.9984)	0.0299	149	125
	BASDAI at baseline		0.7036 (0.5733- 0.8635)	0.0008	149	125
	Comorbidities	Yes	0.3258 (0.1465- 0.7241)	0.0059	149	125
	Psoriasis/nail psoriasis at baseline	Yes	1.5512 (0.7457- 3.2269)	0.2401	149	125
Multivariable Logistic model #					149	117
	Age		0.9542 (0.9112- 0.9993)	0.0465		
	CRP at baseline		1.0015 (1.0002- 1.0028)	0.0241		
	Comorbidities		0.4259 (0.1572- 1.1541)	0.0933		
	DAPSA score at baseline		0.9255 (0.8879- 0.9647)	0.0003		
	Symptoms duration before diagnosis		1.0057 (1.0007- 1.0107)	0.0260		

Notes: # A backward stepwise selection strategy was applied to multivariable logistic model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).
Brier score for the multivariable model is 0.1792; C-statistics is 0.800
Hosmer and Lemeshow Goodness-of-Fit Test: Chi-Square = 9.6682, DF = 8, p-value = 0.2891
Internal validity of the prediction models was tested by bootstrap validation using 500 repetitions (sample size: 50% of the patients included in the model):
the mean C-statistics is 0.8888 and the 95% confidence interval is [0.7711; 1.0000].
Source: MDA_models.sas, run on 09MAY2017

Table 44 - Biomarker-enhanced clinical prediction model of MDA at 6 months

Population: STD

		Considered	OR (95% CI)	p-value	read	used
Univariable Logistic models	Gender	Female	0.3197 (0.1531- 0.6677)	0.0024	149	125
	Age		0.957 (0.9252- 0.9899)	0.0109	149	125
	BMI		0.9884 (0.909- 1.0747)	0.7841	149	125
	Smoking history	Current	1.374 (0.528- 3.5752)	0.5448	149	125
		Past	1.0377 (0.4102- 2.6253)	0.8010		
	Time from diagnosis		1.0024 (0.9973- 1.0075)	0.3576	149	125
	Symptoms duration before diagnosis		1.0018 (0.9979- 1.0056)	0.3680	149	117
	CRP at baseline		1.0003 (0.9991- 1.0015)	0.6371	149	125
	Concurrent DMARD and Glucocorticoids	Yes	1.372 (0.6227- 3.0228)	0.4327	149	125
	DAPSA score at baseline		0.9287 (0.8967- 0.9618)	<.0001	149	125
	HAQ score at baseline		0.2937 (0.1423- 0.6063)	0.0009	149	125
	Patient global assessment of pain (VAS) at baseline		0.9833 (0.9684- 0.9984)	0.0299	149	125
	BASDAI at baseline		0.7036 (0.5733- 0.8635)	0.0008	149	125
	Comorbidities	Yes	0.3258 (0.1465- 0.7241)	0.0059	149	125
	Psoriasis/nail psoriasis at baseline	Yes	1.5512 (0.7457- 3.2269)	0.2401	149	125
	hsCRP		1.0688 (1.008- 1.1334)	0.0261	149	123
	MMP_3		1.0075 (0.9981- 1.017)	0.1199	149	121
	CPII		0.9997 (0.9994- 1.0001)	0.1012	149	108
Multivariable Logistic model #					149	98
	Comorbidities		0.2645 (0.0881- 0.7941)	0.0177		
	DAPSA score at baseline		0.9231 (0.885- 0.9628)	0.0002		
	Psoriasis/nail psoriasis at baseline		2.6207 (0.9597- 7.157)	0.0602		
	hsCRP		1.0853 (0.9985- 1.1797)	0.0542		

Notes: # A backward stepwise selection strategy was applied to multivariable logistic model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).
Brier score for the multivariable model is 0.1722; C-statistics is 0.818
Hosmer and Lemeshow Goodness-of-Fit Test: Chi-Square = 6.8915, DF = 8, p-value = 0.5484
Internal validity of the prediction models was tested by bootstrap validation using 500 repetitions (sample size: 50% of the patients included in the model):
the mean C-statistics is 0.9211 and the 95% confidence interval is [0.7556; 1.0000].
The discrimination slope of the biomarker-enhanced model was 3.1058 % higher than the model without biomarker.
Source: MDA_models.sas, run on 09MAY2017

Table 45 - Clinical prediction model of MDA at 3 months

Population: STD

		Considered	OR (95% CI)	p-value	read	used
Univariable Logistic models	Gender	Female	0.3028 (0.1452- 0.6314)	0.0014	149	138
	Age		0.946 (0.9147- 0.9785)	0.0013	149	138
	BMI		0.9192 (0.8444- 1.0006)	0.0515	149	138
	Smoking history	Current	1.5072 (0.6053- 3.7528)	0.6061	149	138
		Past	1.3996 (0.5687- 3.4444)	0.7783		
	Time from diagnosis		1.0038 (0.9987- 1.0088)	0.1443	149	138
	Symptoms duration before diagnosis		1.0001 (0.9964- 1.0037)	0.9697	149	128
	CRP at baseline		1.0005 (0.9992- 1.0017)	0.4595	149	138
	Concurrent DMARD and Glucocorticoids	Yes	1.0399 (0.486- 2.2252)	0.9197	149	138
	DAPSA score at baseline		0.9328 (0.8999- 0.967)	0.0001	149	138
	HAQ score at baseline		0.1809 (0.0816- 0.401)	<.0001	149	138
	Patient global assessment of pain (VAS) at baseline		0.9849 (0.9711- 0.9989)	0.0345	149	138
	BASDAI at baseline		0.652 (0.5318- 0.7993)	<.0001	149	138
	Comorbidities	Yes	0.2942 (0.1369- 0.6319)	0.0017	149	138
	Psoriasis/nail psoriasis at baseline	Yes	0.6433 (0.3132- 1.3211)	0.2295	149	138
Multivariable Logistic model #					149	128
	Age		0.9438 (0.906- 0.9831)	0.0055		
	CRP at baseline		1.0019 (1.0005- 1.0033)	0.0072		
	DAPSA score at baseline		0.9352 (0.8908- 0.9818)	0.0069		
	HAQ score at baseline		0.373 (0.1413- 0.9844)	0.0464		
	Time from diagnosis		1.0085 (1.0021- 1.0149)	0.0088		

Notes: # A backward stepwise selection strategy was applied to multivariable logistic model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).
Brier score for the multivariable model is 0.1665; C-statistics is 0.816
Hosmer and Lemeshow Goodness-of-Fit Test: Chi-Square = 6.8972, DF = 8, p-value = 0.5478
Internal validity of the prediction models was tested by bootstrap validation using 500 repetitions (sample size: 50% of the patients included in the model):
the mean C-statistics is 0.9039 and the 95% confidence interval is [0.7741; 1.0000].
Source: MDA_models.sas, run on 09MAY2017

Table 46 - Biomarker-enhanced clinical prediction model of MDA at 3 months

Population: STD

		Considered	OR (95% CI)	p-value	read	used
Univariable Logistic models	Gender	Female	0.3028 (0.1452- 0.6314)	0.0014	149	138
	Age		0.946 (0.9147- 0.9785)	0.0013	149	138
	BMI		0.9192 (0.8444- 1.0006)	0.0515	149	138
	Smoking history	Current	1.5072 (0.6053- 3.7528)	0.6061	149	138
		Past	1.3996 (0.5687- 3.4444)	0.7783		
	Time from diagnosis		1.0038 (0.9987- 1.0088)	0.1443	149	138
	Symptoms duration before diagnosis		1.0001 (0.9964- 1.0037)	0.9697	149	128
	CRP at baseline		1.0005 (0.9992- 1.0017)	0.4595	149	138
	Concurrent DMARD and Glucocorticoids	Yes	1.0399 (0.486- 2.2252)	0.9197	149	138
	DAPSA score at baseline		0.9328 (0.8999- 0.967)	0.0001	149	138
	HAQ score at baseline		0.1809 (0.0816- 0.401)	<.0001	149	138
	Patient global assessment of pain (VAS) at baseline		0.9849 (0.9711- 0.9989)	0.0345	149	138
	BASDAI at baseline		0.652 (0.5318- 0.7993)	<.0001	149	138
	Comorbidities	Yes	0.2942 (0.1369- 0.6319)	0.0017	149	138
	Psoriasis/nail psoriasis at baseline	Yes	0.6433 (0.3132- 1.3211)	0.2295	149	138
	hsCRP		1.0342 (0.996- 1.0739)	0.0796	149	136
	MMP_3		1.0062 (0.9982- 1.0142)	0.1295	149	133
	CPII		0.9998 (0.9995- 1.0001)	0.2469	149	116
Multivariable Logistic model #					149	106
	Age		0.932 (0.8902- 0.9758)	0.0027		
	BASDAI at baseline		0.757 (0.5782- 0.9912)	0.0430		
	DAPSA score at baseline		0.9406 (0.8942- 0.9893)	0.0175		
	Time from diagnosis		1.0088 (1.0022- 1.0154)	0.0085		

Notes: # A backward stepwise selection strategy was applied to multivariable logistic model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).
Brier score for the multivariable model is 0.1661; C-statistics is 0.820
Hosmer and Lemeshow Goodness-of-Fit Test: Chi-Square = 4.7810, DF = 8, p-value = 0.7807
Internal validity of the prediction models was tested by bootstrap validation using 500 repetitions (sample size: 50% of the patients included in the model):
the mean C-statistics is 0.9305 and the 95% confidence interval is [0.7961; 1.0000].
The discrimination slope of the biomarker-enhanced model was -0.471 % higher than the model without biomarker.
Source: MDA_models.sas, run on 09MAY2017

Table 47 - Clinical prediction model of change in DAPSA score from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	-.6594	-0.27 (0.7841)	0.000639	149	120
	Age		-.1500	-1.4 (0.1655)	0.016237	149	120
	BMI		0.5779	2.05 (0.0424)	0.034461	149	120
	Smoking history	Past	-.2610	-0.08 (0.9345)			
		Current	-2.602	-0.81 (0.4218)	0.005601	149	120
	Time from diagnosis		-.0311	-2.02 (0.0454)	0.033504	149	120
	Symptoms duration before diagnosis		-.0155	-1.24 (0.2192)	0.013693	149	112
	CRP at baseline		-.0078	-2.07 (0.0407)	0.035016	149	120
	Concurrent DMARD and Glucocorticoids	Yes	1.4182	0.52 (0.6040)	0.002286	149	120
	DAPSA score at baseline		-.5751	-9.33 (<.0001)	0.424406	149	120
	HAQ score at baseline		-6.246	-3.01 (0.0032)	0.071097	149	120
	Patient global assessment of pain (VAS) at baseline		-.2140	-4.68 (<.0001)	0.156788	149	120
	BASDAI at baseline		-1.253	-2.07 (0.0403)	0.035169	149	120
	Comorbidities	Yes	0.5262	0.2 (0.8392)	0.000350	149	120
	Psoriasis/nail psoriasis at baseline	Yes	-1.732	-0.7 (0.4855)	0.004131	149	120
Multivariable linear regression model #						149	112
	Gender	Female	4.1751	2.23 (0.0277)			
	BMI		0.6535	3.05 (0.0029)			
	Symptoms duration before diagnosis		-.0176	-1.94 (0.0547)			
	DAPSA score at baseline		-.5367	-8.05 (<.0001)			
	Patient global assessment of pain (VAS) at baseline		-.1006	-2.36 (0.0201)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.5149

Source: DAPSA_models.sas, run on 17MAY2017

Table 48 - Biomarker-enhanced clinical prediction model of change in DAPSA score from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	-.6594	-0.27 (0.7841)	0.000639	149	120
	Age		-.1500	-1.4 (0.1655)	0.016237	149	120
	BMI		0.5779	2.05 (0.0424)	0.034461	149	120
	Smoking history	Past	-.2610	-0.08 (0.9345)			
		Current	-2.602	-0.81 (0.4218)	0.005601	149	120
	Time from diagnosis		-.0311	-2.02 (0.0454)	0.033504	149	120
	Symptoms duration before diagnosis		-.0155	-1.24 (0.2192)	0.013693	149	112
	CRP at baseline		-.0078	-2.07 (0.0407)	0.035016	149	120
	Concurrent DMARD and Glucocorticoids	Yes	1.4182	0.52 (0.6040)	0.002286	149	120
	DAPSA score at baseline		-.5751	-9.33 (<.0001)	0.424406	149	120
	HAQ score at baseline		-6.246	-3.01 (0.0032)	0.071097	149	120
	Patient global assessment of pain (VAS) at baseline		-.2140	-4.68 (<.0001)	0.156788	149	120
	BASDAI at baseline		-1.253	-2.07 (0.0403)	0.035169	149	120
	Comorbidities	Yes	0.5262	0.2 (0.8392)	0.000350	149	120
	Psoriasis/nail psoriasis at baseline	Yes	-1.732	-0.7 (0.4855)	0.004131	149	120
	hsCRP		-.0556	-0.74 (0.4635)	0.004642	149	118
	MMP_3		0.0009	0.04 (0.9716)	0.000011	149	116
	CPII		0.0002	0.13 (0.8937)	0.000176	149	104
Multivariable linear regression model #						149	94
	Gender	Female	4.3610	2.11 (0.0376)			
	BMI		0.5320	2.28 (0.0251)			
	Time from diagnosis		-.0292	-2.4 (0.0186)			
	DAPSA score at baseline		-.5027	-6.93 (<.0001)			
	Patient global assessment of pain (VAS) at baseline		-.1283	-2.73 (0.0077)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.5399

Source: DAPSA_models.sas, run on 17MAY2017

Table 49 - Clinical prediction model of change in HAQ score from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	-.0187	-0.2 (0.8425)	0.000322	149	125
	Age		0.0003	0.07 (0.9438)	0.000041	149	125
	BMI		0.0038	0.34 (0.7312)	0.000963	149	125
	Smoking history	Past	0.0260	0.21 (0.8328)			
		Current	0.1209	0.97 (0.3360)	0.007588	149	125
	Time from diagnosis		0.0003	0.53 (0.5971)	0.002278	149	125
	Symptoms duration before diagnosis		0.0001	0.27 (0.7901)	0.000619	149	117
	CRP at baseline		0.0002	1.24 (0.2173)	0.012346	149	125
	Concurrent DMARD and Glucocorticoids	Yes	0.1246	1.2 (0.2327)	0.011557	149	125
	DAPSA score at baseline		-.0008	-0.26 (0.7934)	0.000560	149	125
	HAQ score at baseline		-.4504	-6.17 (<.0001)	0.236063	149	125
	Patient global assessment of pain (VAS) at baseline		-.0037	-1.97 (0.0510)	0.030613	149	125
	BASDAI at baseline		-.0664	-2.89 (0.0046)	0.063595	149	125
	Comorbidities	Yes	0.0523	0.53 (0.5976)	0.002271	149	125
	Psoriasis/nail psoriasis at baseline	Yes	-.0627	-0.65 (0.5140)	0.003471	149	125
Multivariable linear regression model #						149	117
	Age		0.0093	2.52 (0.0130)			
	DAPSA score at baseline		0.0098	3.15 (0.0021)			
	HAQ score at baseline		-.6518	-7.53 (<.0001)			
	Psoriasis/nail psoriasis at baseline	Yes	-.1626	-1.99 (0.0493)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.3414

Source: HAQ_models.sas, run on 17MAY2017

Table 50 - Biomarker-enhanced clinical prediction model of change in HAQ score from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	-.0187	-0.2 (0.8425)	0.000322	149	125
	Age		0.0003	0.07 (0.9438)	0.000041	149	125
	BMI		0.0038	0.34 (0.7312)	0.000963	149	125
	Smoking history	Past	0.0260	0.21 (0.8328)			
		Current	0.1209	0.97 (0.3360)	0.007588	149	125
	Time from diagnosis		0.0003	0.53 (0.5971)	0.002278	149	125
	Symptoms duration before diagnosis		0.0001	0.27 (0.7901)	0.000619	149	117
	CRP at baseline		0.0002	1.24 (0.2173)	0.012346	149	125
	Concurrent DMARD and Glucocorticoids	Yes	0.1246	1.2 (0.2327)	0.011557	149	125
	DAPSA score at baseline		-.0008	-0.26 (0.7934)	0.000560	149	125
	HAQ score at baseline		-.4504	-6.17 (<.0001)	0.236063	149	125
	Patient global assessment of pain (VAS) at baseline		-.0037	-1.97 (0.0510)	0.030613	149	125
	BASDAI at baseline		-.0664	-2.89 (0.0046)	0.063595	149	125
	Comorbidities	Yes	0.0523	0.53 (0.5976)	0.002271	149	125
	Psoriasis/nail psoriasis at baseline	Yes	-.0627	-0.65 (0.5140)	0.003471	149	125
	hsCRP		-.0015	-0.52 (0.6065)	0.002199	149	123
	MMP_3		-.0009	-0.88 (0.3802)	0.006478	149	121
	CPII		-.0000	-0.51 (0.6108)	0.002452	149	108
Multivariable linear regression model #						149	98
	Age		0.0090	2.18 (0.0316)			
	CRP at baseline		0.0003	1.88 (0.0639)			
	DAPSA score at baseline		0.0071	2.12 (0.0367)			
	HAQ score at baseline		-.6616	-6.85 (<.0001)			
	Psoriasis/nail psoriasis at baseline	Yes	-.1751	-1.98 (0.0506)			
	MMP_3		-.0018	-2.07 (0.0413)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.3797

Source: HAQ_models.sas, run on 17MAY2017

Table 51 - Clinical prediction model of change in LEI index from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	-.5318	-1.94 (0.0541)	0.029837	149	125
	Age		-.0126	-1.03 (0.3046)	0.008568	149	125
	BMI		-.0040	-0.12 (0.9029)	0.000122	149	125
	Smoking history	Past	0.0207	0.06 (0.9549)			
		Current	0.2795	0.75 (0.4523)	0.004739	149	125
	Time from diagnosis		0.0001	0.06 (0.9492)	0.000033	149	125
	Symptoms duration before diagnosis		-.0003	-0.19 (0.8525)	0.000302	149	117
	CRP at baseline		0.0003	0.76 (0.4477)	0.004694	149	125
	Concurrent DMARD and Glucocorticoids	Yes	0.3940	1.28 (0.2018)	0.013215	149	125
	DAPSA score at baseline		-.0266	-2.94 (0.0040)	0.065463	149	125
	HAQ score at baseline		-.5956	-2.47 (0.0150)	0.047169	149	125
	Patient global assessment of pain (VAS) at baseline		-.0162	-2.98 (0.0035)	0.067235	149	125
	BASDAI at baseline		-.1608	-2.34 (0.0209)	0.042639	149	125
	Comorbidities	Yes	-.3685	-1.27 (0.2079)	0.012866	149	125
	Psoriasis/nail psoriasis at baseline	Yes	0.2313	0.82 (0.4155)	0.005397	149	125
Multivariable linear regression model #						149	117
	DAPSA score at baseline		-.0180	-1.76 (0.0806)			
	Patient global assessment of pain (VAS) at baseline		-.0123	-1.92 (0.0577)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.0970

Source: LEI_models.sas, run on 17MAY2017

Table 52 - Biomarker-enhanced clinical prediction model of change in LEI index from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	-.5318	-1.94 (0.0541)	0.029837	149	125
	Age		-.0126	-1.03 (0.3046)	0.008568	149	125
	BMI		-.0040	-0.12 (0.9029)	0.000122	149	125
	Smoking history	Past	0.0207	0.06 (0.9549)			
		Current	0.2795	0.75 (0.4523)	0.004739	149	125
	Time from diagnosis		0.0001	0.06 (0.9492)	0.000033	149	125
	Symptoms duration before diagnosis		-.0003	-0.19 (0.8525)	0.000302	149	117
	CRP at baseline		0.0003	0.76 (0.4477)	0.004694	149	125
	Concurrent DMARD and Glucocorticoids	Yes	0.3940	1.28 (0.2018)	0.013215	149	125
	DAPSA score at baseline		-.0266	-2.94 (0.0040)	0.065463	149	125
	HAQ score at baseline		-.5956	-2.47 (0.0150)	0.047169	149	125
	Patient global assessment of pain (VAS) at baseline		-.0162	-2.98 (0.0035)	0.067235	149	125
	BASDAI at baseline		-.1608	-2.34 (0.0209)	0.042639	149	125
	Comorbidities	Yes	-.3685	-1.27 (0.2079)	0.012866	149	125
	Psoriasis/nail psoriasis at baseline	Yes	0.2313	0.82 (0.4155)	0.005397	149	125
	hsCRP		0.0070	0.81 (0.4207)	0.005366	149	123
	MMP_3		0.0039	1.32 (0.1900)	0.014390	149	121
	CPII		-.0000	-0.33 (0.7431)	0.001018	149	108
Multivariable linear regression model #						149	98
	DAPSA score at baseline		-.0292	-2.98 (0.0037)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.0847

Source: LEI_models.sas, run on 17MAY2017

Table 53 - Clinical prediction model of change in dactylitis score from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	0.1834	0.91 (0.3659)	0.006653	149	125
	Age		0.0073	0.81 (0.4178)	0.005346	149	125
	BMI		0.0258	1.08 (0.2819)	0.009409	149	125
	Smoking history	Past	0.2641	0.99 (0.3219)			
		Current	0.1159	0.43 (0.6687)	0.008419	149	125
	Time from diagnosis		-.0009	-0.67 (0.5052)	0.003618	149	125
	Symptoms duration before diagnosis		-.0007	-0.64 (0.5233)	0.003552	149	117
	CRP at baseline		0.0001	0.25 (0.8024)	0.000511	149	125
	Concurrent DMARD and Glucocorticoids	Yes	-.0608	-0.27 (0.7881)	0.000590	149	125
	DAPSA score at baseline		0.0044	0.65 (0.5177)	0.003410	149	125
	HAQ score at baseline		0.4637	2.64 (0.0094)	0.053622	149	125
	Patient global assessment of pain (VAS) at baseline		-.0014	-0.35 (0.7271)	0.000993	149	125
	BASDAI at baseline		0.0891	1.76 (0.0810)	0.024541	149	125
	Comorbidities	Yes	-.0616	-0.29 (0.7739)	0.000674	149	125
	Psoriasis/nail psoriasis at baseline	Yes	0.0147	0.07 (0.9435)	0.000041	149	125
Multivariable linear regression model #						149	117
	HAQ score at baseline		0.4758	2.56 (0.0118)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.0538

Source: Dactyl_models.sas, run on 17MAY2017

Table 54 - Biomarker-enhanced clinical prediction model of change in dactylitis score from baseline to Follow-up Visit at 6 months

Population: STD

		Considered	Parameter estimate	T value (p-value)	R-square	Read	Used
Univariable linear regression models	Gender	Female	0.1834	0.91 (0.3659)	0.006653	149	125
	Age		0.0073	0.81 (0.4178)	0.005346	149	125
	BMI		0.0258	1.08 (0.2819)	0.009409	149	125
	Smoking history	Past	0.2641	0.99 (0.3219)			
		Current	0.1159	0.43 (0.6687)	0.008419	149	125
	Time from diagnosis		-.0009	-0.67 (0.5052)	0.003618	149	125
	Symptoms duration before diagnosis		-.0007	-0.64 (0.5233)	0.003552	149	117
	CRP at baseline		0.0001	0.25 (0.8024)	0.000511	149	125
	Concurrent DMARD and Glucocorticoids	Yes	-.0608	-0.27 (0.7881)	0.000590	149	125
	DAPSA score at baseline		0.0044	0.65 (0.5177)	0.003410	149	125
	HAQ score at baseline		0.4637	2.64 (0.0094)	0.053622	149	125
	Patient global assessment of pain (VAS) at baseline		-.0014	-0.35 (0.7271)	0.000993	149	125
	BASDAI at baseline		0.0891	1.76 (0.0810)	0.024541	149	125
	Comorbidities	Yes	-.0616	-0.29 (0.7739)	0.000674	149	125
	Psoriasis/nail psoriasis at baseline	Yes	0.0147	0.07 (0.9435)	0.000041	149	125
	hsCRP		-.0031	-0.49 (0.6237)	0.001996	149	123
	MMP_3		0.0003	0.16 (0.8752)	0.000208	149	121
	CPII		0.0001	1.05 (0.2945)	0.010364	149	108
Multivariable linear regression model #						149	98
	HAQ score at baseline		0.6807	2.81 (0.0061)			
	Patient global assessment of pain (VAS) at baseline		-.0100	-1.83 (0.0709)			

Notes:
A backward stepwise selection strategy was applied to multivariable linear regression model (cut-off to remain in the model: p<0.10).
Polyarthitis variable was not considered in the model (<10% frequency percent). Statistical interactions were not estimated (no model convergence).

R2 for the multivariable model is 0.0811

Source: Dactyl_models.sas, run on 17MAY2017

Table 55.1 - Correlation between disease activity measures at baseline(Pearson)

The CORR Procedure

9 Variables: _68_TJC1 _66_SJC1 VAS1 HAQ1 CRP1 BASDAI1 LEI1 Dactyl1 DAPSA1

Simple Statistics

Variable	N	Mean	Std Dev	Sum	Minimum	Maximum
_68_TJC1	150	11.76667	9.49066	1765	1.00000	55.00000
_66_SJC1	150	4.78667	4.71978	718.00000	0	22.00000
VAS1	150	61.38667	24.41553	9208	3.00000	100.00000
HAQ1	150	0.95500	0.59874	143.25000	0	2.75000
CRP1	149	136.25073	316.55976	20301	0	3048
BASDAI1	150	5.86000	1.93883	879.00000	0.50000	9.80000
LEI1	150	1.92000	1.65282	288.00000	0	6.00000
Dactyl1	150	0.61333	1.39888	92.00000	0	10.00000
DAPSA1	149	30.37013	14.50936	4525	7.75000	82.35000

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	_68_TJC1	_66_SJC1	VAS1	HAQ1	CRP1	BASDAI1	LEI1	Dactyl1	DAPSA1
_68_TJC1	1.00000	0.55130	0.23726	0.38184	-0.11499	0.33833	0.40954	-0.01897	0.89021
		<.0001	0.0035	<.0001	0.1626	<.0001	<.0001	0.8177	<.0001
	150	150	150	150	149	150	150	150	149
_66_SJC1	0.55130	1.00000	0.17439	0.22250	0.00564	0.20031	0.11394	0.18158	0.74435
	<.0001		0.0328	0.0062	0.9456	0.0140	0.1650	0.0262	<.0001
	150	150	150	150	149	150	150	150	149
VAS1	0.23726	0.17439	1.00000	0.47534	-0.06480	0.49353	0.25972	0.03899	0.44399
	0.0035	0.0328		<.0001	0.4324	<.0001	0.0013	0.6357	<.0001
	150	150	150	150	149	150	150	150	149
HAQ1	0.38184	0.22250	0.47534	1.00000	0.03406	0.52397	0.35832	-0.08101	0.48053
	<.0001	0.0062	<.0001		0.6801	<.0001	<.0001	0.3244	<.0001
	150	150	150	150	149	150	150	150	149
CRP1	-0.11499	0.00564	-0.06480	0.03406	1.00000	-0.12117	-0.12410	0.00327	0.14568
	0.1626	0.9456	0.4324	0.6801		0.1410	0.1316	0.9684	0.0763
	149	149	149	149	149	149	149	149	149
BASDAI1	0.33833	0.20031	0.49353	0.52397	-0.12117	1.00000	0.33451	-0.00549	0.41879
	<.0001	0.0140	<.0001	<.0001	0.1410		<.0001	0.9468	<.0001
	150	150	150	150	149	150	150	150	149
LEI1	0.40954	0.11394	0.25972	0.35832	-0.12410	0.33451	1.00000	0.00685	0.35632
	<.0001	0.1650	0.0013	<.0001	0.1316	<.0001		0.9337	<.0001
	150	150	150	150	149	150	150	150	149

Source: Correlation_pearson.sas, run on 17MAY2017

Table 55.1 - Correlation between disease activity measures at baseline(Pearson)

The CORR Procedure

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	_68_TJC1	_66_SJC1	VAS1	HAQ1	CRP1	BASDAI1	LEI1	Dactyl1	DAPSA1
Dactyl1	-0.01897	0.18158	0.03899	-0.08101	0.00327	-0.00549	0.00685	1.00000	0.05585
	0.8177	0.0262	0.6357	0.3244	0.9684	0.9468	0.9337		0.4987
	150	150	150	150	149	150	150	150	149
DAPSA1	0.89021	0.74435	0.44399	0.48053	0.14568	0.41879	0.35632	0.05585	1.00000
	<.0001	<.0001	<.0001	<.0001	0.0763	<.0001	<.0001	0.4987	
	149	149	149	149	149	149	149	149	149

Source: Correlation_pearson.sas, run on 17MAY2017

Table 55.2 - Correlation between disease activity measures at 3 months (Pearson)

The CORR Procedure

9 Variables: _68_TJC3 _66_SJC3 VAS3 HAQ3 CRP3 BASDAI3 LEI3 Dactyl3 DAPSA3

Simple Statistics

Variable	N	Mean	Std Dev	Sum	Minimum	Maximum
_68_TJC3	138	4.82609	6.77254	666.00000	0	34.00000
_66_SJC3	138	1.23913	2.53027	171.00000	0	16.00000
VAS3	138	35.15217	27.52780	4851	0	98.00000
HAQ3	138	0.60809	0.59319	83.91667	0	2.50000
CRP3	131	37.56745	47.67826	4921	0	272.38640
BASDAI3	136	3.93015	2.56937	534.50000	0	9.20000
LEI3	138	0.84058	1.38420	116.00000	0	6.00000
Dactyl3	138	0.15217	0.84493	21.00000	0	9.00000
DAPSA3	131	13.69153	12.13760	1794	0	65.99000

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	_68_TJC3	_66_SJC3	VAS3	HAQ3	CRP3	BASDAI3	LEI3	Dactyl3	DAPSA3
_68_TJC3	1.00000	0.52637	0.63186	0.66410	0.02964	0.60625	0.51559	-0.00044	0.93090
		<.0001	<.0001	<.0001	0.7369	<.0001	<.0001	0.9959	<.0001
	138	138	138	138	131	136	138	138	131
_66_SJC3	0.52637	1.00000	0.32277	0.24040	-0.00840	0.26875	0.34650	0.46768	0.63423
	<.0001		0.0001	0.0045	0.9241	0.0016	<.0001	<.0001	<.0001
	138	138	138	138	131	136	138	138	131
VAS3	0.63186	0.32277	1.00000	0.72036	-0.01095	0.80603	0.35810	-0.07758	0.81543
	<.0001	0.0001		<.0001	0.9012	<.0001	<.0001	0.3658	<.0001
	138	138	138	138	131	136	138	138	131
HAQ3	0.66410	0.24040	0.72036	1.00000	0.08548	0.77197	0.43451	-0.08039	0.72881
	<.0001	0.0045	<.0001		0.3317	<.0001	<.0001	0.3486	<.0001
	138	138	138	138	131	136	138	138	131
CRP3	0.02964	-0.00840	-0.01095	0.08548	1.00000	0.02193	0.00667	-0.07102	0.05775
	0.7369	0.9241	0.9012	0.3317		0.8052	0.9398	0.4202	0.5123
	131	131	131	131	131	129	131	131	131
BASDAI3	0.60625	0.26875	0.80603	0.77197	0.02193	1.00000	0.37173	-0.05398	0.73153
	<.0001	0.0016	<.0001	<.0001	0.8052		<.0001	0.5325	<.0001
	136	136	136	136	129	136	136	136	129
LEI3	0.51559	0.34650	0.35810	0.43451	0.00667	0.37173	1.00000	0.18940	0.49050
	<.0001	<.0001	<.0001	<.0001	0.9398	<.0001		0.0261	<.0001
	138	138	138	138	131	136	138	138	131

Source: Correlation_pearson.sas, run on 17MAY2017

Table 55.2 - Correlation between disease activity measures at 3 months (Pearson)

The CORR Procedure

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	_68_TJC3	_66_SJC3	VAS3	HAQ3	CRP3	BASDAI3	LEI3	Dactyl3	DAPSA3
Dactyl3	-0.00044	0.46768	-0.07758	-0.08039	-0.07102	-0.05398	0.18940	1.00000	0.04650
	0.9959	<.0001	0.3658	0.3486	0.4202	0.5325	0.0261		0.5979
	138	138	138	138	131	136	138	138	131
DAPSA3	0.93090	0.63423	0.81543	0.72881	0.05775	0.73153	0.49050	0.04650	1.00000
	<.0001	<.0001	<.0001	<.0001	0.5123	<.0001	<.0001	0.5979	
	131	131	131	131	131	129	131	131	131

Source: Correlation_pearson.sas, run on 17MAY2017

Table 55.3 - Correlation between disease activity measures at 6 months (Pearson)

The CORR Procedure

9 Variables: _68_TJC6 _66_SJC6 VAS6 HAQ6 CRP6 BASDAI6 LEI6 Dactyl6 DAPSA6

Simple Statistics

Variable	N	Mean	Std Dev	Sum	Minimum	Maximum
_68_TJC6	125	3.99200	6.70038	499.00000	0	44.00000
_66_SJC6	125	0.60800	1.65049	76.00000	0	10.00000
VAS6	125	28.67200	27.07361	3584	0	98.00000
HAQ6	125	0.48700	0.54667	60.87500	0	2.25000
CRP6	120	34.70228	48.40164	4164	0	306.67280
BASDAI6	125	3.35840	2.53906	419.80000	0	8.80000
LEI6	125	0.60000	1.09985	75.00000	0	5.00000
Dactyl6	125	0.15200	0.89853	19.00000	0	9.00000
DAPSA6	120	11.24858	11.71283	1350	0.01000	69.05000

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	_68_TJC6	_66_SJC6	VAS6	HAQ6	CRP6	BASDAI6	LEI6	Dactyl6	DAPSA6
_68_TJC6	1.00000	0.72092	0.54778	0.51269	0.05554	0.54256	0.39242	0.12344	0.91936
		<.0001	<.0001	<.0001	0.5469	<.0001	<.0001	0.1702	<.0001
	125	125	125	125	120	125	125	125	120
_66_SJC6	0.72092	1.00000	0.40822	0.44903	0.05358	0.37441	0.20613	0.11663	0.73899
	<.0001		<.0001	<.0001	0.5611	<.0001	0.0211	0.1952	<.0001
	125	125	125	125	120	125	125	125	120
VAS6	0.54778	0.40822	1.00000	0.67190	0.16614	0.84832	0.34195	0.00240	0.80152
	<.0001	<.0001		<.0001	0.0697	<.0001	<.0001	0.9788	<.0001
	125	125	125	125	120	125	125	125	120
HAQ6	0.51269	0.44903	0.67190	1.00000	0.16614	0.72165	0.25786	0.01226	0.65309
	<.0001	<.0001	<.0001		0.0697	<.0001	0.0037	0.8920	<.0001
	125	125	125	125	120	125	125	125	120
CRP6	0.05554	0.05358	0.16614	0.16614	1.00000	0.12632	-0.03328	-0.01954	0.16583
	0.5469	0.5611	0.0697	0.0697		0.1692	0.7182	0.8323	0.0703
	120	120	120	120	120	120	120	120	120
BASDAI6	0.54256	0.37441	0.84832	0.72165	0.12632	1.00000	0.34833	-0.03821	0.73804
	<.0001	<.0001	<.0001	<.0001	0.1692		<.0001	0.6722	<.0001
	125	125	125	125	120	125	125	125	120
LEI6	0.39242	0.20613	0.34195	0.25786	-0.03328	0.34833	1.00000	0.12730	0.39268
	<.0001	0.0211	<.0001	0.0037	0.7182	<.0001		0.1571	<.0001
	125	125	125	125	120	125	125	125	120

Source: Correlation_pearson.sas, run on 17MAY2017
Table 55.3 - Correlation between disease activity measures at 6 months (Pearson)

The CORR Procedure

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	_68_TJC6	_66_SJC6	VAS6	HAQ6	CRP6	BASDAI6	LEI6	Dactyl6	DAPSA6
Dactyl6	0.12344	0.11663	0.00240	0.01226	-0.01954	-0.03821	0.12730	1.00000	0.08071
	0.1702	0.1952	0.9788	0.8920	0.8323	0.6722	0.1571		0.3809
	125	125	125	125	120	125	125	125	120
DAPSA6	0.91936	0.73899	0.80152	0.65309	0.16583	0.73804	0.39268	0.08071	1.00000
	<.0001	<.0001	<.0001	<.0001	0.0703	<.0001	<.0001	0.3809	
	120	120	120	120	120	120	120	120	120

Source: Correlation_pearson.sas, run on 17MAY2017

Table 56 - Correlation between disease activity measures (Bland and Altman)

Variable 1	Variable 2	Rho	P value
68-TJC	66-SJC	0.3117	<.0001
	VAS	0.2884	<.0001
	HAQ	0.3849	0.0002
	CRP	0.1895	0.0208
	BASDAI	0.4929	<.0001
	LEI	-0.5403	
	Dactyl	0.2939	0.0022
	DAPSA	0.3777	<.0001
66-SJC	VAS	0.3100	<.0001
	HAQ	0.3992	<.0001
	CRP	0.1637	0.0441
	BASDAI	0.4864	<.0001
	LEI	0.3586	0.0002
	Dactyl	0.2287	0.0123
	DAPSA	0.4032	<.0001
VAS	HAQ	0.3996	<.0001
	CRP	0.2442	0.0021
	BASDAI	0.4035	<.0001
	LEI	0.4187	<.0001
	Dactyl	0.3625	0.0002
	DAPSA	0.3480	<.0001
HAQ	CRP	0.2215	0.0077
	BASDAI	0.5061	<.0001
	LEI	0.4321	<.0001
	Dactyl	0.3607	0.0004
	DAPSA	0.4317	<.0001
CRP	BASDAI	-0.8269	
	LEI	-0.8313	
	Dactyl	-0.8334	
	DAPSA	0.3504	<.0001
BASDAI	LEI	0.5036	<.0001
	Dactyl	0.4970	<.0001
	DAPSA	0.4569	<.0001
LEI	Dactyl	0.3192	0.0012
	DAPSA	0.4172	<.0001
Dactyl	DAPSA	0.4274	<.0001

Notes: Analysis is based on a linear mixed model for repeated measures, according to Bland and Altman method.
An unstructured covariance matrix for each patient is considered and the Kenward-Roger adjustment is used for the degrees of freedom.
Correlation coefficients that take into account repeated observations within the same subject are estimated according to Bland and Altman.

Source: Correlation_mixed.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
No. of patients with any concomitant treatment		n	(%)	141	(94.6%)
ANTIPSORIATICS FOR SYSTEMIC USE (D05B)		n	(%)	87	(58.4%)
	Methotrexate	n	(%)	87	(58.4%)
VITAMIN B12 AND FOLIC ACID (B03B)		n	(%)	72	(48.3%)
	Folic acid	n	(%)	71	(47.7%)
	Calcium mefolinate	n	(%)	1	(0.7%)
	Cyanocobalamin	n	(%)	1	(0.7%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS (M01A)		n	(%)	59	(39.6%)
	Etoricoxib	n	(%)	35	(23.5%)
	Ibuprofen	n	(%)	5	(3.4%)
	Diclofenac	n	(%)	4	(2.7%)
	Meloxicam	n	(%)	4	(2.7%)
	Naproxen	n	(%)	4	(2.7%)
	Nimesulide	n	(%)	4	(2.7%)
	Celecoxib	n	(%)	3	(2.0%)
	Hydroxychloroquine	n	(%)	2	(1.3%)
	Ketoprofen	n	(%)	2	(1.3%)
	Aceclofenac	n	(%)	1	(0.7%)
	Indometacin	n	(%)	1	(0.7%)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN (H02A)		n	(%)	55	(36.9%)
	Methylprednisolone	n	(%)	26	(17.4%)
	Prednisone	n	(%)	23	(15.4%)
	Beclometasone	n	(%)	5	(3.4%)
	Triamcinolone	n	(%)	3	(2.0%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN (H02A)	Triamcinolone acetonide	n	(%)	1	(0.7%)
VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO (A11C)		n	(%)	38	(25.5%)
	Colecalciferol	n	(%)	37	(24.8%)
	Calcitriol	n	(%)	1	(0.7%)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)		n	(%)	35	(23.5%)
	Pantoprazole	n	(%)	13	(8.7%)
	Lansoprazole	n	(%)	12	(8.1%)
	Omeprazole	n	(%)	4	(2.7%)
	Rabeprazole	n	(%)	3	(2.0%)
	Esomeprazole	n	(%)	2	(1.3%)
	Sucralfate	n	(%)	1	(0.7%)
INTESTINAL ANTIINFLAMMATORY AGENTS (A07E)		n	(%)	20	(13.4%)
	Sulfasalazine	n	(%)	18	(12.1%)
	Mesalazine	n	(%)	2	(1.3%)
OTHER ANALGESICS AND ANTIPYRETICS (N02B)		n	(%)	20	(13.4%)
	Paracetamol	n	(%)	16	(10.7%)
	Pregabalin	n	(%)	5	(3.4%)
	Codeine phosphate + Paracetamol	n	(%)	1	(0.7%)
THYROID PREPARATIONS (H03A)		n	(%)	19	(12.8%)
	Levothyroxine	n	(%)	19	(12.8%)
LIPID MODIFYING AGENTS, PLAIN (C10A)		n	(%)	15	(10.1%)
	Simvastatin	n	(%)	6	(4.0%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
LIPID MODIFYING AGENTS, PLAIN (C10A)	Atorvastatin	n	(%)	2	(1.3%)
	Ezetimibe	n	(%)	2	(1.3%)
	Lovastatin	n	(%)	2	(1.3%)
	Rosuvastatin	n	(%)	2	(1.3%)
	Pravastatin	n	(%)	1	(0.7%)
ANTIGOUT PREPARATIONS (M04A)		n	(%)	10	(6.7%)
	Allopurinol	n	(%)	9	(6.0%)
	Febuxostat	n	(%)	1	(0.7%)
OPIOIDS (N02A)		n	(%)	10	(6.7%)
	Codeine	n	(%)	5	(3.4%)
	Codeine + Paracetamol	n	(%)	1	(0.7%)
	Oxycodone + Paracetamol	n	(%)	1	(0.7%)
	Oxycodone hydrochloride	n	(%)	1	(0.7%)
	Paracetamol + Tramadol	n	(%)	1	(0.7%)
	Tapentadol	n	(%)	1	(0.7%)
	Tramadol	n	(%)	1	(0.7%)
ANGIOTENSIN II ANTAGONISTS, PLAIN (C09C)		n	(%)	9	(6.0%)
	Olmesartan medoxomil	n	(%)	3	(2.0%)
	Valsartan	n	(%)	3	(2.0%)
	Olmesartan	n	(%)	2	(1.3%)
	Irbesartan	n	(%)	1	(0.7%)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS (C0		n	(%)	9	(6.0%)
	Amlodipine	n	(%)	3	(2.0%)
	Nifedipine	n	(%)	3	(2.0%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS (C0	Lercanidipine	n	(%)	2	(1.3%)
	Amlodipine besilate	n	(%)	1	(0.7%)
ANTITHROMBOTIC AGENTS (B01A)		n	(%)	8	(5.4%)
	Acetylsalicylic acid	n	(%)	6	(4.0%)
	Clopidogrel	n	(%)	2	(1.3%)
ACE INHIBITORS, PLAIN (C09A)		n	(%)	7	(4.7%)
	Ramipril	n	(%)	5	(3.4%)
	Lisinopril	n	(%)	2	(1.3%)
IMMUNOSUPPRESSANTS (L04A)		n	(%)	7	(4.7%)
	Leflunomide	n	(%)	5	(3.4%)
	Adalimumab	n	(%)	1	(0.7%)
	Ciclosporin	n	(%)	1	(0.7%)
ANTIDEPRESSANTS (N06A)		n	(%)	6	(4.0%)
	Amitriptyline	n	(%)	2	(1.3%)
	Sertraline	n	(%)	2	(1.3%)
	Mirtazapine	n	(%)	1	(0.7%)
	Paroxetine	n	(%)	1	(0.7%)
ANTIMETABOLITES (L01B)		n	(%)	6	(4.0%)
	Methotrexate	n	(%)	6	(4.0%)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION (M05B)		n	(%)	6	(4.0%)
	Alendronate sodium	n	(%)	2	(1.3%)
	Alendronic acid	n	(%)	1	(0.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic	N=149	
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION (M05B)	Clodronic acid	n (%)	1	(0.7%)
	Ibandronate sodium	n (%)	1	(0.7%)
	Risedronate sodium	n (%)	1	(0.7%)
DRUGS FOR TREATMENT OF TUBERCULOSIS (J04A)		n (%)	6	(4.0%)
	Isoniazid	n (%)	5	(3.4%)
	Rifampicin	n (%)	1	(0.7%)
BETA BLOCKING AGENTS (C07A)		n (%)	5	(3.4%)
	Bisoprolol	n (%)	3	(2.0%)
	Atenolol	n (%)	1	(0.7%)
	Carvedilol	n (%)	1	(0.7%)
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS (A10B)		n (%)	5	(3.4%)
	Metformin	n (%)	4	(2.7%)
	Empagliflozin	n (%)	1	(0.7%)
	Glimepiride	n (%)	1	(0.7%)
CALCIUM (A12A)		n (%)	5	(3.4%)
	Calcium carbonate	n (%)	4	(2.7%)
	Calcium gluconate	n (%)	1	(0.7%)
MUSCLE RELAXANTS, CENTRALLY ACTING AGENTS (M03B)		n (%)	5	(3.4%)
	Cyclobenzaprine	n (%)	3	(2.0%)
	Tizanidine	n (%)	2	(1.3%)
(N02)		n (%)	4	(2.7%)
	Duloxetine	n (%)	4	(2.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
ANTIHISTAMINES FOR SYSTEMIC USE (R06A)		n	(%)	4	(2.7%)
	Cetirizine hydrochloride	n	(%)	2	(1.3%)
	Hydroxyzine	n	(%)	1	(0.7%)
	Levocetirizine	n	(%)	1	(0.7%)
QUINOLONE ANTIBACTERIALS (J01M)		n	(%)	4	(2.7%)
	Ciprofloxacin	n	(%)	3	(2.0%)
	Levofloxacin	n	(%)	1	(0.7%)
BETA-LACTAM ANTIBACTERIALS, PENICILLINS (J01C)		n	(%)	3	(2.0%)
	Amoxicillin	n	(%)	1	(0.7%)
	Amoxicillin + Clavulanic acid	n	(%)	1	(0.7%)
	Amoxicillin trihydrate	n	(%)	1	(0.7%)
	Clavulanate potassium	n	(%)	1	(0.7%)
	Clavulanic acid	n	(%)	1	(0.7%)
CORTICOSTEROIDS, PLAIN (D07A)		n	(%)	3	(2.0%)
	Fluocinolone acetonide	n	(%)	2	(1.3%)
	Mometasone	n	(%)	1	(0.7%)
LOW-CEILING DIURETICS, THIAZIDES (C03A)		n	(%)	3	(2.0%)
	Hydrochlorothiazide	n	(%)	3	(2.0%)
OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS (R03B)		n	(%)	3	(2.0%)
	Budesonide	n	(%)	1	(0.7%)
	Fluticasone propionate	n	(%)	1	(0.7%)
	Mometasone	n	(%)	1	(0.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic	N=149	
ACE INHIBITORS, COMBINATIONS (C09B)		n (%)	2	(1.3%)
	Amlodipine + Perindopril	n (%)	1	(0.7%)
	Hydrochlorothiazide + Lisinopril	n (%)	1	(0.7%)
ANGIOTENSIN II ANTAGONISTS, COMBINATIONS (C09D)		n (%)	2	(1.3%)
	Amlodipine + Olmesartan	n (%)	1	(0.7%)
	Hydrochlorothiazide + Losartan potassium	n (%)	1	(0.7%)
ANXIOLYTICS (N05B)		n (%)	2	(1.3%)
	Alprazolam	n (%)	1	(0.7%)
	Bromazepam	n (%)	1	(0.7%)
DIRECT ACTING ANTIVIRALS (J05A)		n (%)	2	(1.3%)
	Entecavir	n (%)	2	(1.3%)
DOPAMINERGIC AGENTS (N04B)		n (%)	2	(1.3%)
	Pramipexole	n (%)	2	(1.3%)
	Carbidopa + Melevodopa	n (%)	1	(0.7%)
DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY (G04C)		n (%)	2	(1.3%)
	Alfuzosin hydrochloride	n (%)	1	(0.7%)
	Silodosin	n (%)	1	(0.7%)
ESTROGENS (G03C)		n (%)	2	(1.3%)
	Ethinylestradiol	n (%)	2	(1.3%)
HIGH-CEILING DIURETICS (C03C)		n (%)	2	(1.3%)
	Furosemide	n (%)	2	(1.3%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
INSULINS AND ANALOGUES (A10A)		n	(%)	2	(1.3%)
	Insulin glargine	n	(%)	2	(1.3%)
	Insulin aspart	n	(%)	1	(0.7%)
INTESTINAL ANTIINFECTIVES (A07A)		n	(%)	2	(1.3%)
	Rifaximin	n	(%)	2	(1.3%)
MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS (J01F)		n	(%)	2	(1.3%)
	Clarithromycin	n	(%)	2	(1.3%)
OTHER PLAIN VITAMIN PREPARATIONS (A11H)		n	(%)	2	(1.3%)
	Pyridoxine	n	(%)	1	(0.7%)
	Pyridoxine hydrochloride	n	(%)	1	(0.7%)
PROPULSIVES (A03F)		n	(%)	2	(1.3%)
	Metoclopramide	n	(%)	2	(1.3%)
(H02)		n	(%)	1	(0.7%)
	Corticosteroid nos	n	(%)	1	(0.7%)
(V90)		n	(%)	1	(0.7%)
	Silybum marianum	n	(%)	1	(0.7%)
ADRENERGICS, INHALANTS (R03A)		n	(%)	1	(0.7%)
	Salmeterol	n	(%)	1	(0.7%)
ALL OTHER NON-THERAPEUTIC PRODUCTS (V07A)		n	(%)	1	(0.7%)
	Hyaluronic acid	n	(%)	1	(0.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic	N=149
ALL OTHER THERAPEUTIC PRODUCTS (V03A)		n (%)	1 (0.7%)
	Calcium levofolinate	n (%)	1 (0.7%)
ANTIADRENERGIC AGENTS, CENTRALLY ACTING (C02A)		n (%)	1 (0.7%)
	Clonidine hydrochloride	n (%)	1 (0.7%)
ANTIARRHYTHMICS, CLASS I AND III (C01B)		n (%)	1 (0.7%)
	Flecainide	n (%)	1 (0.7%)
ANTIBIOTICS FOR TOPICAL USE (D06A)		n (%)	1 (0.7%)
	Neomycin	n (%)	1 (0.7%)
ANTIEPILEPTICS (N03A)		n (%)	1 (0.7%)
	Valproate sodium	n (%)	1 (0.7%)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS (S01E)		n (%)	1 (0.7%)
	Latanoprost + Timolol maleate	n (%)	1 (0.7%)
ANTIINFECTIVES AND ANTISEPTICS, EXCL. COMBINATIONS WITH CORTICOSTER		n (%)	1 (0.7%)
	Clotrimazole	n (%)	1 (0.7%)
ANTIMIGRAINE PREPARATIONS (N02C)		n (%)	1 (0.7%)
	Rizatriptan	n (%)	1 (0.7%)
ANTIMYCOTICS FOR SYSTEMIC USE (J02A)		n (%)	1 (0.7%)
	Itraconazole	n (%)	1 (0.7%)
ANTIPSORIATICS FOR TOPICAL USE (D05A)		n (%)	1 (0.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic		N=149	
ANTIPSORIATICS FOR TOPICAL USE (D05A)	Calcipotriol	n	(%)	1	(0.7%)
BILE THERAPY (A05A)		n	(%)	1	(0.7%)
	Ursodeoxycholic acid	n	(%)	1	(0.7%)
CORTICOSTEROIDS, OTHER COMBINATIONS (D07X)		n	(%)	1	(0.7%)
	Betamethasone + Calcipotriol	n	(%)	1	(0.7%)
DRUGS USED IN ADDICTIVE DISORDERS (N07B)		n	(%)	1	(0.7%)
	Naloxone	n	(%)	1	(0.7%)
EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRESSANTS (R05C)		n	(%)	1	(0.7%)
	Acetylcysteine	n	(%)	1	(0.7%)
HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE (G03A)		n	(%)	1	(0.7%)
	Drospirenone	n	(%)	1	(0.7%)
I.V. SOLUTION ADDITIVES (B05X)		n	(%)	1	(0.7%)
	Sodium chloride	n	(%)	1	(0.7%)
LOW-CEILING DIURETICS, EXCL. THIAZIDES (C03B)		n	(%)	1	(0.7%)
	Chlortalidone	n	(%)	1	(0.7%)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS (A16A)		n	(%)	1	(0.7%)
	Acetylcysteine	n	(%)	1	(0.7%)
OTHER ANTIBACTERIALS (J01X)		n	(%)	1	(0.7%)
	Metronidazole	n	(%)	1	(0.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 57 - Summary of concomitant treatments

Population: STD

ATC 3rd level subgroup	Generic Name (WHO-DD)	Statistic	N=149
OTHER ANTIHYPERTENSIVES (C02K)		n (%)	1 (0.7%)
	Other antihypertensives	n (%)	1 (0.7%)
OTHER OPHTHALMOLOGICALS (S01X)		n (%)	1 (0.7%)
	Artificial tears	n (%)	1 (0.7%)
OTHER SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM (G03X)		n (%)	1 (0.7%)
	Bazedoxifene	n (%)	1 (0.7%)
POTASSIUM-SPARING AGENTS (C03D)		n (%)	1 (0.7%)
	Spironolactone	n (%)	1 (0.7%)
PROGESTOGENS (G03D)		n (%)	1 (0.7%)
	Gestodene	n (%)	1 (0.7%)
PROGESTOGENS AND ESTROGENS IN COMBINATION (G03F)		n (%)	1 (0.7%)
	Progestogens and estrogens in combination	n (%)	1 (0.7%)
SULFONAMIDES AND TRIMETHOPRIM (J01E)		n (%)	1 (0.7%)
	Sulfamethoxazole + Trimethoprim	n (%)	1 (0.7%)
TETRACYCLINES (J01A)		n (%)	1 (0.7%)
	Minocycline	n (%)	1 (0.7%)

Notes: Medications were coded using the WHO-DRL Dictionary (DD) version December 2015.
Medications were classified according to 3rd level ATC codes and generic name.
Medications include all medications reported in the eCRF 'Concomitant Medications' form.

Source: Conc_treat.sas, SPARC Consulting. Run on 17MAY2017

Table 58 - Summary of Study Drug administration

Popolazione: STD

	Statistics	N=149
Nr. of injections of Golimumab	n	149
	Mean	6.04
	SD	1.41
	Median	6.00
	Q1,Q3	6.00,7.00
	Min,Max	1.00,8.00
Duration of treatment administration (months)	n	149
	Mean	5.17
	SD	1.33
	Median	5.13
	Q1,Q3	5.07,6.07
	Min,Max	0.03,7.23
Total dose administered (mg)	n	149
	Mean	307.75
	SD	83.75
	Median	300.00
	Q1,Q3	300.00,350.00
	Min,Max	50.00,700.00

Notes:
Duration of treatment administration is calculated as (date of last injection - date of first injection + 1)/30.
Total dose administered is the sum of each dose administered during the study.

Source: Golim.sas, run on 17MAY2017

Table 59 - Overview of adverse events incidence

Population: STD

	Statistic	N=149	
No. of Adverse Events	n	23	
No. of Related Adverse Events	n	20	
No. of Serious Adverse Events	n	3	
No. of Serious Related Adverse Events	n	0	
No. of Temporary discontinuations due to Adverse Events	n	9	
No. of Permanent discontinuations due to Adverse Events	n	6	
No. of Patients with at least one Adverse Event	n (%)	14	(9.4%)
No. of Patients with at least one Related Adverse Event	n (%)	12	(8.1%)
No. of Patients with at least one Serious Adverse Event	n (%)	3	(2.0%)
No. of Patients Dead	n (%)	0	(0.0%)
No. of Patients who temporarily discontinued Golimumab due to AE	n (%)	6	(4.0%)
No. of Patients who permanently discontinued Golimumab due to AE	n (%)	5	(3.4%)

Notes:
Related Adverse Events are those Adverse Events defined as 'correlated to Golimumab'.
Missing category was considered as related to the study drug.
Percentages are calculated on the total number of patients in the STD population.

Source: summary_AE.sas, SPARC Consulting. Run on 08MAY2017

Table 60 - Summary of all adverse events by System Organ Class and Preferred Term

Population: STD

Primary SOC/PT	Statistics		N=149
No. of patients with at least one adverse event	n (%)		14 (9.4%)
Blood And Lymphatic System Disorders	n (%)	E	3 (2.0%) 4
Leukopenia	n (%)	E	2 (1.3%) 2
Lymphadenopathy	n (%)	E	1 (0.7%) 1
Thrombocytopenia	n (%)	E	1 (0.7%) 1
Hepatobiliary Disorders	n (%)	E	1 (0.7%) 1
Drug-Induced Liver Injury	n (%)	E	1 (0.7%) 1
Infections And Infestations	n (%)	E	5 (3.4%) 6
Erysipelas	n (%)	E	2 (1.3%) 2
Bronchitis	n (%)	E	1 (0.7%) 1
Genital Candidiasis	n (%)	E	1 (0.7%) 1
Pharyngotonsillitis	n (%)	E	1 (0.7%) 1
Urinary Tract Infection	n (%)	E	1 (0.7%) 1
Investigations	n (%)	E	3 (2.0%) 4
Alanine Aminotransferase Increased	n (%)	E	2 (1.3%) 2
Aspartate Aminotransferase Increased	n (%)	E	1 (0.7%) 1
Transaminases Increased	n (%)	E	1 (0.7%) 1
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	n (%)	E	1 (0.7%) 1
Basal Cell Carcinoma	n (%)	E	1 (0.7%) 1
Respiratory, Thoracic And Mediastinal Disorders	n (%)	E	1 (0.7%) 1
Dyspnoea	n (%)	E	1 (0.7%) 1
Skin And Subcutaneous Tissue Disorders	n (%)	E	5 (3.4%) 6
Alopecia	n (%)	E	1 (0.7%) 1
Pruritus	n (%)	E	1 (0.7%) 1
Psoriasis	n (%)	E	1 (0.7%) 1
Pustular Psoriasis	n (%)	E	1 (0.7%) 1
Rash Erythematous	n (%)	E	1 (0.7%) 1

Notes:
Percentages are based on number of subjects in the STD sample.
N = number of patients, % = percentage of patients, E = number of events.
If a subject experienced more than one AE with the same PT or primary SOC, the AE with the maximum intensity was counted.
AEs were coded using MedDRA version 18.1 or higher.

Source: AE_PT_SOC.sas, SPARC Consulting. Run on 17MAY2017

Table 60 - Summary of all adverse events by System Organ Class and Preferred Term

Population: STD

Primary SOC/PT	Statistics	N=149
Rash Papular	n (%) E	1 (0.7%) 1

Notes:
Percentages are based on number of subjects in the STD sample.
N = number of patients, % = percentage of patients, E = number of events.
If a subject experienced more than one AE with the same PT or primary SOC, the AE with the maximum intensity was counted.
AEs were coded using MedDRA version 18.1 or higher.

Source: AE_PT_SOC.sas, SPARC Consulting. Run on 17MAY2017

Table 61 - Summary of adverse events by maximum intensity by System Organ Class and Preferred Term

Population: STD

Primary SOC/PT	Statistics	N=149 Mild	Moderate
Blood And Lymphatic System Disorders	n (%) E	1 (0.7%) 1	2 (1.3%) 3
Leukopenia	n (%) E	1 (0.7%) 1	1 (0.7%) 1
Lymphadenopathy	n (%) E		1 (0.7%) 1
Thrombocytopenia	n (%) E		1 (0.7%) 1
Hepatobiliary Disorders	n (%) E		1 (0.7%) 1
Drug-Induced Liver Injury	n (%) E		1 (0.7%) 1
Infections And Infestations	n (%) E	3 (2.0%) 4	2 (1.3%) 2
Bronchitis	n (%) E		1 (0.7%) 1
Erysipelas	n (%) E	1 (0.7%) 1	1 (0.7%) 1
Genital Candidiasis	n (%) E	1 (0.7%) 1	
Pharyngotonsillitis	n (%) E	1 (0.7%) 1	
Urinary Tract Infection	n (%) E	1 (0.7%) 1	
Investigations	n (%) E	3 (2.0%) 4	
Alanine Aminotransferase Increased	n (%) E	2 (1.3%) 2	
Aspartate Aminotransferase Increased	n (%) E	1 (0.7%) 1	
Transaminases Increased	n (%) E	1 (0.7%) 1	
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	n (%) E	1 (0.7%) 1	
Basal Cell Carcinoma	n (%) E	1 (0.7%) 1	
Respiratory, Thoracic And Mediastinal Disorders	n (%) E		1 (0.7%) 1
Dyspnoea	n (%) E		1 (0.7%) 1
Skin And Subcutaneous Tissue Disorders	n (%) E	1 (0.7%) 1	4 (2.7%) 5
Alopecia	n (%) E		1 (0.7%) 1
Pruritus	n (%) E		1 (0.7%) 1
Psoriasis	n (%) E	1 (0.7%) 1	
Pustular Psoriasis	n (%) E		1 (0.7%) 1
Rash Erythematous	n (%) E		1 (0.7%) 1
Rash Papular	n (%) E		1 (0.7%) 1

Notes:
Percentages are based on number of subjects in the STD sample.
N = number of patients, % = percentage of patients, E = number of events.
If a subject experienced more than one AE with the same PT or primary SOC, the AE with the maximum severity was counted.
AEs were coded using MedDRA version 18.1 or higher.

Source: AE_intensity.sas, SPARC Consulting. Run on 17MAY2017

Table 62 - Summary of all serious adverse events by System Organ Class and Preferred Term

Population: STD

Primary SOC/PT	Statistics		N=149
No. of patients with at least one serious adverse event	n (%)		3 (2.0%)
Blood And Lymphatic System Disorders	n (%)	E	1 (0.7%) 1
Lymphadenopathy	n (%)	E	1 (0.7%) 1
Hepatobiliary Disorders	n (%)	E	1 (0.7%) 1
Drug-Induced Liver Injury	n (%)	E	1 (0.7%) 1
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	n (%)	E	1 (0.7%) 1
Basal Cell Carcinoma	n (%)	E	1 (0.7%) 1

Notes:
Percentages are based on number of subjects in the STD sample.
N = number of patients, % = percentage of patients, E = number of events.
If a subject experienced more than one AE with the same PT or primary SOC, the AE with the maximum intensity was counted.
AEs were coded using MedDRA version 18.1 or higher.

Source: SAE_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 63 - Summary of all related adverse events by System Organ Class and Preferred Term

Population: STD

Primary SOC/PT	Statistics		N=149
No. of patients with at least one related adverse event	n (%)		12 (8.1%)
Blood And Lymphatic System Disorders	n (%)	E	2 (1.3%) 3
Leukopenia	n (%)	E	2 (1.3%) 2
Thrombocytopenia	n (%)	E	1 (0.7%) 1
Infections And Infestations	n (%)	E	5 (3.4%) 6
Erysipelas	n (%)	E	2 (1.3%) 2
Bronchitis	n (%)	E	1 (0.7%) 1
Genital Candidiasis	n (%)	E	1 (0.7%) 1
Pharyngotonsillitis	n (%)	E	1 (0.7%) 1
Urinary Tract Infection	n (%)	E	1 (0.7%) 1
Investigations	n (%)	E	3 (2.0%) 4
Alanine Aminotransferase Increased	n (%)	E	2 (1.3%) 2
Aspartate Aminotransferase Increased	n (%)	E	1 (0.7%) 1
Transaminases Increased	n (%)	E	1 (0.7%) 1
Respiratory, Thoracic And Mediastinal Disorders	n (%)	E	1 (0.7%) 1
Dyspnoea	n (%)	E	1 (0.7%) 1
Skin And Subcutaneous Tissue Disorders	n (%)	E	5 (3.4%) 6
Alopecia	n (%)	E	1 (0.7%) 1
Pruritus	n (%)	E	1 (0.7%) 1
Psoriasis	n (%)	E	1 (0.7%) 1
Pustular Psoriasis	n (%)	E	1 (0.7%) 1
Rash Erythematous	n (%)	E	1 (0.7%) 1
Rash Papular	n (%)	E	1 (0.7%) 1

Notes:
Percentages are based on number of subjects in the STD sample.
N = number of patients, % = percentage of patients, E = number of events.
If a subject experienced more than one AE with the same PT or primary SOC, the AE with the maximum intensity was counted.
AEs were coded using MedDRA version 18.1 or higher.

Source: related_AE_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 64 - Summary of all serious related adverse events by System Organ Class and Preferred Term

Population: STD

NO SERIOUS RELATED ADVERSE EVENTS WERE REPORTED IN THE STUDY

Source: related_SAE_pt_soc.sas, SPARC Consulting. Run on 17MAY2017

Table 65 - Line listing of all adverse events

PPD

Table 65 - Line listing of all adverse events

Table 66 - Line listing of serious adverse events

Table 67 - Line listing of related serious adverse events

NO SERIOUS RELATED ADVERSE EVENTS WERE REPORTED IN THE STUDY

Source: AE_lists.sas, SPARC Consulting. Run on 17MAY2017

Table 68 - Line listing of adverse events leading to permanent discontinuation of Golimumab

Table 69 - Line listing of adverse events leading to temporary discontinuation of Golimumab

Table 70 - Line listing of deaths

NO DEATHS WERE REPORTED IN THE STUDY

Source: AE_lists.sas, SPARC Consulting. Run on 17MAY2017

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