NON-INTERVENTIONAL (NI) FINAL STUDY REPORT

PASS Information

Title	Real-world evaluation of effectiveness, persistence and usage patterns of tofacitinib in treatment of psoriatic arthritis in Australia.
Protocol Number	A3921398
Protocol Version Identifier	Version 1.0
Date	19 July 2022
EU Post Authorization Study (PAS) Register Number	EUPAS39635
Active Substance	Tofacitinib Citrate
Medicinal Product	Xeljanz®
Research Question and Objectives	To understand the treatment patterns (lines of therapy, combination with other therapies or monotherapy), clinical effectiveness, patient reported outcomes and treatment persistence among Australian adult patients with psoriatic arthritis who are receiving tofacitinib.
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1. ABSTRACT (STAND-ALONE DOCUMENT)

In Annex 1 as a stand-alone document.

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical (Classification)
bDMARD	Biologic Disease-Modifying Antiheumatic Drug
CDAI	Clinical Disease Activity Index
cDMARD	Conventional Disease-Modifying Antirheumatic Drug
CRP	C-Reactive Protein
DAPSA	Disease Activity in Psoriatic Arthritis
DAS28	Disease Activity Score in 28 joints
DMARD	Disease-Modifying Antirheumatic Drug
ESR	Erythrocyte Sedimentation Rate
FACIT	Functional Assessment Of Chronic Illness Therapy
GPP	Good Pharmacoepidemiology Practices
HAQ-DI	Health Assessment Questionnaire Disease Index
HCRU	Health Care Resource Utilisation
HL7	Health Level Seven
HREC	Human Research Ethics Committee
ICD-10	International Classification of Diseases 10
ICMJE	International Committee of Medical Journal Editors
IEC	Independent Ethics Committee

Abbreviation	Definition
IL17	Interleukin 17 Inhibitor
IRB	Institutional Review Board
ISPE	International Society for PharmacoEpidemiology
JAK	Janus Kinase
KM	Kaplan-Meier
LOINC	Logical Observation Identifiers Names and Codes
MP	Multiprocessor
MTX	Methotrexate
NSAID	Non-Steroidal Anti-Inflammatory Drug
OPAL	OPAL Optimising Patient Outcome in Australian RheumatoLogy
PBS	Pharmaceutical Benefits Scheme
PRO	Patient Reported Outcome
PsA	Psoriatic Arthritis
QoL	Quality of Life
QUMI	Quality Use of Medicines Initiative
S4S	Software 4 Specialists (Clinical Software Developers For OPAL)
SAP	Statistical Analysis Plan
SDAI	Simple Disease Activity Index
TNFi	Tumor Necrosis Factor Inhibitor
tsDMARD	Targeted Synthetic Disease Modifying Antirheumatic Drug

Abbreviation	Definition
WHO	World Health Organisation

3. INVESTIGATORS

Principal Investigator(s) of the Protocol (N/A)

Name, degree(s)	Job Title	Affiliation	Address
Redacted	Redacted Redacted	Redacted	Redacted Redacted Redacted
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4. OTHER RESPONSIBLE PARTIES

Not applicable.

5. MILESTONES

Milestone	Planned Date	Actual Date	Comments
Start of Data Collection	15 April 2021	15 May 2021	
End of Data Collection	01 December 2021	11 October 2022	
Planned Date of EUPASS Registration	01 April 2021	17 May 2021	
Final Study Report	01 November 2022		

6. RATIONALE AND BACKGROUND

Chronic inflammatory diseases such as psoriatic arthritis (PsA) have a significant negative impact on patients' health-related quality of life (QoL), and present a significant economic burden. Maximisation of health-related QoL is the primary goal of treatment. This is achieved through symptom and inflammation control, prevention of progressive structural damage, preservation or normalisation of function and social participation, and targeting remission.[1] Treatment of PsA usually involves a multifaceted approach that includes pharmacologic and non-pharmacologic strategies. Non-pharmacologic therapy may include physical, occupational, and psychological therapy, and surgery, while pharmacological therapy usually consists of various combinations of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, corticosteroids, and synthetic or biologic disease modifying anti-rheumatic drugs (DMARDs).

Recently, tofacitinib, a new oral, targeted synthetic DMARD (tsDMARD), has become available for the treatment of PsA. Tofacitinib is a potent, selective inhibitor of the Janus Kinase (JAK) family of kinases with a high degree of selectivity against other kinases in the human genome. It was approved for use in Australia in May 2018 and included in the Pharmaceutical Benefits Scheme (PBS) (reimbursement) in May 2019. Limited data exist to describe the characteristics and outcomes of patients who receive tofacitinib in the real-world setting.

Patient reported outcomes (PROs) complement physician and laboratory measures in providing scientific evidence to support decisions regarding clinical therapy. The Outcome Measures in Rheumatology International consensus effort, the American College of Rheumatology, and the European League Against Rheumatism have recognized the importance of including a variety of PROs in randomized controlled trials.[2]

This study aimed to use the Optimising Patient outcome in Australian rheumatoLogy (OPAL)3 dataset to provide real-world evidence regarding general treatment patterns, clinical effectiveness, treatment persistence and PROs among PsA patients being treated with tofacitinib in the post-approval setting. Similar data were collected for patients treated with bDMARDs that provides context from a real-world clinical practice setting. No formal comparisons between patients treated with tofacitinib and bDMARDs were performed. An exploratory analysis and description of the most common reasons for discontinuation of treatments are described. No safety analysis or analysis of adverse events were performed.

This non-interventional study is designated as a Post-Authorization Safety Study (PASS) and was conducted voluntarily by Pfizer.

7. RESEARCH QUESTION AND OBJECTIVES

To understand the patterns of treatment (lines of therapy, and use as combination or monotherapy), clinical effectiveness, PROs and treatment persistence among Australian adult patients with PsA treated with tofacitinib. Similar data were also collected for patients treated with bDMARDs to provide descriptive information about clinical management of PsA in real-world Australian clinical practice.

Objectives

7.1. Primary Objective

1. To describe tofacitinib, interleukin 17 inhibitor (IL17i), and tumor necrosis factor inhibitor (TNFi) treatment patterns among Australian adult patients with PsA, including:

    - Line of use (eg, first-line, second-line);
    - Mean dose;
    - Proportion of patients receiving monotherapy;
    - Proportion of patients using in combination with NSAIDs, corticosteroids and conventional disease-modifying antirheumatic drugs (cDMARDs);
    - Reasons for discontinuation.

7.2. Secondary Objectives

1. To describe treatment persistence to IL17i, TNFi and tofacitinib in Australian patients with PsA.

2. To describe the clinical effectiveness of tofacitinib, IL17i, and TNFi, as defined by disease severity markers Disease Activity Score in 28 joints - erythrocyte sedimentation rate, (DAS28-ESR) Clinical Disease Activity Index (CDAI), Simple Disease Activity Index (SDAI), Disease Activity in Psoriatic Arthritis (DAPSA) [if available]) and the percentage of patients reaching targeted treatment goals (remission or low disease activity), in Australia.

3. To describe patient reported outcomes (HAQ-DI, FACIT-Fatigue, HCRU) in Australian adult patients with PsA between those prescribed tofacitinib and those prescribed other IL17i, or TNFi.

8. RESEARCH METHODS

8.1. Study Design

This is a retrospective, non-interventional, secondary structured data analysis cohort study of treatment patterns in patients prescribed IL17i, TNFi, or tofacitinib and involved extracting real-world patient data from the Australian OPAL dataset.

Tofacitinib was listed on the Pharmaceutical Benefits Scheme (PBS) in May 2019. TNFi (adalimumab, certolizumab, etanercept, golimumab infliximab) and IL17i (secukinumab, ixekizumab) were already listed on the Pharmaceutical Benefits Scheme at this time.

Data were extracted for the period 01 May 2019 until 30 September 2021 (sample window).

Patients included in this study were followed for a minimum of 1 year following their prescription of the index DMARD (IL17i, TNFi, or tofacitinib). Patients who discontinued their index DMARD were also followed up for at least 1 year from time of the initial prescription of that treatment.

All drugs were prescribed, and all follow-up visits were captured as part of normal medical practice. Patient therapeutic strategies were not determined by the study protocol.

8.2. Setting

Data were extracted from the Australian OPAL dataset database. The OPAL database collects information from individual clinicians' servers during routine clinical consultations, using purpose-built worksheets in Audit4 software. Pathology and imaging reports were electronically transferred from the pathology and radiology providers and were incorporated into the patient's medical record. This software serves as the patient's medical record.[3,4]

The activities of OPAL Rheumatology Ltd received overarching ethics approval from the University of New South Wales Human Research Ethics Committee (HREC), based on a patient opt-out arrangement. De-identified data were exported from the clinician's server and encrypted. Aggregated data were sent to the OPAL Study Committee and the study statistician. All research undertaken by OPAL requires the prospective approval of a properly constituted Australian HREC.

The database has collected information on more than 192,000 unique patients during 1 million clinical consultations from 43 rheumatologist clinics (and approximately 104 individual rheumatologists) around Australia. Of these 14,372 have a diagnosis of PsA.

Tofacitinib was reimbursed by the PBS in May 2019. Therefore, the start of the sample selection window corresponded to the time of approval.

The sample selection window was 01 May 2019 to 30 September 2020. Patients were followed for a minimum one year. Therefore, the sampling window was 01 May 2019 to 30 September 2021.

460 patients taking tofacitinib, and 1,080 patients taking bDMARDs were enrolled in this study, and all relevant and available data were extracted. Data cuts used are from September 2020 and September 2021.

This study included adult patients (aged 18 years or older) with a diagnosis of PsA, who received treatment with tofacitinib or a bDMARD and had at least 1 year of follow-up.

8.2.1. Inclusion Criteria

Patients meeting each of the following inclusion criteria were eligible for inclusion in the study:

1. Diagnosed with PsA;
2. Aged 18 years but under 95 years of age on the index date (date of commencement of IL17i, TNFi, or tofacitinib);
3. Received at least 1 prescription for IL17i, TNFi, or tofacitinib; and
4. Have at least 1 year of follow-up since prescription of IL17i, TNFi, or tofacitinib.

8.2.2. Exclusion Criteria

Patients meeting any of the following criteria were not included in the study:

1. Diagnosis with any autoimmune rheumatic disease except for PsA (eg, rheumatoid arthritis, ankylosing spondylitis).
2. Patients who have no visit data recorded within the sample window.
3. Patients who have missing start dates for IL17i, TNFi, or tofacitinib during the sample selection window.

8.2.3. Propensity Score Matching

Because of the observational nature of the data, analyses were repeated both in the overall population, as well as, in a propensity score matched population. Propensity score matching increases the comparability of the observed baseline characteristics in patients treated with tofacitinib and other bDMARDs. The propensity score is the conditional probability of receiving treatment (eg, tofacitinib versus TNFi or tofacitinib versus IL17i), which is estimated using logistic regression.

The following independent covariates were included as predictor variables in the propensity score:

- Patient age group at index:
  - 18-34;
  - 35-44;
  - 45-54;
  - 55-64;
  - 65-74;
  - >75.
- Sex:
  - Male;
  - Female.
- Disease Severity:
  - DAS28-ESR, DAS28-CRP, CDAI, SDAI or DAPSA*

*Note choice of measure depended on the availability of data.

- Select baseline treatments combinations (where baseline is the index date):
  - Methotrexate monotherapy;
  - Methotrexate + other conventional DMARD(s);
  - Conventional DMARD(S) other than methotrexate;
  - Neither methotrexate nor other conventional DMARD(s).

Tofacitinib users were matched to TNFi users based on their propensity score from the above model. In the initial instance, 2 matches for each tofacitinib patient were sought. If 2 matches could not be found for 80% of tofacitinib patients, the matching were repeated, seeking only 1 match for each tofacitinib patient. The use of a caliper width of 0.20 was the starting point and this was varied as needed.[5] For example, the caliper width could be increased if there were numerous tofacitinib patients for whom matches could not be found.

A second propensity score matching model matched tofacitinib users to IL17i users based on their propensity score from the above model. In the initial instance, 2 matches for each tofacitinib patient were sought. If 2 matches could not be found for 80% of tofacitinib patients, the matching were repeated, seeking only 1 match for each tofacitinib patient. The use of a caliper width of 0.20 was the starting point and this was varied as needed. For example, the caliper width could be increased if there are numerous tofacitinib patients for whom matches could not be found.

In the comparative secondary outcomes, regression adjustment were used to reduce bias due to residual differences (imbalance) in observed baseline covariates between the 2 treatment groups ie, those variables where a substantial difference still exists after matching will be included in any formal analyses as covariates.

Propensity score matching might not have been feasible for reasons such as insufficient sample size within treatment groups of interest or insufficient overlap between groups (a loss of 50% or more tofacitinib patients ie, there are zero appropriate matches found for over 50% of tofacitinib patients during the propensity score matching exercise). In this instance, only descriptive analyses would have been conducted rather than matching analyses.

Further information on the propensity score matching method is available in the Statistical Analysis Plan (SAP).

8.3. Variables

Table 1. Baseline and Outcome Variables

Variable	Role	Data Source(s) Operational Definition	Operational Definition
Patient Characteristics	Baseline Characteristic	OPAL	Age, sex and presence of comorbidities
Clinical Characteristics	Baseline Characteristic	OPAL	Disease duration, disease severity, disease activity (DAS28, SDAI, CDAI, Tender Joint Count (TJC), Swollen Joint Count (SJC) DAPSA, Disease Activity in PSoriatic Arthritis)
Patient Reported Outcomes	Baseline Characteristic Outcome	OPAL	General health HAQ-DI, HCRU, Visual Analogue Scale VAS pain, FACIT-fatigue
Treatment History	Baseline Characteristic, Potential Confounder	OPAL	Number, sequence and duration of previous DMARDs

Variable	Role	Data Source(s) Operational Definition	Operational Definition
Concomitant Therapy	Baseline Characteristic, Potential Confounder	OPAL	Type and dose of concomitant cDMARDs
Treatment Duration	Outcome		Duration of treatment of the index b/tsDMARD
Clinical Characteristics	Outcome	OPAL	Disease activity (DAS28, SDAI, CDAI, Tender Joint Count (TJC), Swollen Joint Count (SJC) DAPSA, Disease Activity in PSoriatic Arthritis)

*Detailed definitions are included in the SAP.

The following endpoints were looked at within the different treatment groups to characterise the type of patients being prescribed IL17i, TNFi or tofacitinib, and to determine how these treatments are being used in clinical practice.

8.3.1. Patient Characteristics

Baseline demographic characteristics of each patient were extracted based on data captured on the index date, or the closest measurements prior to the index date. These data include:

- Age, sex and baseline comorbidities.

8.3.2. Clinical Characteristics

Clinical characteristics of each patient include:

- Time since symptom onset at index.
- Disease severity:
  - DAS28-ESR/DAS28-CRP.
- Clinical Disease Activity Index (CDAI).
- Simple disease activity index (SDAI).
- DAPSA.
- Health assessment questionnaire for disease index (HAQ-DI).
- Health-care resource use questionnaire (HCRU).

- Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue)
- Baseline medication of interest:
  - NSAIDs/analgesics;
  - Corticosteroids;
  - Disease modifying antirheumatic drugs (DMARDs) *The number, sequence, and duration of previous DMARDs were collected. The duration of current bDMARD prior to the index date were collected. The number and dose of concurrent conventional DMARDs were also collected.*

8.3.3. Prior Biologic Treatment

Information on the number of prior bDMARD treatments will be summarised.

For the episodes of prior biologic treatment, the number falling into each of the following categories will be summarised:

- Combination – with methotrexate (MTX) and a cDMARD;
- Combination – with MTX only;
- Combination – with cDMARD only;
- Monotherapy.

8.3.4. Treatment Information

The number of patients prescribed the index DMARD in each treatment group were summarised together with information on length of follow-up. The following summaries were performed to assess the treatment patterns for patients in the IL17i, TNFi or tofacitinib treatment groups.

The dose of the index DMARD, line of use and concomitant cDMARD use were summarised at the index date.

The number and percentage of subjects in each treatment group falling into the following categories at the index date were summarized.

- Combination – with MTX and a cDMARD;
- Combination – with MTX only;
- Combination – with cDMARD only;

- Monotherapy.

The demographic characteristics of patients in each of the above categories were examined.

Duration of treatment of the index DMARD were summarised using Kaplan-Meier (KM) methods where subjects who had not discontinued were censored at the last available assessment. Additionally, for those who received monotherapy treatment at the index date, duration of monotherapy treatment (ie, until either a switch to combination therapy with the same index DMARD or until discontinuation of the index DMARD) were summarised.

Similarly, for those who received combination treatment at the index date, duration of combination treatment with the index DMARD were summarised.

Reasons for discontinuation were also summarised, overall, and by treatment combination (monotherapy, combination therapy).

8.3.5. Baseline

Baseline is defined as the measurements taken at the index date, or the closest measurement before the index date.

8.3.6. Outcomes

Analyses were presented for the overall population and for the propensity score match population.

8.3.6.1. Treatment Patterns

Treatment patterns for patients in the 'tofacitinib group' the 'TNFi group' and 'IL17i group' included line of usage, dose, frequency, and concomitant cDMARDs. Reasons for discontinuation were noted.

8.3.6.2. Clinical Effectiveness

Clinical effectiveness was assessed using disease severity (remission, low, moderate, high), DAS28, CDAI, SDAI and DAPSA scores. The proportion of patients reaching targeted treatment goals were reported.

8.3.6.3. Patient Reported Outcomes

Patient reported outcomes include the health assessment questionnaire for disease index (HAQ-DI) score, the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue) score, and the Health Care Resource Utilisation (HCRU) score.

8.4. Data Sources

All data for this study were obtained from the OPAL dataset. The OPAL – Quality Use of Medicines Initiative is a point of care observational dataset database.[3,4] Currently, approximately 104 Australian rheumatologists and more than 192,000 unique patients with

rheumatic disease are participating in the dataset. Participating rheumatologists use an electronic patient management program that captures patient- and disease-specific details during routine physician-patient consultations.

OPAL members are based largely in private practice; however, this is representative of the Australian rheumatology community. OPAL members run clinics and collect data from both urban and rural clinics.

Data are captured into individual clinician's servers during routine clinical consultations, using the purpose-built worksheets in the Audit4 software.3 Audit4 serves as the patient's medical record and produces the clinical correspondence for the consultation. Diagnoses are made by individual rheumatologists rather than being criteria based. Pathology and imaging reports are electronically transferred from the providers and incorporated into the patient's medical record.

The primary rheumatological condition and comorbidities are coded using the World Health Organisation (WHO) International Classification of Diseases 10 (ICD-10), and medications are mapped to the WHO Anatomical Therapeutic Chemical (classification) (ATC) System.

There are condition specific "clinical worksheets" such as a homunculus for tender and swollen joint counts, visual analogue scales and automatic calculation of DAS28 (Erythrocyte Sedimentation Rate (ESR) or C-reactive protein (CRP)).

Data de-identified for patient, clinic and clinician can be exported from each of the OPAL member's local server to a central server for analysis based on a predefined ethics-approved protocol.

8.5. Study Size

Sample size calculations are not applicable however, with 250 tofacitinib patients, proportions (eg, the proportion of first line users) can be estimated with a precision (ie, standard error of the estimate) of at worst ±7%. This is based on an estimated proportion of 50%. For lower or higher estimates the precision will be improved. (The size of the propensity score matched population of tofacitinib and IL17i /TNFi users may be smaller than this ie, if not all tofacitinib patients can be found matches).

8.6. Data Management

De-identified data were extracted from the OPAL database. Permission to extract the data from the individual clinician's Audit4 software was obtained 3 to 4 weeks prior to the data extraction.

The sample selection window was 01 May 2019 to 30 Sept 2020 and all patients with a bDMARD prescription, during this time, who meet the other eligibility criteria, were included in the extracted data set. A minimum of 1 year time period occurred for all sampled patients. Therefore, data up to 30 September 2021 are included in the study.

The number and percentage of missing values were included in the description of baseline characteristics. Missing values were be imputed.

The patterns and predictors of missing variables were explored for those covariates with 10% or greater missing values.

Analyses were conducted using the Stata Multiprocessor (MP) V14 (or higher), or equivalent statistical software.

8.7. Data Anlysis

Patients meeting the inclusion and exclusion criteria described in Section 8.2.1 and Section 8.2.3 were categorised into 1 of 2 mutually exclusive drug cohorts, based on the type of DMARD received:

- Tofacitinib;
- All bDMARDs.

Baseline has been defined in Section 8.3.5.

All continuous variables were summarised using n (non-missing sample size), mean, standard deviation, median, minimum and maximum. The frequency and percentages (based on the non-missing sample size) or observed levels were reported for all categorical measures.

Descriptive summaries were produced for each data cut, providing there was sufficient data available, and again at the final analysis.

All summaries are descriptive, and there was no comparative analyses undertakened. Therefore, no adjustments for multiple data cuts and multiple endpoints were required.

Patients who discontinued their index treatment (tofacitinib, TNFi or IL17i) were followed for a 1 year period.

Detailed methodology for summary and statistical analyses of data collected in this study are documented in a statistical analysis plan (SAP), which is dated, filed, and maintained by the sponsor. The SAP modified the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses are reflected in a protocol amendment.

8.7.1. Patient Demographics

Patient demographics were summarised descriptively. Data were presented, overall, and by treatment group (tofacitinib and bDMARD).

8.7.2. Treatment Patterns

The number of patients prescribed tofacitinib or another bDMARD were summarised. Information on length of follow-up (eg, mean, standard deviation, median, minimum, maximum) for the tofacitinib and bDMARD groups were calculated. Persistence to treatment was calculated. Further information can be found in the SAP.

8.7.3. Clinical Effectiveness

The following summaries were performed for patients in the tofacitinib treatment group. Summaries were performed at baseline, 3, 9, 15, and 24 months with change from baseline also summarised at each post-baseline time-point.

- DAS28;
- DAS28 change from baseline;
- CDAI;
- CDAI change from baseline;
- SDAI;
- SDAI change from baseline;
- DAPSA;
- DAPSA change from baseline;
- Number and % of patients reaching targeted treatment goals.

8.7.4. Patient Reported Outcomes

The following summaries were performed for patients in the tofacitinib treatment group. Summaries were performed at baseline, 3, 9, 15, and 24 months with change from baseline also summarised at each post-baseline time-point.

- HAQ-DI;
- HAQ-DI change from baseline;
- FACIT-Fatigue;
- FACIT-Fatigue change from baseline;
- HCRU;

- HCRU change from baseline.

8.8. Quality Control

The Audit4 software is used at the point of care, and as such is a source document. Thus the data that is provided by clinicians to OPAL is a subset of the data that is a legal document which the clinician must ensure is accurate. For chemical pathology results, Audit4 has an internal quality control and only accepts values in the database where there is a corresponding Logical Observation Identifiers Names and Codes (LOINC) code and matching units as provided in the Health Level Seven (HL7) message from the pathology provider service.

No additional formal quality control procedures were in place for OPAL.

8.9. Limitations of the Research Methods

This is a retrospective study based on data in the OPAL dataset. The analyses were therefore limited by the availability of data in this database. Data fields in the Audit4 software are not mandatory. So, it is likely to be missing data points. The sample size, variables, and study duration were selected to minimize the impact of this.

The Audit4 software records medically significant events, which are not necessarily serious adverse events (AE). Therefore, it was not be possible to stratify data into serious and non-serious AE.

The source data were subject to logic checks in the software programming, and individual clinicians were responsible for accurate data entry. Patient classifications were based solely on the physician's diagnosis.

The database only covered outpatient visits; inpatient visits were not included in this analysis.

9. PROTECTION OF HUMAN SUBJECTS

9.1. Patient Information

This study involved data that exist in anonymized structured format and contains no patient personal information.

9.2. Patient Consent

As this study involves anonymized structured data, which according to applicable legal requirements, do not contain data subject to privacy laws, obtaining informed consent from patients by Pfizer was not required.

9.3. Patient Withdrawal

Not applicable.

9.4. Institutional Review Board

(IRB)/Independent Ethics Committee (IEC) The activities of OPAL Rheumatology Ltd have received overarching ethics approval from University of New South Wales Human Research Ethics. There must be prospective approval of the study protocol, protocol amendments, and other relevant documents (eg, informed consent forms if applicable) from the relevant IRBs/IECs. All correspondence with the IRB/IEC must be retained. Copies of IRB/IEC approvals must be forwarded to Pfizer.

9.5. Ethical Conduct of the Study

The study was conducted in accordance with legal and regulatory requirements, as well as, with scientific purpose, value, and rigor, and follows generally accepted research practices described in Guidelines for Good Pharmacoepidemiology Practices (GPP) issued by the International Society for PharmacoEpidemiology (ISPE).[6]

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study involved data that exist as structured data from the time of study start, or a combination of existing structured data, and unstructured data, which were converted to structured form during the implementation of the protocol, solely, by a computer using automated/algorithmic methods, such as natural language processing.

From these data sources, individual patient data were not retrieved, or validated. Therefore, it was not possible to link (ie, identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (AE) (ie, identifiable patient, identifiable reporter, a suspect product, and event) could not be met.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

This protocol was registered on the Register of Post-Authorisation Studies. A clinical study report of all results was generated, and results of this study will be submitted to a peer-reviewed journal. Authorship of the manuscript is based on International Committee of Medical Journal Editors (ICMJE) criteria.

There was no event of any prohibition or restriction imposed (eg, clinical hold) by an applicable competent authority in any area of the world. Nor was the investigator aware of any new information that might have influenced the evaluation of the benefits and risks of a Pfizer product.

12. OTHER ASPECTS

Not applicable.

13. AMENDMENTS AND UPDATES

14. RESEARCH METHODS

15. RESULTS

Pfizer NIS Protocol A3921398 (TOPsA) FINAL ANALYSIS TABLES AND FIGURES
Version 1.0 FINAL dated 21 Mar 2022

Real-world evaluation of effectiveness, persistence and usage patterns of tofacitinib in treatment of psoriatic arthritis in Australia

INTRODUCTION

CHANGES AND CLARIFICATIONS OF ANALYSIS METHODS

Full Analysis Set (All Eligible Patients) At this final analysis the primary focus is on the Full Analysis Set (FAS) population, that is, those meeting the eligibility criteria with a minimum of 12 months follow-up after the index date as defined in the SAP. Following team discussion, the follow-up definition has been clarified to be the time elapsed from the index date to the date of data extraction. Therefore, at this final analysis this includes all eligible patients (i.e. meeting the other inclusion and exclusion) since the end of the sample selection window (30 Sept 2020) was 12 months from the date of the data cut for this analysis (extracted on 11 Oct 2021). Note that outcomes data is not available for all of these patients across the 12-month follow-up period as not all patients had visits at or after 12 months. The extent of post-index information (ie. the time from the index date to the latest visit post-index) is shown in Table 0 (Disposition).

Enrichment of Tofacitinib Group: the SAP stated that if the patient has been prescribed more than one of the drugs of interest (ie, IL-17Ai, TNFi, or tofacitinib) during the sample selection window, the index DMARD was designated as tofacitinib (if received) or the first prescription of a new IL-17Ai or TNFi within the sample selection window if the patient had never received tofacitinib. This was done to maximise the amount of tofacitinib data included. Around 9% of eligible patients (82/905) assigned to the tofacitinib group had started another bDMARD of interest earlier in the sample section window. It should be noted that this enrichment increased the number of later line patients in the tofacitinib group. This enrichment of the tofacitinib group would also tend to increase the proportion of later line patients in the IL-17Ai/TNFi groups, as their earlier line of treatment with a IL17Ai/TNFi would not be selected as the index bDMARD. Within the tofacitinib group, the discontinuation rate was lower in patients receiving tofacitinib as their first ts/bDMARD in the window compared to those receiving tofacitinib later in the window, again probably reflecting the difference in line of treatment between the two groups. Among those who discontinued there were slightly lower proportions who discontinued due to adverse reaction (approximately 15% vs 28%), and completion of treatment/no longer required (18% vs 22%) but similar rates due to reasons related to lack of efficacy between those receiving tofacitinib as their first ts/bDMARD in the window compared to those receiving it later in the window.

It should be noted that the reasons that could be selected for treatment discontinuation evolved over time and this could influence these observed differences.

Other Group: patients on bDMARDs other than tofacitinib, IL-17Ai or TNFi were planned to be included. However, there were too few patients (n=59) on other bDMARDs who were eligible. Therefore, this group is only included in Table 0 (Disposition).

Data at Index Date: not all patients have a visit at or around the Index date (ie, the initiation of the new bDMARD). This was not an inclusion criterion. /**Doses:** all doses in tables are as recorded in the 'mgdoseperday' field in the Doses dataset. Note that some medications are not given daily, however. Dose in follow-up is calculated as the average daily dose of all the dose records. .**Windows:** to include as much information as possible windows around timepoints have been extended so that all records in the follow-up period are assigned to a timepoint. For example, the index visit window is from -3 months to 1.5 months, the 3-month visit is from 1.5 months to 4.5 months and so on. Where multiple readings are present within a window those prior to Index are prioritised (Index only), followed by those closest to the nominal timepoint. All tables related to disease activity over time (i.e. Table 8A to 8G) are now presented by nominal timepoint and the time period has been extended to 15 months in this final analysis.

Concomitant Medical Conditions: if a condition had a missing onset date it was assumed that it started prior to the index date and hence was included as a condition at index unless a stop date was recorded prior to the index date.

DAS28-CRP(3): this variable was derived as:

(0.56*sqrt(tjc28)+0.28*sqrt(sjc28)+0.36*ln(CRP+1))*1.10+1.15

This measure was then included in summaries of disease activity at Index and during follow-up. Boundaries of categories for remission/low/high/very high were taken to be the same as DAS28-CRP (which included 4 domains including patient global score).

DAPSA: this variable was derived for the interim analysis. For the updated data cut this variable was included in the data extract. However, the patient global and pain scores used to derive this variable were scaled from 0 to 100 rather than 0 to 10. In addition, some patients had all components needed to derive the DAPSA present in the data cut, but no DAPSA was present. Therefore, the patient global and pain VAS scores were re-scaled by dividing by 10 and the DAPSA variable re-derived for all patients using the following formula:

tjc68+sjc66+CRP+patientglobal+patientpain

TJC68 and SJC66: these measures are now available in the data cut and have been added to relevant tables (Tables 2, 5, 8).

Skin Assessments: physician and patient skin assessments are now available in the data cut and therefore these variables have been added to relevant tables (Tables 2, 5 and 8).

Subgroups: KM plots for additional subgroups of first line, second line, third or higher line and the combinations of first/second line and mono/combo subgroups have been added for this final analysis. Monotherapy/Combination information: if a cDMARD had missing start date, if the stop date was after a timepoint/follow-up period or if no stop date was provided, then that cDMARD was assumed to be being taken at that timepoint/follow-up period. If a cDMARD was taken at any point during a follow-up period, then that was included in the combination being used in that follow-up period. A patient was assumed to be on monotherapy at a timepoint or during a follow-up period if there was no record of a cDMARD being taken at that timepoint or during that follow-up period. Monotherapy/combination status during follow-up is only included while the patient is on their index treatment, and if no stop date for the index treatment is recorded, only up to a patient's last visit. At the interim analysis only data from the Medications dataset was used. For this final analysis this has been supplemented with information from the MedicationDoses dataset.

Sankey Plot: a Sankey plot has been added to show the flow between monotherapy and combination therapy during index bDMARD treatment for all eligible patients.

Treatment Duration: in the interim analysis, duration of treatment was defined as the date of last dose - index date. To reflect the fact that the treatment was taken on the date of last dose, duration of treatment is now defined as date of last dose - index date + 1. Similarly, the censoring date for patients not known to have discontinued is now defined as date of last visit - indexdate + 1.

Propensity Score modelling and matching: some updates were made to the SAP specified methods and to the methods used for the interim analysis. See below section for more information.

DETAILS ON CONSTRUCTION OF MATCHED POPULATIONS

Because of the observational nature of the data, matched analysis sets (also referred to as propensity score matched populations) were constructed. Propensity score matching increases the comparability of the observed baseline characteristics in patients treated with tofacitinib and other bDMARDs. The propensity score is the conditional probability of receiving treatment (eg, tofacitinib versus IL-17Ai or tofacitinib vs TNFi), which is estimated using logistic regression.

At this final cut all eligible patients were used in the matching process.

Propensity Score Model covariates: According to the SAP, age group at index, sex, treatment combination at Index and disease severity measures were to be considered for inclusion in the propensity score model, with the choice of disease severity measure (DAS28-

ESR, DAS28-CRP, CDAI, SDAI or DAPSA) to be made depending on availability of data. Although not mentioned in the SAP, DAS28-CRP(3) was also considered. However, less than 50% of patients had data available for each disease severity measure (see below table) so it was not possible to include any of these measures. Although also not in the SAP, line of therapy and time from diagnosis (i.e., time from first seen) were considered to be important variables. Time from first seen was only available for around a third of patients so this could not be included. Line of therapy was observed to be unbalanced between the tofacitinib group and each other group. At the interim analysis a categorical variable for line (first vs second or greater) was added to the propensity score model. However, the matched populations were still unbalanced in terms of second line treatment. Therefore, for this final analysis a categorical variable for line with three levels (First vs Second vs Third or greater) was used in the model. Although time from first seen and DAS-CRP3 (the disease activity variable available for the most patients at baseline) could not be fitted to the propensity score model the impact of the matching on balance between groups for these variables was also assessed.

PS Matching - potential covariates, number of patients with non-missing values in FAS

	Total	Tofacitinib	IL-17Ai	TNFi
	1,486	406	416	664
Age Category at Index (Years)	1,486	406	416	664
Gender Combination Information	1,474 1,486	406 406	410 416	658 664
Line	1,486	406	416	664
Time since first seen(months)	482	139	141	202
DAS28CRP	291	66	80	145
DAS28CRP(3)	638	171	174	293
DAS28ESR	287	65	78	144
CDAI	289	61	82	146
SDAI	281	61	78	142

The final propensity score model included age category, sex, treatment combination at Index and line of therapy (First vs Second vs Third or greater). Treatment combination at index (4 levels) and age category (6 levels) were included using indicator variables.

Matching Process: Tofacitinib users were matched to TNFi users based on their propensity score from the above model. In the SAP it stated that in the initial instance two matches for each tofacitinib patient were to be sought. However, given that there were less than twice as many TNFi or IL17Ai users as tofacitinib users only one match was sought. A caliper width of 0.20 resulted in most (>60%) of tofacitinib patients having a match selected for both matched populations and hence this caliper width was not varied.

Missing Values on Covariates: Unfortunately, most patients were missing all measures of disease severity at Index and therefore the SAP-specified processes around using both DAS28-CRP and DAS-28ESR to minimise the overall level of missingness could not be employed. The impact of matching on the standardised bias of DAS28-CRP(3) between groups (the measure with the least missing data) was assessed for the patients with this measure recorded alongside the covariates included in the PS models.

Evaluation of the Success of Matching Process: The success of the matching was determined by examining the propensity score distribution (density plot) in both the original sample and the matched sample, and by comparing standardized difference (in means and proportions) between the matched groups. A difference above 10% (0.1) is generally considered indicative of substantial difference/bias in that covariate. The below results tables and graphs indicate that the matching process was a success as the standardized differences were generally reduced to below 10%, with the exception of age category where the matching actually increased imbalances between the numbers in each category. However, the age category was not significant in the propensity score model, and hence was not as important in determining which treatment was received, as line or sex.

Success of Matching: Tofacitinib with IL-17Ai Patients

The below table shows the logistic regression output for the propensity score model. Line category and sex were highly significant predictors of treatment choice. Some younger age categories (compared to the 18-34 year old category) and combination categories (compared to the "Methotrexate plus Other cDMARD" category) were not significant but are retained in the model as these were prespecified covariate.

16. LIST OF SOURCE TABLES AND FIGURES

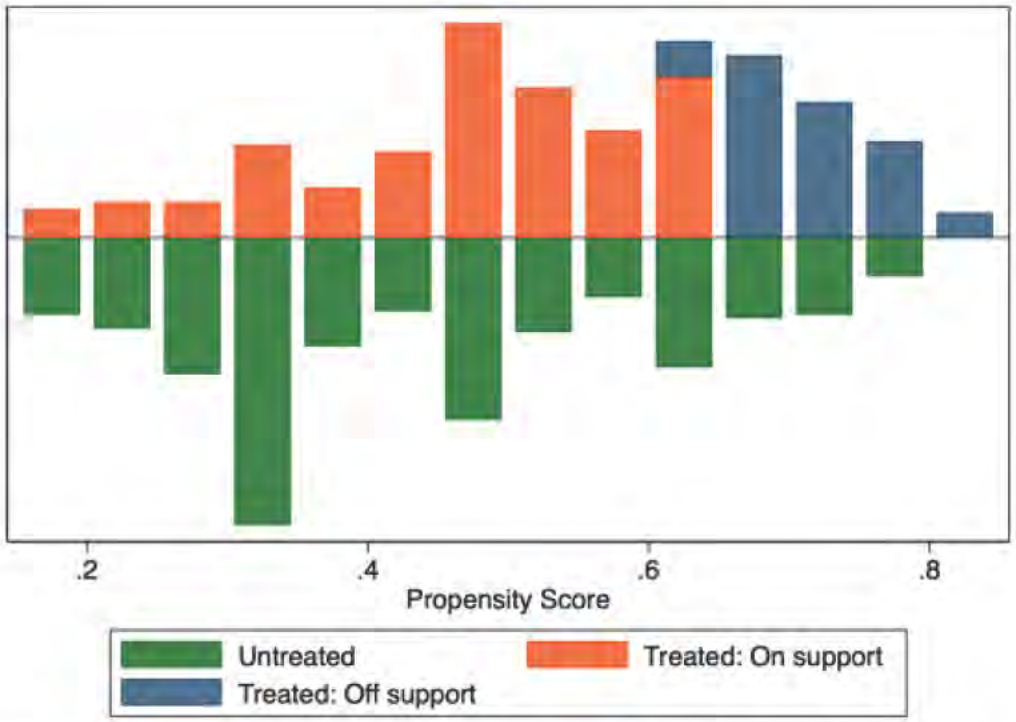
PS Matching - Propensity Score Model Tofacitinib/IL17Ai

Covariates	Estimate	Se	Ci	Pvalue
Age: 35 to 44 yrs	0.1071	0.3350	(-0.5496,0.7637)	0.7493
Age: 45 to 54 yrs	0.2422	0.3051	(-0.3558,0.8402)	0.4273
Age: 55 to 64 yrs	0.4026	0.3053	(-0.1958,1.0009)	0.1873

Age: 65 to 74 yrs	0.7224	0.3256	(0.0843,1.3605)	0.0265
Age:75 to 94 yrs	1.0074	0.4362	(0.1525,1.8624)	0.0209
Sex Combo: Methotrexate Only	0.6188 0.0448	0.1631 0.2084	(0.2991,0.9385) (-0.3637,0.4533)	0.0001 0.8298
Combo: Other cDMARD	0.0196	0.2440	(-0.4586,0.4978)	0.9361
Combo: Monotherapy	-0.0886	0.1925	(-0.4659,0.2888)	0.6455
Line 2	0.6387	0.1990	(0.2486,1.0289)	0.0013
Line 3 Plus	1.4126	0.1845	(1.0511,1.7742)	0.0000
Constant	-2.1988	0.4231	(-3.0281,-1.3694)	0.0000

Combination categories compared to Methotrexate plus Other category, Age categories compared to 18-34 year old category, Line categories compared to Line1.

The below graph shows the distribution of propensity scores for "Treated" (ie, Tofacitinib) vs "Untreated" (i.e. IL-17Ai) patients. For lower values of the propensity score there were sufficient IL-17Ai patients to make good matches. However, for higher values the "Treated" patients were "Off support" meaning that there were insufficient IL-17Ai patients with these values to select good matches based on the propensity
score.



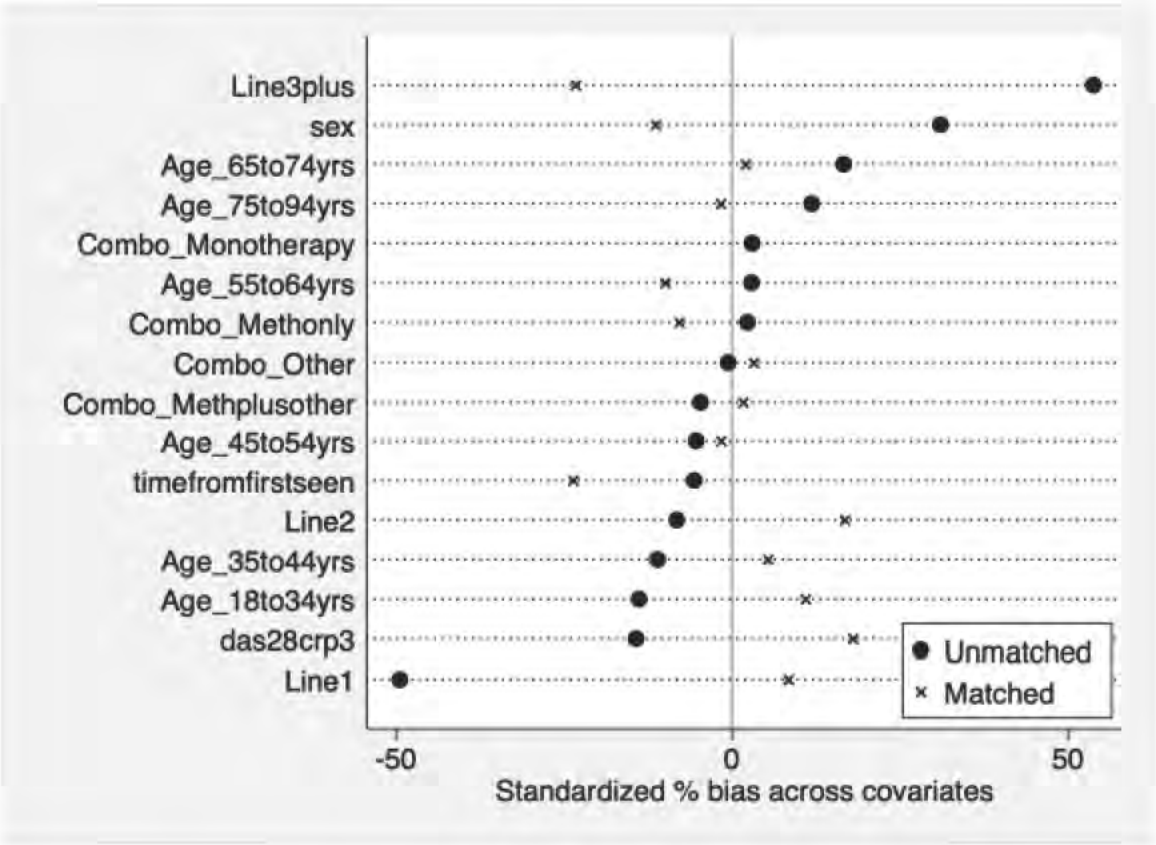
To further investigate the types of tofacitinib patients for whom good matches could not be found, the below table compares the covariate values for matched and unmatched tofacitinib patients. Unmatched patients were female or unassigned, tended to be older and were less likely to be on bDMARD monotherapy. The overwhelming majority of unmatched tofacitinib patient were on their third or greater line of treatment. Time since first seen was slightly higher in unmatched tofacitinib patients.

PS Matching - Comparison of Matched and Unmatched Tofacitinib Patients

Factor	Unmatched	Matched	P-value
N	137	269	
Age Category at Index (Years)			<0.001
18-34 years	1 (0.7%)	25 (9.3%)	
35-44 years	0 (0.0%)	50 (18.6%)	
45-54 years	43 (31.4%)	66 (24.5%)	
55-64 years	47 (34.3%)	67 (24.9%)	

65-74 years	33 (24.1%)	49 (18.2%)	
75-94 years	13 (9.5%)	12 (4.5%)	
Gender			<0.001
Female	133 (97.1%)	173 (64.3%)	
Male	0 (0.0%)	96 (35.7%)	
Unassigned	4 (2.9%)	0 (0.0%)	
Combination Information			0.55
With Meth + Other cDMARD	43 (31.4%)	70 (26.0%)	
With Methotrexate Only	34 (24.8%)	63 (23.4%)	
With Other cDMARD	16 (11.7%)	41 (15.2%)	
bDMARD Monotherapy	44 (32.1%)	95 (35.3%)	
Line			<0.001
First	1 (0.7%)	77 (28.6%)	
Second	2 (1.5%)	99 (36.8%)	
>=Third	134 (97.8%)	93 (34.6%)	
DAS28CRP(3), mean (SD)	2.9 (1.3) (n=59)	3.5 (1.4) (n=112)	0.003
Time Since First Seen(Months), Mean (SD)	75.2 (40.6) (n=47)	62.1 (69.6) (n=92)	0.23

The below figure and table show the characteristics of the groups before and after matching. Overall, the matching did make the groups more comparable, however some differences in age remained, particularly in the younger age categories. However, these younger age categories were not significant in the propensity score model, and therefore these issues were not considered to unduly affect the success of the matching process. Although not included in the propensity score modelling, the matching did not seem to majorly impact the comparability of DAS28-CRP(3) between groups. However, the standardised bias increased for time from first seen after matching, although this measure was only available for a relatively small subset of patients.



PS Matching - Tofacitinib and IL17Ai Groups Before and After Matching

Factor	Tofacitinib, Before	IL-17Ai, Before	Tofacitinib, After	IL-17Ai, After
N	406	416	269	269
Age at Index (Years), Mean (SD)	55.6 (12.7) (n=406)	52.6 (12.7) (n=416)	53.3 (13.3) (n=269)	54.6 (12.7) (n=269)
Age Category at Index (Years)				
18 - 34 Years	26 (6.4%)	116 (17.5%)	25 (9.8%)	23 (9.0%)
35 - 44 Years	50 (12.3%)	115 (17.3%)	50 (19.5%)	40 (15.6%)
45 - 54 Years	109 (26.8%)	155 (23.3%)	64 (25.0%)	65 (25.4%)

Factor	Tofacitinib, Before	IL-17Ai, Before	Tofacitinib, After	IL-17Ai, After
55 - 64 Years	114 (28.1%)	160 (24.1%)	61 (23.8%)	67 (26.2%)
65 - 74 Years	82 (20.2%)	90 (13.6%)	42 (16.4%)	45 (17.6%)
75 - 94 Years	25 (6.2%)	28 (4.2%)	14 (5.5%)	16 (6.2%)
Sex				
Male	96 (23.9%)	222 (34.0%)	77 (30.1%)	64 (25.0%)
Female Combination Information	306 (76.1%)	430 (66.0%)	179 (69.9%)	192 (75.0%)
With Meth + Other cDMARD	113 (27.8%)	237 (35.7%)	76 (29.7%)	70 (27.3%)
With Methotrexate Only	97 (23.9%)	147 (22.1%)	59 (23.0%)	68 (26.6%)
With other cDMARD	57 (14.0%)	105 (15.8%)	50 (19.5%)	47 (18.4%)
bDMARD Monotherapy	139 (34.2%)	175 (26.4%)	71 (27.7%)	71 (27.7%)
Line				
First	78 (19.2%)	417 (62.8%)	77 (30.1%)	79 (30.9%)
Second	101 (24.9%)	145 (21.8%)	101 (39.5%)	82 (32.0%)
>=Third	227 (55.9%)	102 (15.4%)	78 (30.5%)	95 (37.1%)
DAS28CRP(3), Mean (SD)	3.3 (1.4) (n=171)	3.9 (1.5) (n=293)	3.5 (1.4) (n=106)	3.5 (1.4) (n=118)
DAS28CRP(3), Median (Range)	3.2 (1.3, 7.6) (n=171)	3.8 (1.3, 7.1) (n=293)	3.4 (1.3, 6.6) (n=106)	3.3 (1.4, 7.1) (n=118)
Time Since First Seen (Months), Mean (SD)	66.5 (61.5) (n=139)	46.4 (60.4) (n=202)	53.0 (58.8) (n=86)	54.2 (60.5) (n=86)

TABLE NUMBERING CONVENTION

As there were a number of populations and subgroups examined the following numbering convention has been implemented:

Overall tables:

- Table Xi : All Eligible patients
- Table Xii: Matched population (Tofacitinib/IL-17Ai)
- Table Xiii: Matched population (Tofacitinib/TNFi)

Subgroup tables are denoted by e.g., Xai (Monotherapy) and Xbi (Combination). Selected tables (Table 1, Table 2, Table 4 and the set under Table 6) are presented by Line and these are denoted by e.g., Xci (First Line) and Xdi (Second line or greater). Additional subgroups were explored for the KM plots and these are denoted e.g., Xei Second Line, Xfi Third Line, Xgi Monotherapy/First Line, Xhi Monotherapy/Second Line, Xii Combination/First Line, Xij Combination/Second Line

TABLES AND FIGURES

Section 0: Patient Disposition

Table 0 Patient Disposition

	Total	Tofacitinib	IL-17Ai	TNFi	Other
	N=219,812	N=1,071	N=668	N=2,978	N=1,693
Has PsA	16,692 (7.6%)	521 (48.6%)	523 (78.3%)	857 (28.8%)	93 (5.5%)
First prescription of any bDMARD/tsDMARD in selection window	1,994 (11.9%)	521 (100.0%)	523 (100.0%)	857 (100.0%)	93 (100.0%)
Aged Over 18 Years But Under 95 Years at Index	1,991 (99.8%)	521 (100.0%)	523 (100.0%)	854 (99.6%)	93 (100.0%)
Has Other Autoimmune Rheumatic Disease	316 (15.9%)	77 (14.8%)	63 (12.0%)	143 (16.7%)	33 (35.5%)
Has No Visit Data	110 (	31 (7.0%)	38 (8.3%)	40 (5.6%)	1 (1.7%)

Recorded Within Sample window	6.6%)				
Has Missing Start Dates For Any Trt of Interest in Selection Window	16 (1.0%)	7 (1.7%)	3 (0.7%)	6 (0.9%)	0 (0.0%)
Patient Died	4 (0.3%)	0 (0.0%)	3 (0.7%)	1 (0.2%)	0 (0.0%)
Eligible (Any bDMARD/tsDMARD)	1,545 (0.7%)	406 (37.9%)	416 (62.3%)	664 (22.3%)	59 (3.5%)
Pre-Index Information (Time From Earliest Visit to Index)					
0 to < 6 Months	308 (19.9%)	40 (9.9%)	99 (23.8%)	161 (24.2%)	8 (13.6%)
> = 6 to <12 Months	178 (11.5%)	27 (6.7%)	25 (6.0%)	118 (17.8%)	8 (13.6%)
> = 12 to <12 Months	231 (15.0%)	58 (14.3%)	56 (13.5%)	112 (16.9%)	5 (8.5%)
> = 24 Months	828 (53.6%)	281 (69.2%)	236 (56.7%)	273 (41.1%)	38 (64.4%)
Post-Index Information (Time from Index to Latest Visit)					
0 to <6 Months	238 (15.4%)	67 (16.5%)	65 (15.6%)	95 (14.3%)	11 (18.6%)
> = 6 to <12 Months	218 (14.1%)	64 (15.8%)	57 (13.7%)	90 (13.6%)	7 (11.9%)
> = 12 to <24 Months	865 (56.0%)	220 (54.2%)	239 (57.5%)	369 (55.6%)	37 (62.7%)
> = 24 Months	224	55 (13.5%)	55	110 (16.6%)	4 (6.8%)

	(14.5%)		(13.2%)		
Has Visit > = 12 Months Post-Index	1,089 (70.5%)	275 (67.7%)	294 (70.7%)	479 (72.1%)	41 (69.5%)

Percentages for each inc/exc criterion use patients who were eligible up to that point as denominator; percentages for eligibility use total N as denominator; percentages for pre/post index information use eligible patients as denominator. Other group includes those prescribed an alternative bDMARD, not included in Tofacitinib, IL-17Ai or TNFi groups Table 0ii Patient Disposition - Matched Population: Tofacitinib/IL-17Ai Groups

Table 0ii Patient Disposition - Matched Population: Tofacitinib/IL-17Ai Groups

	Total	Tofacitinib	IL-17Ai
	N=538	N=269	N=269
Eligible	538 (100.0%)	269 (100.0%)	269 (100.0%)
Pre-Index Information (Time from Earliest Visit to Index)			
0 to < 6 Months	76 (14.1%)	36 (13.4%)	40 (14.9%)
> = 6 to < 12 Months	39 (7.2%)	24 (8.9%)	15 (5.6%)
>=12 to < 24 Months	79 (14.7%)	47 (17.5%)	32 (11.9%)
> = 24 Months	344 (63.9%)	162 (60.2%)	182 (67.7%)
Post-Index Information (Time from Index to Latest Visit)			
0 to < 6 Months	93 (17.3%)	51 (19.0%)	42 (15.6%)
> = 6 to < 12 Months	81 (15.1%)	49 (18.2%)	32 (11.9%)
>=12 to < 24 Months	288 (53.5%)	135 (50.2%)	153 (56.9%)

> = 24 Months	76 (14.1%)	34 (12.6%)	42 (15.6%)
Has Visit >=12 Months Post-Index	364 (67.7%)	169 (62.8%)	195 (72.5%)

Percentages Calculated from the Total N in each Group

Table 0iii Patient Disposition - Matched Population: Tofacitinib/TNFi Groups

	Total	Tofacitinib	TNFi
	N=512	N=256	N=256
Eligible	512 (100.0%)	256 (100.0%)	256 (100.0%)
Pre-Index Information (Time from Earliest Visit to Index)			
0 to < 6 Months	72 (14.1%)	36 (14.1%)	36 (14.1%)
>=6 to < 12 Months	58 (11.3%)	22 (8.6%)	36 (14.1%)
>=12 to < 24 Months	81 (15.8%)	44 (17.2%)	37 (14.5%)
>=24 Months	301 (58.8%)	154 (60.2%)	147 (57.4%)
Post-Index Information (Time from Index to Latest Visit)			
0 to < 6 Months	89 (17.4%)	43 (16.8%)	46 (18.0%)
>=6 to < 12 Months	73 (14.3%)	46 (18.0%)	27 (10.5%)
>=12 to < 24 Months	269 (52.5%)	133 (52.0%)	136 (53.1%)
>=24 Months	81 (15.8%)	34 (13.3%)	47 (18.4%)
Has Visit >=12 Months Post-Index	350 (68.4%)	167 (65.2%)	183 (71.5%)

Percentages Calculated from the Total N in each Group

Section 1: Patient Demographics

Table 1i Demographics - All Eligible Patients

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
Age at index (years), mean (SD)	55.56 (12.68) (n=406)	52.65 (12.72) (n=416)	50.32 (14.57) (n=664)	52.40 (13.73) (n=1486)
Age at index (years), median (range)	56.00 (19.00, 93.00) (n=406)	53.00 (20.00, 79.00) (n=416)	51.00 (20.00, 83.00) (n=664)	53.00 (19.00, 93.00) (n=1486)
Age category at index (years)				
18-34 years	26 (6.4%)	43 (10.3%)	116 (17.5%)	185 (12.4%)
35-44 years	50 (12.3%)	69 (16.6%)	115 (17.3%)	234 (15.7%)
45-54 years	109 (26.8%)	120 (28.8%)	155 (23.3%)	384 (25.8%)
55-64 years	114 (28.1%)	111 (26.7%)	160 (24.1%)	385 (25.9%)
65-74 years	82 (20.2%)	58 (13.9%)	90 (13.6%)	230 (15.5%)
75-94 years	25 (6.2%)	15 (3.6%)	28 (4.2%)	68 (4.6%)
Gender				
Female	306 (75.4%)	254 (61.1%)	430 (64.8%)	990 (66.6%)
Male	96 (23.6%)	156 (37.5%)	222 (33.4%)	474 (31.9%)
Unassigned	4 (1.0%)	0 (0.0%)	6 (0.9%)	10 (0.7%)
0 (0.0%)	6 (1.4%)	6 (0.9%)	12 (0.8%)	
One or more co-morbid condition				
No	206 (50.7%)	195 (46.9%)	306 (46.1%)	707 (47.6%)

Yes	200 (49.3%)	221 (53.1%)	358 (53.9%)	779 (52.4%)
Heart disease				
Not reported	406 (100.0%)	416 (100.0%)	664 (100.0%)	1486 (100.0%)
Acute myocardial infarction				
Not reported	405 (99.8%)	415 (99.8%)	664 (100.0%)	1484 (99.9%)
Yes	1 (0.2%)	1 (0.2%)	0 (0.0%)	2 (0.1%)
Angina				
Not reported	406 (100.0%)	416 (100.0%)	664 (100.0%)	1486 (100.0%)
Certain complications following acute myocardial infarction				
Not reported	406 (100.0%)	416 (100.0%)	664 (100.0%)	1486 (100.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
Other acute ischemic heart disease				
Not reported	406 (100.0%)	416 (100.0%)	664 (100.0%)	1486 (100.0%)
Chronic ischaemic heart disease				
Not reported	395 (97.3%)	409 (98.3%)	656 (98.8%)	1460 (98.3%)
Yes	11 (2.7%)	7 (1.7%)	8 (1.2%)	26 (1.7%)
Hypertension				
Not reported	335 (82.5%)	347 (83.4%)	569 (85.7%)	1251 (84.2%)
Yes	71 (17.5%)	69 (16.6%)	95 (14.3%)	235 (15.8%)
Atrioventricular block				
Not reported	406 (100.0%)	416 (100.0%)	664 (100.0%)	1486 (100.0%)

Peripheral vascular disease				
Not reported	402 (99.0%)	413 (99.3%)	660 (99.4%)	1475 (99.3%)
Yes	4 (1.0%)	3 (0.7%)	4 (0.6%)	11 (0.7%)
Chronic obstructive pulmonary disease				
Not reported	401 (98.8%)	414 (99.5%)	661 (99.5%)	1476 (99.3%)
Yes	5 (1.2%)	2 (0.5%)	3 (0.5%)	10 (0.7%)
Diabetes mellitus				
Not reported	387 (95.3%)	393 (94.5%)	636 (95.8%)	1416 (95.3%)
Yes	19 (4.7%)	23 (5.5%)	28 (4.2%)	70 (4.7%)
Hyperlipidaemia				
Not reported	363 (89.4%)	389 (93.5%)	625 (94.1%)	1377 (92.7%)
Yes	43 (10.6%)	27 (6.5%)	39 (5.9%)	109 (7.3%)
Obesity				
Not reported	397 (97.8%)	402 (96.6%)	646 (97.3%)	1445 (97.2%)
Yes	9 (2.2%)	14 (3.4%)	18 (2.7%)	41 (2.8%)
Hiatal hernia				
Not reported	406 (100.0%)	414 (99.5%)	658 (99.1%)	1478 (99.5%)
Yes	0 (0.0%)	2 (0.5%)	6 (0.9%)	8 (0.5%)
Gastrooesophageal reflux disease				
Not reported	357 (87.9%)	370 (88.9%)	609 (91.7%)	1336 (89.9%)
Yes	49 (12.1%)	46 (11.1%)	55 (8.3%)	150 (10.1%)
Factor	Tofacitinib	IL-17Ai	TNFi	All

N	406	416	664	1486
Peptic ulcer disease				
Not reported	405 (99.8%)	413 (99.3%)	660 (99.4%)	1478 (99.5%)
Yes	1 (0.2%)	3 (0.7%)	4 (0.6%)	8 (0.5%)
Crohn's disease				
Not reported	401 (98.8%)	414 (99.5%)	656 (98.8%)	1471 (99.0%)
Yes	5 (1.2%)	2 (0.5%)	8 (1.2%)	15 (1.0%)
Ulcerative colitis				
Not reported	398 (98.0%)	415 (99.8%)	655 (98.6%)	1468 (98.8%)
Yes	8 (2.0%)	1 (0.2%)	9 (1.4%)	18 (1.2%)
Non-alcoholic fatty liver disease				
Not reported	396 (97.5%)	399 (95.9%)	637 (95.9%)	1432 (96.4%)
Yes	10 (2.5%)	17 (4.1%)	27 (4.1%)	54 (3.6%)
Any tumour				
Not reported	406 (100.0%)	416 (100.0%)	664 (100.0%)	1486 (100.0%)
Osteoporosis				
Not reported	404 (99.5%)	416 (100.0%)	662 (99.7%)	1482 (99.7%)
Yes	2 (0.5%)	0 (0.0%)	2 (0.3%)	4 (0.3%)
Iridocylitis (uveitis)				
Not reported	403 (99.3%)	413 (99.3%)	653 (98.3%)	1469 (98.9%)
Yes	3 (0.7%)	3 (0.7%)	11 (1.7%)	17 (1.1%)
Psoriasis				

Not reported	311 (76.6%)	283 (68.0%)	446 (67.2%)	1040 (70.0%)
Yes	95 (23.4%)	133 (32.0%)	218 (32.8%)	446 (30.0%)
Malignancy				
Not reported	355 (87.4%)	372 (89.4%)	596 (89.8%)	1323 (89.0%)
Yes	51 (12.6%)	44 (10.6%)	68 (10.2%)	163 (11.0%)

Table 1ii Demographics - Matched Population: Tofacitinib/IL-17Ai groups

Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
Age at index (years), mean (SD)	53.25 (13.31) (n=269)	54.64 (12.67) (n=269)	53.95 (13.00) (n=538)
Age at index (years), median (range)	53.00 (19.00, 93.00) (n=269)	55.00 (23.00, 79.00) (n=269)	54.00 (19.00, 93.00) (n=538)
Age category at index (years)			
18-34 years	25 (9.3%)	17 (6.3%)	42 (7.8%)
35-44 years	50 (18.6%)	45 (16.7%)	95 (17.7%)
45-54 years	66 (24.5%)	68 (25.3%)	134 (24.9%)
55-64 years	67 (24.9%)	79 (29.4%)	146 (27.1%)
65-74 years	49 (18.2%)	47 (17.5%)	96 (17.8%)
75-94 years	12 (4.5%)	13 (4.8%)	25 (4.6%)
Gender			
Female	173 (64.3%)	187 (69.5%)	360 (66.9%)
Male	96 (35.7%)	82 (30.5%)	178 (33.1%)
One or more co-morbid condition			

No	128 (47.6%)	129 (48.0%)	257 (47.8%)
Yes	141 (52.4%)	140 (52.0%)	281 (52.2%)
Heart disease			
Not reported	269 (100.0%)	269 (100.0%)	538 (100.0%)
Acute myocardial infarction			
Not reported	268 (99.6%)	268 (99.6%)	536 (99.6%)
Yes	1 (0.4%)	1 (0.4%)	2 (0.4%)
Angina			
Not reported	269 (100.0%)	269 (100.0%)	538 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	269 (100.0%)	269 (100.0%)	538 (100.0%)
Other acute ischemic heart disease			
Not reported	269 (100.0%)	269 (100.0%)	538 (100.0%)
Chronic ischaemic heart disease			
Not reported	261 (97.0%)	264 (98.1%)	525 (97.6%)
Yes	8 (3.0%)	5 (1.9%)	13 (2.4%)
Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
Hypertension			
Not reported	217 (80.7%)	219 (81.4%)	436 (81.0%)
Yes	52 (19.3%)	50 (18.6%)	102 (19.0%)
Atrioventricular block			

Not reported	269 (100.0%)	269 (100.0%)	538 (100.0%)
Peripheral vascular disease			
Not reported	268 (99.6%)	267 (99.3%)	535 (99.4%)
Yes	1 (0.4%)	2 (0.7%)	3 (0.6%)
Chronic obstructive pulmonary disease			
Not reported	266 (98.9%)	268 (99.6%)	534 (99.3%)
Yes	3 (1.1%)	1 (0.4%)	4 (0.7%)
Diabetes mellitus			
Not reported	259 (96.3%)	252 (93.7%)	511 (95.0%)
Yes	10 (3.7%)	17 (6.3%)	27 (5.0%)
Hyperlipidaemia			
Not reported	241 (89.6%)	254 (94.4%)	495 (92.0%)
Yes	28 (10.4%)	15 (5.6%)	43 (8.0%)
Obesity			
Not reported	264 (98.1%)	259 (96.3%)	523 (97.2%)
Yes	5 (1.9%)	10 (3.7%)	15 (2.8%)
Hiatal hernia			
Not reported	269 (100.0%)	267 (99.3%)	536 (99.6%)
Yes	0 (0.0%)	2 (0.7%)	2 (0.4%)
Gastrooesophageal reflux disease			
Not reported	235 (87.4%)	240 (89.2%)	475 (88.3%)
Yes	34 (12.6%)	29 (10.8%)	63 (11.7%)

Peptic ulcer disease			
Not reported	268 (99.6%)	268 (99.6%)	536 (99.6%)
Yes	1 (0.4%)	1 (0.4%)	2 (0.4%)
Crohn's disease			
Not reported	265 (98.5%)	267 (99.3%)	532 (98.9%)
Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
Yes	4 (1.5%)	2 (0.7%)	6 (1.1%)
Ulcerative colitis			
Not reported	265 (98.5%)	268 (99.6%)	533 (99.1%)
Yes	4 (1.5%)	1 (0.4%)	5 (0.9%)
Non-alcoholic fatty liver disease			
Not reported	264 (98.1%)	260 (96.7%)	524 (97.4%)
Yes	5 (1.9%)	9 (3.3%)	14 (2.6%)
Any tumour			
Not reported	269 (100.0%)	269 (100.0%)	538 (100.0%)
Osteoporosis			
Not reported	267 (99.3%)	269 (100.0%)	536 (99.6%)
Yes	2 (0.7%)	0 (0.0%)	2 (0.4%)
Iridocylitis (uveitis)			
Not reported	266 (98.9%)	268 (99.6%)	534 (99.3%)
Yes	3 (1.1%)	1 (0.4%)	4 (0.7%)

Psoriasis			
Not reported	205 (76.2%)	196 (72.9%)	401 (74.5%)
Yes	64 (23.8%)	73 (27.1%)	137 (25.5%)
Malignancy			
Not reported	234 (87.0%)	234 (87.0%)	468 (87.0%)
Yes	35 (13.0%)	35 (13.0%)	70 (13.0%)

Table 1iii Demographics - Matched Population: Tofacitinib/TNFi groups

Factor	Tofacitinib	TNFi	All
N	256	256	512
Age at index (years), mean (SD)	53.04 (13.55) (n=256)	53.88 (13.70) (n=256)	53.46 (13.62) (n=512)
Age at index (years), median (range)	53.00 (19.00, 93.00) (n=256)	54.50 (24.00, 81.00) (n=256)	53.00 (19.00, 93.00) (n=512)
Age category at index (years)			
18-34 years	25 (9.8%)	23 (9.0%)	48 (9.4%)
35-44 years	50 (19.5%)	40 (15.6%)	90 (17.6%)
45-54 years	64 (25.0%)	65 (25.4%)	129 (25.2%)
55-64 years	61 (23.8%)	67 (26.2%)	128 (25.0%)
65-74 years	42 (16.4%)	45 (17.6%)	87 (17.0%)
75-94 years	14 (5.5%)	16 (6.2%)	30 (5.9%)
Gender			
Female	179 (69.9%)	192 (75.0%)	371 (72.5%)

Male	77 (30.1%)	64 (25.0%)	141 (27.5%)
One or more co-morbid condition			
No	131 (51.2%)	120 (46.9%)	251 (49.0%)
Yes	125 (48.8%)	136 (53.1%)	261 (51.0%)
Heart disease			
Not reported	256 (100.0%)	256 (100.0%)	512 (100.0%)
Acute myocardial infarction			
Not reported	255 (99.6%)	256 (100.0%)	511 (99.8%)
Yes	1 (0.4%)	0 (0.0%)	1 (0.2%)
Angina			
Not reported	256 (100.0%)	256 (100.0%)	512 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	256 (100.0%)	256 (100.0%)	512 (100.0%)
Other acute ischemic heart disease			
Not reported	256 (100.0%)	256 (100.0%)	512 (100.0%)
Chronic ischaemic heart disease			
Not reported	252 (98.4%)	251 (98.0%)	503 (98.2%)
Yes	4 (1.6%)	5 (2.0%)	9 (1.8%)
Factor	Tofacitinib	TNFi	All
N	256	256	512
Hypertension			
Not reported	209 (81.6%)	214 (83.6%)	423 (82.6%)

Yes	47 (18.4%)	42 (16.4%)	89 (17.4%)
Atrioventricular block			
Not reported	256 (100.0%)	256 (100.0%)	512 (100.0%)
Peripheral vascular disease			
Not reported	254 (99.2%)	253 (98.8%)	507 (99.0%)
Yes	2 (0.8%)	3 (1.2%)	5 (1.0%)
Chronic obstructive pulmonary disease			
Not reported	254 (99.2%)	256 (100.0%)	510 (99.6%)
Yes	2 (0.8%)	0 (0.0%)	2 (0.4%)
Diabetes mellitus			
Not reported	246 (96.1%)	245 (95.7%)	491 (95.9%)
Yes	10 (3.9%)	11 (4.3%)	21 (4.1%)
Hyperlipidaemia			
Not reported	233 (91.0%)	234 (91.4%)	467 (91.2%)
Yes	23 (9.0%)	22 (8.6%)	45 (8.8%)
Obesity			
Not reported	252 (98.4%)	249 (97.3%)	501 (97.9%)
Yes	4 (1.6%)	7 (2.7%)	11 (2.1%)
Hiatal hernia			
Not reported	256 (100.0%)	254 (99.2%)	510 (99.6%)
Yes	0 (0.0%)	2 (0.8%)	2 (0.4%)
Gastrooesaphogeal reflux disease			

Not reported	227 (88.7%)	230 (89.8%)	457 (89.3%)
Yes	29 (11.3%)	26 (10.2%)	55 (10.7%)
Peptic ulcer disease			
Not reported	255 (99.6%)	256 (100.0%)	511 (99.8%)
Yes	1 (0.4%)	0 (0.0%)	1 (0.2%)
Crohn's disease			
Not reported	252 (98.4%)	250 (97.7%)	502 (98.0%)
Factor	Tofacitinib	TNFi	All
N	256	256	512
Yes	4 (1.6%)	6 (2.3%)	10 (2.0%)
Ulcerative colitis			
Not reported	253 (98.8%)	254 (99.2%)	507 (99.0%)
Yes	3 (1.2%)	2 (0.8%)	5 (1.0%)
Non-alcoholic fatty liver disease			
Not reported	253 (98.8%)	245 (95.7%)	498 (97.3%)
Yes	3 (1.2%)	11 (4.3%)	14 (2.7%)
Any tumour			
Not reported	256 (100.0%)	256 (100.0%)	512 (100.0%)
Osteoporosis			
Not reported	254 (99.2%)	254 (99.2%)	508 (99.2%)
Yes	2 (0.8%)	2 (0.8%)	4 (0.8%)
Iridocylitis (uveitis)			

Not reported	254 (99.2%)	252 (98.4%)	506 (98.8%)
Yes	2 (0.8%)	4 (1.6%)	6 (1.2%)
Psoriasis			
Not reported	200 (78.1%)	182 (71.1%)	382 (74.6%)
Yes	56 (21.9%)	74 (28.9%)	130 (25.4%)
Malignancy			
Not reported	227 (88.7%)	230 (89.8%)	457 (89.3%)
Yes	29 (11.3%)	26 (10.2%)	55 (10.7%)

Table 1ai Demographics - All Eligible patients , Subgroup: Monotherapy

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
Age at index (years), mean (SD)	55.27 (12.63) (n=139)	53.69 (13.24) (n=137)	49.26 (15.50) (n=175)	52.46 (14.20) (n=451)
Age at index (years), median (range)	56.00 (27.00, 93.00) (n=139)	54.00 (23.00, 79.00) (n=137)	48.00 (20.00, 83.00) (n=175)	52.00 (20.00, 93.00) (n=451)
Age category at index (years)				
18-34 years	10 (7.2%)	10 (7.3%)	36 (20.6%)	56 (12.4%)
35-44 years	12 (8.6%)	30 (21.9%)	31 (17.7%)	73 (16.2%)
45-54 years	43 (30.9%)	35 (25.5%)	43 (24.6%)	121 (26.8%)
55-64 years	41 (29.5%)	30 (21.9%)	36 (20.6%)	107 (23.7%)

65-74 years	25 (18.0%)	23 (16.8%)	15 (8.6%)	63 (14.0%)
75-94 years	8 (5.8%)	9 (6.6%)	14 (8.0%)	31 (6.9%)
Gender				
Female	101 (72.7%)	78 (56.9%)	108 (61.7%)	287 (63.6%)
Male	36 (25.9%)	56 (40.9%)	61 (34.9%)	153 (33.9%)
Unassigned	2 (1.4%)	0 (0.0%)	3 (1.7%)	5 (1.1%)
0 (0.0%)	3 (2.2%)	3 (1.7%)	6 (1.3%)	
One or more co-morbid condition				
No	59 (42.4%)	52 (38.0%)	85 (48.6%)	196 (43.5%)
Yes	80 (57.6%)	85 (62.0%)	90 (51.4%)	255 (56.5%)
Heart disease				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Acute myocardial infarction				
Not reported	139 (100.0%)	136 (99.3%)	175 (100.0%)	450 (99.8%)
Yes	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.2%)
Angina				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Certain complications following acute myocardial infarction				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Other acute ischemic heart disease				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All

N	139	137	175	451
Chronic ischaemic heart disease				
Not reported	136 (97.8%)	133 (97.1%)	172 (98.3%)	441 (97.8%)
Yes	3 (2.2%)	4 (2.9%)	3 (1.7%)	10 (2.2%)
Hypertension				
Not reported	114 (82.0%)	106 (77.4%)	152 (86.9%)	372 (82.5%)
Yes	25 (18.0%)	31 (22.6%)	23 (13.1%)	79 (17.5%)
Atrioventricular block				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Peripheral vascular disease				
Not reported	139 (100.0%)	136 (99.3%)	174 (99.4%)	449 (99.6%)
Yes	0 (0.0%)	1 (0.7%)	1 (0.6%)	2 (0.4%)
Chronic obstructive pulmonary disease				
Not reported	138 (99.3%)	136 (99.3%)	175 (100.0%)	449 (99.6%)
Yes	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (0.4%)
Diabetes mellitus				
Not reported	131 (94.2%)	129 (94.2%)	168 (96.0%)	428 (94.9%)
Yes	8 (5.8%)	8 (5.8%)	7 (4.0%)	23 (5.1%)
Hyperlipidaemia				
Not reported	118 (84.9%)	125 (91.2%)	164 (93.7%)	407 (90.2%)
Yes	21 (15.1%)	12 (8.8%)	11 (6.3%)	44 (9.8%)
Obesity				

Not reported	133 (95.7%)	133 (97.1%)	169 (96.6%)	435 (96.5%)
Yes	6 (4.3%)	4 (2.9%)	6 (3.4%)	16 (3.5%)
Hiatal hernia				
Not reported	139 (100.0%)	137 (100.0%)	174 (99.4%)	450 (99.8%)
Yes	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.2%)
Gastrooesophageal reflux disease				
Not reported	116 (83.5%)	118 (86.1%)	157 (89.7%)	391 (86.7%)
Yes	23 (16.5%)	19 (13.9%)	18 (10.3%)	60 (13.3%)
Peptic ulcer disease				
Not reported	139 (100.0%)	137 (100.0%)	174 (99.4%)	450 (99.8%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
Yes	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.2%)
Crohn's disease				
Not reported	138 (99.3%)	136 (99.3%)	174 (99.4%)	448 (99.3%)
Yes	1 (0.7%)	1 (0.7%)	1 (0.6%)	3 (0.7%)
Ulcerative colitis				
Not reported	136 (97.8%)	136 (99.3%)	174 (99.4%)	446 (98.9%)
Yes	3 (2.2%)	1 (0.7%)	1 (0.6%)	5 (1.1%)
Non-alcoholic fatty liver disease				
Not reported	132 (95.0%)	126 (92.0%)	170 (97.1%)	428 (94.9%)
Yes	7 (5.0%)	11 (8.0%)	5 (2.9%)	23 (5.1%)

Any tumour				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Osteoporosis				
Not reported	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)
Iridocylitis (uveitis)				
Not reported	138 (99.3%)	136 (99.3%)	175 (100.0%)	449 (99.6%)
Yes	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (0.4%)
Psoriasis				
Not reported	99 (71.2%)	91 (66.4%)	122 (69.7%)	312 (69.2%)
Yes	40 (28.8%)	46 (33.6%)	53 (30.3%)	139 (30.8%)
Malignancy				
Not reported	118 (84.9%)	125 (91.2%)	153 (87.4%)	396 (87.8%)
Yes	21 (15.1%)	12 (8.8%)	22 (12.6%)	55 (12.2%)

Table 1aii Demographics - Matched Population: Tofacitinib/IL-17Ai groups , Subgroup: Monotherapy

Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
Age at index (years), mean (SD)	53.24 (13.19) (n=95)	55.84 (12.72) (n=91)	54.51 (12.99) (n=186)
Age at index (years), median (range)	52.00 (27.00, 93.00) (n=95)	56.00 (23.00, 79.00) (n=91)	54.00 (23.00, 93.00) (n=186)

Age category at index (years)			
18-34 years	9 (9.5%)	4 (4.4%)	13 (7.0%)
35-44 years	12 (12.6%)	15 (16.5%)	27 (14.5%)
45-54 years	32 (33.7%)	24 (26.4%)	56 (30.1%)
55-64 years	23 (24.2%)	24 (26.4%)	47 (25.3%)
65-74 years	15 (15.8%)	16 (17.6%)	31 (16.7%)
75-94 years	4 (4.2%)	8 (8.8%)	12 (6.5%)
Gender			
Female	59 (62.1%)	58 (63.7%)	117 (62.9%)
Male	36 (37.9%)	33 (36.3%)	69 (37.1%)
One or more co-morbid condition			
No	37 (38.9%)	34 (37.4%)	71 (38.2%)
Yes	58 (61.1%)	57 (62.6%)	115 (61.8%)
Heart disease			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Acute myocardial infarction			
Not reported	95 (100.0%)	90 (98.9%)	185 (99.5%)
Yes	0 (0.0%)	1 (1.1%)	1 (0.5%)
Angina			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)

Other acute ischemic heart disease			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Chronic ischaemic heart disease			
Not reported	92 (96.8%)	87 (95.6%)	179 (96.2%)
Yes	3 (3.2%)	4 (4.4%)	7 (3.8%)
Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
Hypertension			
Not reported	74 (77.9%)	65 (71.4%)	139 (74.7%)
Yes	21 (22.1%)	26 (28.6%)	47 (25.3%)
Atrioventricular block			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Peripheral vascular disease			
Not reported	95 (100.0%)	90 (98.9%)	185 (99.5%)
Yes	0 (0.0%)	1 (1.1%)	1 (0.5%)
Chronic obstructive pulmonary disease			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Diabetes mellitus			
Not reported	88 (92.6%)	83 (91.2%)	171 (91.9%)
Yes	7 (7.4%)	8 (8.8%)	15 (8.1%)
Hyperlipidaemia			
Not reported	79 (83.2%)	84 (92.3%)	163 (87.6%)

Yes	16 (16.8%)	7 (7.7%)	23 (12.4%)
Obesity			
Not reported	91 (95.8%)	89 (97.8%)	180 (96.8%)
Yes	4 (4.2%)	2 (2.2%)	6 (3.2%)
Hiatal hernia			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Gastrooesophageal reflux disease			
Not reported	78 (82.1%)	79 (86.8%)	157 (84.4%)
Yes	17 (17.9%)	12 (13.2%)	29 (15.6%)
Peptic ulcer disease			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Crohn's disease			
Not reported	95 (100.0%)	90 (98.9%)	185 (99.5%)
Yes	0 (0.0%)	1 (1.1%)	1 (0.5%)
Ulcerative colitis			
Not reported	93 (97.9%)	90 (98.9%)	183 (98.4%)
Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
Yes	2 (2.1%)	1 (1.1%)	3 (1.6%)
Non-alcoholic fatty liver disease			
Not reported	92 (96.8%)	85 (93.4%)	177 (95.2%)
Yes	3 (3.2%)	6 (6.6%)	9 (4.8%)

Any tumour			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Osteoporosis			
Not reported	95 (100.0%)	91 (100.0%)	186 (100.0%)
Iridocylitis (uveitis)			
Not reported	94 (98.9%)	90 (98.9%)	184 (98.9%)
Yes	1 (1.1%)	1 (1.1%)	2 (1.1%)
Psoriasis			
Not reported	68 (71.6%)	65 (71.4%)	133 (71.5%)
Yes	27 (28.4%)	26 (28.6%)	53 (28.5%)
Malignancy			
Not reported	79 (83.2%)	81 (89.0%)	160 (86.0%)
Yes	16 (16.8%)	10 (11.0%)	26 (14.0%)

Table 1aiii Demographics - Matched Population: Tofacitinib/TNFi groups , Subgroup: Monotherapy

Factor	Tofacitinib	TNFi	All
N	71	71	142
Age at index (years), mean (SD)	52.38 (14.40) (n=71)	51.15 (14.30) (n=71)	51.77 (14.31) (n=142)
Age at index (years), median (range)	50.00 (27.00, 93.00) (n=71)	50.00 (26.00, 81.00) (n=71)	50.00 (26.00, 93.00) (n=142)
Age category at index (years)			

18-34 years	9 (12.7%)	9 (12.7%)	18 (12.7%)
35-44 years	12 (16.9%)	13 (18.3%)	25 (17.6%)
45-54 years	21 (29.6%)	22 (31.0%)	43 (30.3%)
55-64 years	15 (21.1%)	14 (19.7%)	29 (20.4%)
65-74 years	10 (14.1%)	6 (8.5%)	16 (11.3%)
75-94 years	4 (5.6%)	7 (9.9%)	11 (7.7%)
Gender			
Female	48 (67.6%)	51 (71.8%)	99 (69.7%)
Male	23 (32.4%)	20 (28.2%)	43 (30.3%)
One or more co-morbid condition			
No	30 (42.3%)	32 (45.1%)	62 (43.7%)
Yes	41 (57.7%)	39 (54.9%)	80 (56.3%)
Heart disease			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Acute myocardial infarction			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Angina			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Other acute ischemic heart disease			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)

Chronic ischaemic heart disease			
Not reported	71 (100.0%)	69 (97.2%)	140 (98.6%)
Yes	0 (0.0%)	2 (2.8%)	2 (1.4%)
Hypertension			
Factor	Tofacitinib	TNFi	All
N	71	71	142
Not reported	56 (78.9%)	61 (85.9%)	117 (82.4%)
Yes	15 (21.1%)	10 (14.1%)	25 (17.6%)
Atrioventricular block			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Peripheral vascular disease			
Not reported	71 (100.0%)	70 (98.6%)	141 (99.3%)
Yes	0 (0.0%)	1 (1.4%)	1 (0.7%)
Chronic obstructive pulmonary disease			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Diabetes mellitus			
Not reported	65 (91.5%)	69 (97.2%)	134 (94.4%)
Yes	6 (8.5%)	2 (2.8%)	8 (5.6%)
Hyperlipidaemia			
Not reported	61 (85.9%)	67 (94.4%)	128 (90.1%)
Yes	10 (14.1%)	4 (5.6%)	14 (9.9%)
Obesity			

Not reported	68 (95.8%)	69 (97.2%)	137 (96.5%)
Yes	3 (4.2%)	2 (2.8%)	5 (3.5%)
Hiatal hernia			
Not reported	71 (100.0%)	70 (98.6%)	141 (99.3%)
Yes	0 (0.0%)	1 (1.4%)	1 (0.7%)
Gastrooesophageal reflux disease			
Not reported	59 (83.1%)	64 (90.1%)	123 (86.6%)
Yes	12 (16.9%)	7 (9.9%)	19 (13.4%)
Peptic ulcer disease			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Crohn's disease			
Not reported	71 (100.0%)	70 (98.6%)	141 (99.3%)
Yes	0 (0.0%)	1 (1.4%)	1 (0.7%)
Ulcerative colitis			
Not reported	70 (98.6%)	71 (100.0%)	141 (99.3%)
Factor	Tofacitinib	TNFi	All
N	71	71	142
Yes	1 (1.4%)	0 (0.0%)	1 (0.7%)
Non-alcoholic fatty liver disease			
Not reported	70 (98.6%)	68 (95.8%)	138 (97.2%)
Yes	1 (1.4%)	3 (4.2%)	4 (2.8%)
Any tumour			

Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Osteoporosis			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Iridocylitis (uveitis)			
Not reported	71 (100.0%)	71 (100.0%)	142 (100.0%)
Psoriasis			
Not reported	54 (76.1%)	49 (69.0%)	103 (72.5%)
Yes	17 (23.9%)	22 (31.0%)	39 (27.5%)
Malignancy			
Not reported	61 (85.9%)	62 (87.3%)	123 (86.6%)
Yes	10 (14.1%)	9 (12.7%)	19 (13.4%)

Table 1bi Demographics - All Eligible patients , Subgroup: Combination

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	267	279	489	1035
Age at index (years), mean (SD)	55.71 (12.72) (n=267)	52.14 (12.45) (n=279)	50.70 (14.22) (n=489)	52.38 (13.53) (n=1035)
Age at index (years), median (range)	57.00 (19.00, 84.00) (n=267)	53.00 (20.00, 79.00) (n=279)	52.00 (21.00, 82.00) (n=489)	53.00 (19.00, 84.00) (n=1035)
Age category at index (years)				
18-34 years	16 (6.0%)	33 (11.8%)	80 (16.4%)	129 (12.5%)

35-44 years	38 (14.2%)	39 (14.0%)	84 (17.2%)	161 (15.6%)
45-54 years	66 (24.7%)	85 (30.5%)	112 (22.9%)	263 (25.4%)
55-64 years	73 (27.3%)	81 (29.0%)	124 (25.4%)	278 (26.9%)
65-74 years	57 (21.3%)	35 (12.5%)	75 (15.3%)	167 (16.1%)
75-94 years	17 (6.4%)	6 (2.2%)	14 (2.9%)	37 (3.6%)
Gender				
Female	205 (76.8%)	176 (63.1%)	322 (65.8%)	703 (67.9%)
Male	60 (22.5%)	100 (35.8%)	161 (32.9%)	321 (31.0%)
Unassigned	2 (0.7%)	0 (0.0%)	3 (0.6%)	5 (0.5%)
0 (0.0%)	3 (1.1%)	3 (0.6%)	6 (0.6%)	
One or more co-morbid condition				
No	147 (55.1%)	143 (51.3%)	221 (45.2%)	511 (49.4%)
Yes	120 (44.9%)	136 (48.7%)	268 (54.8%)	524 (50.6%)
Heart disease				
Not reported	267 (100.0%)	279 (100.0%)	489 (100.0%)	1035 (100.0%)
Acute myocardial infarction				
Not reported	266 (99.6%)	279 (100.0%)	489 (100.0%)	1034 (99.9%)
Yes	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Angina				
Not reported	267 (100.0%)	279 (100.0%)	489 (100.0%)	1035 (100.0%)
Certain complications following acute myocardial infarction				
Not reported	267 (100.0%)	279 (100.0%)	489 (100.0%)	1035 (100.0%)

Other acute ischemic heart disease				
Not reported	267 (100.0%)	279 (100.0%)	489 (100.0%)	1035 (100.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	267	279	489	1035
Chronic ischaemic heart disease				
Not reported	259 (97.0%)	276 (98.9%)	484 (99.0%)	1019 (98.5%)
Yes	8 (3.0%)	3 (1.1%)	5 (1.0%)	16 (1.5%)
Hypertension				
Not reported	221 (82.8%)	241 (86.4%)	417 (85.3%)	879 (84.9%)
Yes	46 (17.2%)	38 (13.6%)	72 (14.7%)	156 (15.1%)
Atrioventricular block				
Not reported	267 (100.0%)	279 (100.0%)	489 (100.0%)	1035 (100.0%)
Peripheral vascular disease				
Not reported	263 (98.5%)	277 (99.3%)	486 (99.4%)	1026 (99.1%)
Yes	4 (1.5%)	2 (0.7%)	3 (0.6%)	9 (0.9%)
Chronic obstructive pulmonary disease				
Not reported	263 (98.5%)	278 (99.6%)	486 (99.4%)	1027 (99.2%)
Yes	4 (1.5%)	1 (0.4%)	3 (0.6%)	8 (0.8%)
Diabetes mellitus				
Not reported	256 (95.9%)	264 (94.6%)	468 (95.7%)	988 (95.5%)
Yes	11 (4.1%)	15 (5.4%)	21 (4.3%)	47 (4.5%)
Hyperlipidaemia				

Not reported	245 (91.8%)	264 (94.6%)	461 (94.3%)	970 (93.7%)
Yes	22 (8.2%)	15 (5.4%)	28 (5.7%)	65 (6.3%)
Obesity				
Not reported	264 (98.9%)	269 (96.4%)	477 (97.5%)	1010 (97.6%)
Yes	3 (1.1%)	10 (3.6%)	12 (2.5%)	25 (2.4%)
Hiatal hernia				
Not reported	267 (100.0%)	277 (99.3%)	484 (99.0%)	1028 (99.3%)
Yes	0 (0.0%)	2 (0.7%)	5 (1.0%)	7 (0.7%)
Gastrooesophageal reflux disease				
Not reported	241 (90.3%)	252 (90.3%)	452 (92.4%)	945 (91.3%)
Yes	26 (9.7%)	27 (9.7%)	37 (7.6%)	90 (8.7%)
Peptic ulcer disease				
Not reported	266 (99.6%)	276 (98.9%)	486 (99.4%)	1028 (99.3%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	267	279	489	1035
Yes	1 (0.4%)	3 (1.1%)	3 (0.6%)	7 (0.7%)
Crohn's disease				
Not reported	263 (98.5%)	278 (99.6%)	482 (98.6%)	1023 (98.8%)
Yes	4 (1.5%)	1 (0.4%)	7 (1.4%)	12 (1.2%)
Ulcerative colitis				
Not reported	262 (98.1%)	279 (100.0%)	481 (98.4%)	1022 (98.7%)
Yes	5 (1.9%)	0 (0.0%)	8 (1.6%)	13 (1.3%)

Non-alcoholic fatty liver disease				
Not reported	264 (98.9%)	273 (97.8%)	467 (95.5%)	1004 (97.0%)
Yes	3 (1.1%)	6 (2.2%)	22 (4.5%)	31 (3.0%)
Any tumour				
Not reported	267 (100.0%)	279 (100.0%)	489 (100.0%)	1035 (100.0%)
Osteoporosis				
Not reported	265 (99.3%)	279 (100.0%)	487 (99.6%)	1031 (99.6%)
Yes	2 (0.7%)	0 (0.0%)	2 (0.4%)	4 (0.4%)
Iridocylitis (uveitis)				
Not reported	265 (99.3%)	277 (99.3%)	478 (97.8%)	1020 (98.6%)
Yes	2 (0.7%)	2 (0.7%)	11 (2.2%)	15 (1.4%)
Psoriasis				
Not reported	212 (79.4%)	192 (68.8%)	324 (66.3%)	728 (70.3%)
Yes	55 (20.6%)	87 (31.2%)	165 (33.7%)	307 (29.7%)
Malignancy				
Not reported	237 (88.8%)	247 (88.5%)	443 (90.6%)	927 (89.6%)
Yes	30 (11.2%)	32 (11.5%)	46 (9.4%)	108 (10.4%)

Table 1bii Demographics - Matched Population: Tofacitinib/IL-17Ai groups , Subgroup: Combination

Factor	Tofacitinib	IL-17Ai	All
N	174	178	352
Age at index (years), mean	53.26 (13.41) (n=174)	54.03 (12.64) (n=178)	53.65 (13.01) (n=352)

(SD)			
Age at index (years), median (range)	54.00 (19.00, 84.00) (n=174)	55.00 (24.00, 79.00) (n=178)	55.00 (19.00, 84.00) (n=352)
Age category at index (years)			
18-34 years	16 (9.2%)	13 (7.3%)	29 (8.2%)
35-44 years	38 (21.8%)	30 (16.9%)	68 (19.3%)
45-54 years	34 (19.5%)	44 (24.7%)	78 (22.2%)
55-64 years	44 (25.3%)	55 (30.9%)	99 (28.1%)
65-74 years	34 (19.5%)	31 (17.4%)	65 (18.5%)
75-94 years	8 (4.6%)	5 (2.8%)	13 (3.7%)
Gender			
Female	114 (65.5%)	129 (72.5%)	243 (69.0%)
Male	60 (34.5%)	49 (27.5%)	109 (31.0%)
One or more co-morbid condition			
No	91 (52.3%)	95 (53.4%)	186 (52.8%)
Yes	83 (47.7%)	83 (46.6%)	166 (47.2%)
Heart disease			
Not reported	174 (100.0%)	178 (100.0%)	352 (100.0%)
Acute myocardial infarction			
Not reported	173 (99.4%)	178 (100.0%)	351 (99.7%)
Yes	1 (0.6%)	0 (0.0%)	1 (0.3%)
Angina			

Not reported	174 (100.0%)	178 (100.0%)	352 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	174 (100.0%)	178 (100.0%)	352 (100.0%)
Other acute ischemic heart disease			
Not reported	174 (100.0%)	178 (100.0%)	352 (100.0%)
Chronic ischaemic heart disease			
Not reported	169 (97.1%)	177 (99.4%)	346 (98.3%)
Yes	5 (2.9%)	1 (0.6%)	6 (1.7%)
Factor	Tofacitinib	IL-17Ai	All
N	174	178	352
Hypertension			
Not reported	143 (82.2%)	154 (86.5%)	297 (84.4%)
Yes	31 (17.8%)	24 (13.5%)	55 (15.6%)
Atrioventricular block			
Not reported	174 (100.0%)	178 (100.0%)	352 (100.0%)
Peripheral vascular disease			
Not reported	173 (99.4%)	177 (99.4%)	350 (99.4%)
Yes	1 (0.6%)	1 (0.6%)	2 (0.6%)
Chronic obstructive pulmonary disease			
Not reported	171 (98.3%)	177 (99.4%)	348 (98.9%)
Yes	3 (1.7%)	1 (0.6%)	4 (1.1%)
Diabetes mellitus			

Not reported	171 (98.3%)	169 (94.9%)	340 (96.6%)
Yes	3 (1.7%)	9 (5.1%)	12 (3.4%)
Hyperlipidaemia			
Not reported	162 (93.1%)	170 (95.5%)	332 (94.3%)
Yes	12 (6.9%)	8 (4.5%)	20 (5.7%)
Obesity			
Not reported	173 (99.4%)	170 (95.5%)	343 (97.4%)
Yes	1 (0.6%)	8 (4.5%)	9 (2.6%)
Hiatal hernia			
Not reported	174 (100.0%)	176 (98.9%)	350 (99.4%)
Yes	0 (0.0%)	2 (1.1%)	2 (0.6%)
Gastrooesophageal reflux disease			
Not reported	157 (90.2%)	161 (90.4%)	318 (90.3%)
Yes	17 (9.8%)	17 (9.6%)	34 (9.7%)
Peptic ulcer disease			
Not reported	173 (99.4%)	177 (99.4%)	350 (99.4%)
Yes	1 (0.6%)	1 (0.6%)	2 (0.6%)
Crohn's disease			
Not reported	170 (97.7%)	177 (99.4%)	347 (98.6%)
Factor	Tofacitinib	IL-17Ai	All
N	174	178	352
Yes	4 (2.3%)	1 (0.6%)	5 (1.4%)

Ulcerative colitis			
Not reported	172 (98.9%)	178 (100.0%)	350 (99.4%)
Yes	2 (1.1%)	0 (0.0%)	2 (0.6%)
Non-alcoholic fatty liver disease			
Not reported	172 (98.9%)	175 (98.3%)	347 (98.6%)
Yes	2 (1.1%)	3 (1.7%)	5 (1.4%)
Any tumour			
Not reported	174 (100.0%)	178 (100.0%)	352 (100.0%)
Osteoporosis			
Not reported	172 (98.9%)	178 (100.0%)	350 (99.4%)
Yes	2 (1.1%)	0 (0.0%)	2 (0.6%)
Iridocylitis (uveitis)			
Not reported	172 (98.9%)	178 (100.0%)	350 (99.4%)
Yes	2 (1.1%)	0 (0.0%)	2 (0.6%)
Psoriasis			
Not reported	137 (78.7%)	131 (73.6%)	268 (76.1%)
Yes	37 (21.3%)	47 (26.4%)	84 (23.9%)
Malignancy			
Not reported	155 (89.1%)	153 (86.0%)	308 (87.5%)
Yes	19 (10.9%)	25 (14.0%)	44 (12.5%)

Table 1biii Demographics - Matched Population: Tofacitinib/TNFi groups , Subgroup: Combination

Factor	Tofacitinib	TNFi	All
N	185	185	370
Age at index (years), mean (SD)	53.29 (13.23) (n=185)	54.92 (13.36) (n=185)	54.11 (13.30) (n=370)
Age at index (years), median (range)	53.00 (19.00, 84.00) (n=185)	57.00 (24.00, 80.00) (n=185)	55.00 (19.00, 84.00) (n=370)
Age category at index (years)			
18-34 years	16 (8.6%)	14 (7.6%)	30 (8.1%)
35-44 years	38 (20.5%)	27 (14.6%)	65 (17.6%)
45-54 years	43 (23.2%)	43 (23.2%)	86 (23.2%)
55-64 years	46 (24.9%)	53 (28.6%)	99 (26.8%)
65-74 years	32 (17.3%)	39 (21.1%)	71 (19.2%)
75-94 years	10 (5.4%)	9 (4.9%)	19 (5.1%)
Gender			
Female	131 (70.8%)	141 (76.2%)	272 (73.5%)
Male	54 (29.2%)	44 (23.8%)	98 (26.5%)
One or more co-morbid condition			
No	101 (54.6%)	88 (47.6%)	189 (51.1%)
Yes	84 (45.4%)	97 (52.4%)	181 (48.9%)
Heart disease			
Not reported	185 (100.0%)	185 (100.0%)	370 (100.0%)
Acute myocardial infarction			
Not reported	184 (99.5%)	185 (100.0%)	369 (99.7%)

Yes	1 (0.5%)	0 (0.0%)	1 (0.3%)
Angina			
Not reported	185 (100.0%)	185 (100.0%)	370 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	185 (100.0%)	185 (100.0%)	370 (100.0%)
Other acute ischemic heart disease			
Not reported	185 (100.0%)	185 (100.0%)	370 (100.0%)
Chronic ischaemic heart disease			
Not reported	181 (97.8%)	182 (98.4%)	363 (98.1%)
Yes	4 (2.2%)	3 (1.6%)	7 (1.9%)
Factor	Tofacitinib	TNFi	All
N	185	185	370
Hypertension			
Not reported	153 (82.7%)	153 (82.7%)	306 (82.7%)
Yes	32 (17.3%)	32 (17.3%)	64 (17.3%)
Atrioventricular block			
Not reported	185 (100.0%)	185 (100.0%)	370 (100.0%)
Peripheral vascular disease			
Not reported	183 (98.9%)	183 (98.9%)	366 (98.9%)
Yes	2 (1.1%)	2 (1.1%)	4 (1.1%)
Chronic obstructive pulmonary disease			
Not reported	183 (98.9%)	185 (100.0%)	368 (99.5%)

Yes	2 (1.1%)	0 (0.0%)	2 (0.5%)
Diabetes mellitus			
Not reported	181 (97.8%)	176 (95.1%)	357 (96.5%)
Yes	4 (2.2%)	9 (4.9%)	13 (3.5%)
Hyperlipidaemia			
Not reported	172 (93.0%)	167 (90.3%)	339 (91.6%)
Yes	13 (7.0%)	18 (9.7%)	31 (8.4%)
Obesity			
Not reported	184 (99.5%)	180 (97.3%)	364 (98.4%)
Yes	1 (0.5%)	5 (2.7%)	6 (1.6%)
Hiatal hernia			
Not reported	185 (100.0%)	184 (99.5%)	369 (99.7%)
Yes	0 (0.0%)	1 (0.5%)	1 (0.3%)
Gastrooesophageal reflux disease			
Not reported	168 (90.8%)	166 (89.7%)	334 (90.3%)
Yes	17 (9.2%)	19 (10.3%)	36 (9.7%)
Peptic ulcer disease			
Not reported	184 (99.5%)	185 (100.0%)	369 (99.7%)
Yes	1 (0.5%)	0 (0.0%)	1 (0.3%)
Crohn's disease			
Not reported	181 (97.8%)	180 (97.3%)	361 (97.6%)
Factor	Tofacitinib	TNFi	All

N	185	185	370
Yes	4 (2.2%)	5 (2.7%)	9 (2.4%)
Ulcerative colitis			
Not reported	183 (98.9%)	183 (98.9%)	366 (98.9%)
Yes	2 (1.1%)	2 (1.1%)	4 (1.1%)
Non-alcoholic fatty liver disease			
Not reported	183 (98.9%)	177 (95.7%)	360 (97.3%)
Yes	2 (1.1%)	8 (4.3%)	10 (2.7%)
Any tumour			
Not reported	185 (100.0%)	185 (100.0%)	370 (100.0%)
Osteoporosis			
Not reported	183 (98.9%)	183 (98.9%)	366 (98.9%)
Yes	2 (1.1%)	2 (1.1%)	4 (1.1%)
Iridocylitis (uveitis)			
Not reported	183 (98.9%)	181 (97.8%)	364 (98.4%)
Yes	2 (1.1%)	4 (2.2%)	6 (1.6%)
Psoriasis			
Not reported	146 (78.9%)	133 (71.9%)	279 (75.4%)
Yes	39 (21.1%)	52 (28.1%)	91 (24.6%)
Malignancy			
Not reported	166 (89.7%)	168 (90.8%)	334 (90.3%)
Yes	19 (10.3%)	17 (9.2%)	36 (9.7%)

Table 1ci Demographics - All Eligible patients , Subgroup: First Line

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	78	174	417	669
Age at index (years), mean (SD)	57.71 (13.41) (n=78)	50.96 (13.31) (n=174)	50.05 (14.85) (n=417)	51.18 (14.48) (n=669)
Age at index (years), median (range)	59.50 (29.00, 84.00) (n=78)	52.00 (24.00, 79.00) (n=174)	50.00 (20.00, 83.00) (n=417)	52.00 (20.00, 84.00) (n=669)
Age category at index (years)				
18-34 years	5 (6.4%)	29 (16.7%)	75 (18.0%)	109 (16.3%)
35-44 years	10 (12.8%)	27 (15.5%)	78 (18.7%)	115 (17.2%)
45-54 years	14 (17.9%)	46 (26.4%)	92 (22.1%)	152 (22.7%)
55-64 years	22 (28.2%)	44 (25.3%)	96 (23.0%)	162 (24.2%)
65-74 years	19 (24.4%)	22 (12.6%)	55 (13.2%)	96 (14.3%)
75-94 years	8 (10.3%)	6 (3.4%)	21 (5.0%)	35 (5.2%)
Gender				
Female	56 (71.8%)	108 (62.1%)	252 (60.4%)	416 (62.2%)
Male	21 (26.9%)	61 (35.1%)	157 (37.6%)	239 (35.7%)
Unassigned	1 (1.3%)	0 (0.0%)	3 (0.7%)	4 (0.6%)
0 (0.0%)	5 (2.9%)	5 (1.2%)	10 (1.5%)	
One or more co-morbid condition				
No	40 (51.3%)	74 (42.5%)	186 (44.6%)	300 (44.8%)
Yes	38 (48.7%)	100 (57.5%)	231 (55.4%)	369 (55.2%)

Heart disease				
Not reported	78 (100.0%)	174 (100.0%)	417 (100.0%)	669 (100.0%)
Acute myocardial infarction				
Not reported	77 (98.7%)	174 (100.0%)	417 (100.0%)	668 (99.9%)
Yes	1 (1.3%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Angina				
Not reported	78 (100.0%)	174 (100.0%)	417 (100.0%)	669 (100.0%)
Certain complications following acute myocardial infarction				
Not reported	78 (100.0%)	174 (100.0%)	417 (100.0%)	669 (100.0%)
Other acute ischemic heart disease				
Not reported	78 (100.0%)	174 (100.0%)	417 (100.0%)	669 (100.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	78	174	417	669
Chronic ischaemic heart disease				
Not reported	77 (98.7%)	173 (99.4%)	413 (99.0%)	663 (99.1%)
Yes	1 (1.3%)	1 (0.6%)	4 (1.0%)	6 (0.9%)
Hypertension				
Not reported	64 (82.1%)	152 (87.4%)	355 (85.1%)	571 (85.4%)
Yes	14 (17.9%)	22 (12.6%)	62 (14.9%)	98 (14.6%)
Atrioventricular block				
Not reported	78 (100.0%)	174 (100.0%)	417 (100.0%)	669 (100.0%)
Peripheral vascular disease				

Not reported	78 (100.0%)	173 (99.4%)	416 (99.8%)	667 (99.7%)
Yes	0 (0.0%)	1 (0.6%)	1 (0.2%)	2 (0.3%)
Chronic obstructive pulmonary disease				
Not reported	77 (98.7%)	173 (99.4%)	416 (99.8%)	666 (99.6%)
Yes	1 (1.3%)	1 (0.6%)	1 (0.2%)	3 (0.4%)
Diabetes mellitus				
Not reported	75 (96.2%)	168 (96.6%)	401 (96.2%)	644 (96.3%)
Yes	3 (3.8%)	6 (3.4%)	16 (3.8%)	25 (3.7%)
Hyperlipidaemia				
Not reported	73 (93.6%)	164 (94.3%)	396 (95.0%)	633 (94.6%)
Yes	5 (6.4%)	10 (5.7%)	21 (5.0%)	36 (5.4%)
Obesity				
Not reported	75 (96.2%)	169 (97.1%)	408 (97.8%)	652 (97.5%)
Yes	3 (3.8%)	5 (2.9%)	9 (2.2%)	17 (2.5%)
Hiatal hernia				
Not reported	78 (100.0%)	173 (99.4%)	413 (99.0%)	664 (99.3%)
Yes	0 (0.0%)	1 (0.6%)	4 (1.0%)	5 (0.7%)
Gastrooesophageal reflux disease				
Not reported	72 (92.3%)	153 (87.9%)	383 (91.8%)	608 (90.9%)
Yes	6 (7.7%)	21 (12.1%)	34 (8.2%)	61 (9.1%)
Peptic ulcer disease				
Not reported	78 (100.0%)	171 (98.3%)	413 (99.0%)	662 (99.0%

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	78	174	417	669
Yes	0 (0.0%)	3 (1.7%)	4 (1.0%)	7 (1.0%)
Crohn's disease				
Not reported	77 (98.7%)	174 (100.0%)	414 (99.3%)	665 (99.4%)
Yes	1 (1.3%)	0 (0.0%)	3 (0.7%)	4 (0.6%)
Ulcerative colitis				
Not reported	78 (100.0%)	174 (100.0%)	414 (99.3%)	666 (99.6%)
Yes	0 (0.0%)	0 (0.0%)	3 (0.7%)	3 (0.4%)
Non-alcoholic fatty liver disease				
Not reported	78 (100.0%)	171 (98.3%)	406 (97.4%)	655 (97.9%)
Yes	0 (0.0%)	3 (1.7%)	11 (2.6%)	14 (2.1%)
Any tumour				
Not reported	78 (100.0%)	174 (100.0%)	417 (100.0%)	669 (100.0%)
Osteoporosis				
Not reported	78 (100.0%)	174 (100.0%)	416 (99.8%)	668 (99.9%)
Yes	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
Iridocylitis (uveitis)				
Not reported	78 (100.0%)	173 (99.4%)	409 (98.1%)	660 (98.7%)
Yes	0 (0.0%)	1 (0.6%)	8 (1.9%)	9 (1.3%)
Psoriasis				
Not reported	57 (73.1%)	107 (61.5%)	270 (64.7%)	434 (64.9%)

Yes	21 (26.9%)	67 (38.5%)	147 (35.3%)	235 (35.1%)
Malignancy				
Not reported	68 (87.2%)	155 (89.1%)	370 (88.7%)	593 (88.6%)
Yes	10 (12.8%)	19 (10.9%)	47 (11.3%)	76 (11.4%)

Table 1cii Demographics - Matched Population: Tofacitinib/IL-17Ai groups , Subgroup: First Line

Factor	Tofacitinib	IL-17Ai	All
N	77	67	144
Age at index (years), mean (SD)	57.66 (13.49) (n=77)	54.90 (13.23) (n=67)	56.38 (13.40) (n=144)
Age at index (years), median (range)	59.00 (29.00, 84.00) (n=77)	57.00 (24.00, 79.00) (n=67)	57.50 (24.00, 84.00) (n=144)
Age category at index (years)			
18-34 years	5 (6.5%)	5 (7.5%)	10 (6.9%)
35-44 years	10 (13.0%)	11 (16.4%)	21 (14.6%)
45-54 years	14 (18.2%)	14 (20.9%)	28 (19.4%)
55-64 years	21 (27.3%)	21 (31.3%)	42 (29.2%)
65-74 years	19 (24.7%)	12 (17.9%)	31 (21.5%)
75-94 years	8 (10.4%)	4 (6.0%)	12 (8.3%)
Gender			
Female	56 (72.7%)	44 (65.7%)	100 (69.4%)
Male	21 (27.3%)	23 (34.3%)	44 (30.6%)

One or more co-morbid condition			
No	39 (50.6%)	27 (40.3%)	66 (45.8%)
Yes	38 (49.4%)	40 (59.7%)	78 (54.2%)
Heart disease			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Acute myocardial infarction			
Not reported	76 (98.7%)	67 (100.0%)	143 (99.3%)
Yes	1 (1.3%)	0 (0.0%)	1 (0.7%)
Angina			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Other acute ischemic heart disease			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Chronic ischaemic heart disease			
Not reported	76 (98.7%)	66 (98.5%)	142 (98.6%)
Yes	1 (1.3%)	1 (1.5%)	2 (1.4%)
Factor	Tofacitinib	IL-17Ai	All
N	77	67	144
Hypertension			
Not reported	63 (81.8%)	56 (83.6%)	119 (82.6%)
Yes	14 (18.2%)	11 (16.4%)	25 (17.4%)

Atrioventricular block			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Peripheral vascular disease			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Chronic obstructive pulmonary disease			
Not reported	76 (98.7%)	67 (100.0%)	143 (99.3%)
Yes	1 (1.3%)	0 (0.0%)	1 (0.7%)
Diabetes mellitus			
Not reported	74 (96.1%)	65 (97.0%)	139 (96.5%)
Yes	3 (3.9%)	2 (3.0%)	5 (3.5%)
Hyperlipidaemia			
Not reported	72 (93.5%)	63 (94.0%)	135 (93.8%)
Yes	5 (6.5%)	4 (6.0%)	9 (6.2%)
Obesity			
Not reported	74 (96.1%)	64 (95.5%)	138 (95.8%)
Yes	3 (3.9%)	3 (4.5%)	6 (4.2%)
Hiatal hernia			
Not reported	77 (100.0%)	66 (98.5%)	143 (99.3%)
Yes	0 (0.0%)	1 (1.5%)	1 (0.7%)
Gastrooesophageal reflux disease			
Not reported	71 (92.2%)	57 (85.1%)	128 (88.9%)
Yes	6 (7.8%)	10 (14.9%)	16 (11.1%)

Peptic ulcer disease			
Not reported	77 (100.0%)	66 (98.5%)	143 (99.3%)
Yes	0 (0.0%)	1 (1.5%)	1 (0.7%)
Crohn's disease			
Not reported	76 (98.7%)	67 (100.0%)	143 (99.3%)
Yes	1 (1.3%)	0 (0.0%)	1 (0.7%)
Factor	Tofacitinib	IL-17Ai	All
N	77	67	144
Ulcerative colitis			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Non-alcoholic fatty liver disease			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Any tumour			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Osteoporosis			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Iridocylitis (uveitis)			
Not reported	77 (100.0%)	67 (100.0%)	144 (100.0%)
Psoriasis			
Not reported	56 (72.7%)	46 (68.7%)	102 (70.8%)
Yes	21 (27.3%)	21 (31.3%)	42 (29.2%)
Malignancy			

Not reported	67 (87.0%)	56 (83.6%)	123 (85.4%)
Yes	10 (13.0%)	11 (16.4%)	21 (14.6%)

Table 1ciii Demographics - Matched Population: Tofacitinib/TNFi groups , Subgroup: First Line

Factor	Tofacitinib	TNFi	All
N	77	79	156
Age at index (years), mean (SD)	57.66 (13.49) (n=77)	57.54 (14.04) (n=79)	57.60 (13.73) (n=156)
Age at index (years), median (range)	59.00 (29.00, 84.00) (n=77)	60.00 (24.00, 81.00) (n=79)	60.00 (24.00, 84.00) (n=156)
Age category at index (years)			
18-34 years	5 (6.5%)	5 (6.3%)	10 (6.4%)
35-44 years	10 (13.0%)	10 (12.7%)	20 (12.8%)
45-54 years	14 (18.2%)	14 (17.7%)	28 (17.9%)
55-64 years	21 (27.3%)	21 (26.6%)	42 (26.9%)
65-74 years	19 (24.7%)	20 (25.3%)	39 (25.0%)
75-94 years	8 (10.4%)	9 (11.4%)	17 (10.9%)
Gender			
Female	56 (72.7%)	57 (72.2%)	113 (72.4%)
Male	21 (27.3%)	22 (27.8%)	43 (27.6%)
One or more co-morbid condition			
No	39 (50.6%)	31 (39.2%)	70 (44.9%)

Yes	38 (49.4%)	48 (60.8%)	86 (55.1%)
Heart disease			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Acute myocardial infarction			
Not reported	76 (98.7%)	79 (100.0%)	155 (99.4%)
Yes	1 (1.3%)	0 (0.0%)	1 (0.6%)
Angina			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Other acute ischemic heart disease			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Chronic ischaemic heart disease			
Not reported	76 (98.7%)	78 (98.7%)	154 (98.7%
Factor	Tofacitinib	TNFi	All
N	77	79	156
Hypertension			
Not reported	63 (81.8%)	62 (78.5%)	125 (80.1%)
Yes	14 (18.2%)	17 (21.5%)	31 (19.9%)
Atrioventricular block			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Peripheral vascular disease			

Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Chronic obstructive pulmonary disease			
Not reported	76 (98.7%)	79 (100.0%)	155 (99.4%)
Yes	1 (1.3%)	0 (0.0%)	1 (0.6%)
Diabetes mellitus			
Not reported	74 (96.1%)	75 (94.9%)	149 (95.5%)
Yes	3 (3.9%)	4 (5.1%)	7 (4.5%)
Hyperlipidaemia			
Not reported	72 (93.5%)	71 (89.9%)	143 (91.7%)
Yes	5 (6.5%)	8 (10.1%)	13 (8.3%)
Obesity			
Not reported	74 (96.1%)	78 (98.7%)	152 (97.4%)
Yes	3 (3.9%)	1 (1.3%)	4 (2.6%)
Hiatal hernia			
Not reported	77 (100.0%)	78 (98.7%)	155 (99.4%)
Yes	0 (0.0%)	1 (1.3%)	1 (0.6%)
Gastrooesophageal reflux disease			
Not reported	71 (92.2%)	71 (89.9%)	142 (91.0%)
Yes	6 (7.8%)	8 (10.1%)	14 (9.0%)
Peptic ulcer disease			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Crohn's disease			

Not reported	76 (98.7%)	77 (97.5%)	153 (98.1%)
Yes	1 (1.3%)	2 (2.5%)	3 (1.9%)
Ulcerative colitis			
Factor	Tofacitinib	TNFi	All
N	77	79	156
Not reported	77 (100.0%)	78 (98.7%)	155 (99.4%)
Yes	0 (0.0%)	1 (1.3%)	1 (0.6%)
Non-alcoholic fatty liver disease			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Any tumour			
Not reported	77 (100.0%)	79 (100.0%)	156 (100.0%)
Osteoporosis			
Not reported	77 (100.0%)	78 (98.7%)	155 (99.4%)
Yes	0 (0.0%)	1 (1.3%)	1 (0.6%)
Iridocylitis (uveitis)			
Not reported	77 (100.0%)	77 (97.5%)	154 (98.7%)
Yes	0 (0.0%)	2 (2.5%)	2 (1.3%)
Psoriasis			
Not reported	56 (72.7%)	51 (64.6%)	107 (68.6%)
Yes	21 (27.3%)	28 (35.4%)	49 (31.4%)
Malignancy			
Not reported	67 (87.0%)	65 (82.3%)	132 (84.6%)

Yes	10 (13.0%)	14 (17.7%)	24 (15.4%)

Table 1di Demographics - All Eligible patients , Subgroup: Second or later Line

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	328	242	247	817
Age at index (years), mean (SD)	55.05 (12.46) (n=328)	53.86 (12.17) (n=242)	50.78 (14.10) (n=247)	53.41 (13.01) (n=817)
Age at index (years), median (range)	56.00 (19.00, 93.00) (n=328)	54.00 (20.00, 77.00) (n=242)	52.00 (23.00, 80.00) (n=247)	54.00 (19.00, 93.00) (n=817)
Age category at index (years)				
18-34 years	21 (6.4%)	14 (5.8%)	41 (16.6%)	76 (9.3%)
35-44 years	40 (12.2%)	42 (17.4%)	37 (15.0%)	119 (14.6%)
45-54 years	95 (29.0%)	74 (30.6%)	63 (25.5%)	232 (28.4%)
55-64 years	92 (28.0%)	67 (27.7%)	64 (25.9%)	223 (27.3%)
65-74 years	63 (19.2%)	36 (14.9%)	35 (14.2%)	134 (16.4%)
75-94 years	17 (5.2%)	9 (3.7%)	7 (2.8%)	33 (4.0%)
Gender				
Female	250 (76.2%)	146 (60.3%)	178 (72.1%)	574 (70.3%)
Male	75 (22.9%)	95 (39.3%)	65 (26.3%)	235 (28.8%)
Unassigned	3 (0.9%)	0 (0.0%)	3 (1.2%)	6 (0.7%)
0 (0.0%)	1 (0.4%)	1 (0.4%)	2 (0.2%)	
One or more co-morbid condition				

No	166 (50.6%)	121 (50.0%)	120 (48.6%)	407 (49.8%)
Yes	162 (49.4%)	121 (50.0%)	127 (51.4%)	410 (50.2%)
Heart disease				
Not reported	328 (100.0%)	242 (100.0%)	247 (100.0%)	817 (100.0%)
Acute myocardial infarction				
Not reported	328 (100.0%)	241 (99.6%)	247 (100.0%)	816 (99.9%)
Yes	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (0.1%)
Angina				
Not reported	328 (100.0%)	242 (100.0%)	247 (100.0%)	817 (100.0%)
Certain complications following acute myocardial infarction				
Not reported	328 (100.0%)	242 (100.0%)	247 (100.0%)	817 (100.0%)
Other acute ischemic heart disease				
Not reported	328 (100.0%)	242 (100.0%)	247 (100.0%)	817 (100.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	328	242	247	817
Chronic ischaemic heart disease				
Not reported	318 (97.0%)	236 (97.5%)	243 (98.4%)	797 (97.6%)
Yes	10 (3.0%)	6 (2.5%)	4 (1.6%)	20 (2.4%)
Hypertension				
Not reported	271 (82.6%)	195 (80.6%)	214 (86.6%)	680 (83.2%)
Yes	57 (17.4%)	47 (19.4%)	33 (13.4%)	137 (16.8%)
Atrioventricular block				

Not reported	328 (100.0%)	242 (100.0%)	247 (100.0%)	817 (100.0%)
Peripheral vascular disease				
Not reported	324 (98.8%)	240 (99.2%)	244 (98.8%)	808 (98.9%)
Yes	4 (1.2%)	2 (0.8%)	3 (1.2%)	9 (1.1%)
Chronic obstructive pulmonary disease				
Not reported	324 (98.8%)	241 (99.6%)	245 (99.2%)	810 (99.1%)
Yes	4 (1.2%)	1 (0.4%)	2 (0.8%)	7 (0.9%)
Diabetes mellitus				
Not reported	312 (95.1%)	225 (93.0%)	235 (95.1%)	772 (94.5%)
Yes	16 (4.9%)	17 (7.0%)	12 (4.9%)	45 (5.5%)
Hyperlipidaemia				
Not reported	290 (88.4%)	225 (93.0%)	229 (92.7%)	744 (91.1%)
Yes	38 (11.6%)	17 (7.0%)	18 (7.3%)	73 (8.9%)
Obesity				
Not reported	322 (98.2%)	233 (96.3%)	238 (96.4%)	793 (97.1%)
Yes	6 (1.8%)	9 (3.7%)	9 (3.6%)	24 (2.9%)
Hiatal hernia				
Not reported	328 (100.0%)	241 (99.6%)	245 (99.2%)	814 (99.6%)
Yes	0 (0.0%)	1 (0.4%)	2 (0.8%)	3 (0.4%)
Gastrooesophageal reflux disease				
Not reported	285 (86.9%)	217 (89.7%)	226 (91.5%)	728 (89.1%)
Yes	43 (13.1%)	25 (10.3%)	21 (8.5%)	89 (10.9%)

Peptic ulcer disease				
Not reported	327 (99.7%)	242 (100.0%)	247 (100.0%)	816 (99.9%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	328	242	247	817
Yes	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Crohn's disease				
Not reported	324 (98.8%)	240 (99.2%)	242 (98.0%)	806 (98.7%)
Yes	4 (1.2%)	2 (0.8%)	5 (2.0%)	11 (1.3%)
Ulcerative colitis				
Not reported	320 (97.6%)	241 (99.6%)	241 (97.6%)	802 (98.2%)
Yes	8 (2.4%)	1 (0.4%)	6 (2.4%)	15 (1.8%)
Non-alcoholic fatty liver disease				
Not reported	318 (97.0%)	228 (94.2%)	231 (93.5%)	777 (95.1%)
Yes	10 (3.0%)	14 (5.8%)	16 (6.5%)	40 (4.9%)
Any tumour				
Not reported	328 (100.0%)	242 (100.0%)	247 (100.0%)	817 (100.0%)
Osteoporosis				
Not reported	326 (99.4%)	242 (100.0%)	246 (99.6%)	814 (99.6%)
Yes	2 (0.6%)	0 (0.0%)	1 (0.4%)	3 (0.4%)
Iridocylitis (uveitis)				
Not reported	325 (99.1%)	240 (99.2%)	244 (98.8%)	809 (99.0%)
Yes	3 (0.9%)	2 (0.8%)	3 (1.2%)	8 (1.0%)

Psoriasis				
Not reported	254 (77.4%)	176 (72.7%)	176 (71.3%)	606 (74.2%)
Yes	74 (22.6%)	66 (27.3%)	71 (28.7%)	211 (25.8%)
Malignancy				
Not reported	287 (87.5%)	217 (89.7%)	226 (91.5%)	730 (89.4%)
Yes	41 (12.5%)	25 (10.3%)	21 (8.5%)	87 (10.6%)

Table 1dii Demographics - Matched Population: Tofacitinib/IL-17Ai groups , Subgroup: Second or later Line

Factor	Tofacitinib	IL-17Ai	All
N	192	202	394
Age at index (years), mean (SD)	51.48 (12.85) (n=192)	54.55 (12.52) (n=202)	53.06 (12.75) (n=394)
Age at index (years), median (range)	50.00 (19.00, 93.00) (n=192)	55.00 (23.00, 77.00) (n=202)	53.00 (19.00, 93.00) (n=394)
Age category at index (years)			
18-34 years	20 (10.4%)	12 (5.9%)	32 (8.1%)
35-44 years	40 (20.8%)	34 (16.8%)	74 (18.8%)
45-54 years	52 (27.1%)	54 (26.7%)	106 (26.9%)
55-64 years	46 (24.0%)	58 (28.7%)	104 (26.4%)
65-74 years	30 (15.6%)	35 (17.3%)	65 (16.5%)
75-94 years	4 (2.1%)	9 (4.5%)	13 (3.3%)
Gender			

Female	117 (60.9%)	143 (70.8%)	260 (66.0%)
Male	75 (39.1%)	59 (29.2%)	134 (34.0%)
One or more co-morbid condition			
No	89 (46.4%)	102 (50.5%)	191 (48.5%)
Yes	103 (53.6%)	100 (49.5%)	203 (51.5%)
Heart disease			
Not reported	192 (100.0%)	202 (100.0%)	394 (100.0%)
Acute myocardial infarction			
Not reported	192 (100.0%)	201 (99.5%)	393 (99.7%)
Yes	0 (0.0%)	1 (0.5%)	1 (0.3%)
Angina			
Not reported	192 (100.0%)	202 (100.0%)	394 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	192 (100.0%)	202 (100.0%)	394 (100.0%)
Other acute ischemic heart disease			
Not reported	192 (100.0%)	202 (100.0%)	394 (100.0%)
Chronic ischaemic heart disease			
Not reported	185 (96.4%)	198 (98.0%)	383 (97.2%)
Yes	7 (3.6%)	4 (2.0%)	11 (2.8%)
Factor	Tofacitinib	IL-17Ai	All
N	192	202	394
Hypertension			

Not reported	154 (80.2%)	163 (80.7%)	317 (80.5%)
Yes	38 (19.8%)	39 (19.3%)	77 (19.5%)
Atrioventricular block			
Not reported	192 (100.0%)	202 (100.0%)	394 (100.0%)
Peripheral vascular disease			
Not reported	191 (99.5%)	200 (99.0%)	391 (99.2%)
Yes	1 (0.5%)	2 (1.0%)	3 (0.8%)
Chronic obstructive pulmonary disease			
Not reported	190 (99.0%)	201 (99.5%)	391 (99.2%)
Yes	2 (1.0%)	1 (0.5%)	3 (0.8%)
Diabetes mellitus			
Not reported	185 (96.4%)	187 (92.6%)	372 (94.4%)
Yes	7 (3.6%)	15 (7.4%)	22 (5.6%)
Hyperlipidaemia			
Not reported	169 (88.0%)	191 (94.6%)	360 (91.4%)
Yes	23 (12.0%)	11 (5.4%)	34 (8.6%)
Obesity			
Not reported	190 (99.0%)	195 (96.5%)	385 (97.7%)
Yes	2 (1.0%)	7 (3.5%)	9 (2.3%)
Hiatal hernia			
Not reported	192 (100.0%)	201 (99.5%)	393 (99.7%)
Yes	0 (0.0%)	1 (0.5%)	1 (0.3%)

Gastrooesophageal reflux disease			
Not reported	164 (85.4%)	183 (90.6%)	347 (88.1%)
Yes	28 (14.6%)	19 (9.4%)	47 (11.9%)
Peptic ulcer disease			
Not reported	191 (99.5%)	202 (100.0%)	393 (99.7%)
Yes	1 (0.5%)	0 (0.0%)	1 (0.3%)
Crohn's disease			
Not reported	189 (98.4%)	200 (99.0%)	389 (98.7%)
Factor	Tofacitinib	IL-17Ai	All
N	192	202	394
Yes	3 (1.6%)	2 (1.0%)	5 (1.3%)
Ulcerative colitis			
Not reported	188 (97.9%)	201 (99.5%)	389 (98.7%)
Yes	4 (2.1%)	1 (0.5%)	5 (1.3%)
Non-alcoholic fatty liver disease			
Not reported	187 (97.4%)	193 (95.5%)	380 (96.4%)
Yes	5 (2.6%)	9 (4.5%)	14 (3.6%)
Any tumour			
Not reported	192 (100.0%)	202 (100.0%)	394 (100.0%)
Osteoporosis			
Not reported	190 (99.0%)	202 (100.0%)	392 (99.5%)
Yes	2 (1.0%)	0 (0.0%)	2 (0.5%)

Iridocylitis (uveitis)			
Not reported	189 (98.4%)	201 (99.5%)	390 (99.0%)
Yes	3 (1.6%)	1 (0.5%)	4 (1.0%)
Psoriasis			
Not reported	149 (77.6%)	150 (74.3%)	299 (75.9%)
Yes	43 (22.4%)	52 (25.7%)	95 (24.1%)
Malignancy			
Not reported	167 (87.0%)	178 (88.1%)	345 (87.6%)
Yes	25 (13.0%)	24 (11.9%)	49 (12.4%)

Table 1diii Demographics - Matched Population: Tofacitinib/TNFi groups , Subgroup: Second or later Line

Factor	Tofacitinib	TNFi	All
N	179	177	356
Age at index (years), mean (SD)	51.05 (13.11) (n=179)	52.24 (13.26) (n=177)	51.64 (13.18) (n=356)
Age at index (years), median (range)	50.00 (19.00, 93.00) (n=179)	52.00 (25.00, 80.00) (n=177)	51.00 (19.00, 93.00) (n=356)
Age category at index (years)			
18-34 years	20 (11.2%)	18 (10.2%)	38 (10.7%)
35-44 years	40 (22.3%)	30 (16.9%)	70 (19.7%)
45-54 years	50 (27.9%)	51 (28.8%)	101 (28.4%)
55-64 years	40 (22.3%)	46 (26.0%)	86 (24.2%)

65-74 years	23 (12.8%)	25 (14.1%)	48 (13.5%)
75-94 years	6 (3.4%)	7 (4.0%)	13 (3.7%)
Gender			
Female	123 (68.7%)	135 (76.3%)	258 (72.5%)
Male	56 (31.3%)	42 (23.7%)	98 (27.5%)
One or more co-morbid condition			
No	92 (51.4%)	89 (50.3%)	181 (50.8%)
Yes	87 (48.6%)	88 (49.7%)	175 (49.2%)
Heart disease			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Acute myocardial infarction			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Angina			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Certain complications following acute myocardial infarction			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Other acute ischemic heart disease			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Chronic ischaemic heart disease			
Not reported	176 (98.3%)	173 (97.7%)	349 (98.0%)
Yes	3 (1.7%)	4 (2.3%)	7 (2.0%)
Hypertension			

Factor	Tofacitinib	TNFi	All
N	179	177	356
Not reported	146 (81.6%)	152 (85.9%)	298 (83.7%)
Yes	33 (18.4%)	25 (14.1%)	58 (16.3%)
Atrioventricular block			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Peripheral vascular disease			
Not reported	177 (98.9%)	174 (98.3%)	351 (98.6%)
Yes	2 (1.1%)	3 (1.7%)	5 (1.4%)
Chronic obstructive pulmonary disease			
Not reported	178 (99.4%)	177 (100.0%)	355 (99.7%)
Yes	1 (0.6%)	0 (0.0%)	1 (0.3%)
Diabetes mellitus			
Not reported	172 (96.1%)	170 (96.0%)	342 (96.1%)
Yes	7 (3.9%)	7 (4.0%)	14 (3.9%)
Hyperlipidaemia			
Not reported	161 (89.9%)	163 (92.1%)	324 (91.0%)
Yes	18 (10.1%)	14 (7.9%)	32 (9.0%)
Obesity			
Not reported	178 (99.4%)	171 (96.6%)	349 (98.0%)
Yes	1 (0.6%)	6 (3.4%)	7 (2.0%)
Hiatal hernia			

Not reported	179 (100.0%)	176 (99.4%)	355 (99.7%)
Yes	0 (0.0%)	1 (0.6%)	1 (0.3%)
Gastrooesophageal reflux disease			
Not reported	156 (87.2%)	159 (89.8%)	315 (88.5%)
Yes	23 (12.8%)	18 (10.2%)	41 (11.5%)
Peptic ulcer disease			
Not reported	178 (99.4%)	177 (100.0%)	355 (99.7%)
Yes	1 (0.6%)	0 (0.0%)	1 (0.3%)
Crohn's disease			
Not reported	176 (98.3%)	173 (97.7%)	349 (98.0%)
Yes	3 (1.7%)	4 (2.3%)	7 (2.0%)
Factor	Tofacitinib	TNFi	All
N	179	177	356
Ulcerative colitis			
Not reported	176 (98.3%)	176 (99.4%)	352 (98.9%)
Yes	3 (1.7%)	1 (0.6%)	4 (1.1%)
Non-alcoholic fatty liver disease			
Not reported	176 (98.3%)	166 (93.8%)	342 (96.1%)
Yes	3 (1.7%)	11 (6.2%)	14 (3.9%)
Any tumour			
Not reported	179 (100.0%)	177 (100.0%)	356 (100.0%)
Osteoporosis			

Not reported	177 (98.9%)	176 (99.4%)	353 (99.2%)
Yes	2 (1.1%)	1 (0.6%)	3 (0.8%)
Iridocylitis (uveitis)			
Not reported	177 (98.9%)	175 (98.9%)	352 (98.9%)
Yes	2 (1.1%)	2 (1.1%)	4 (1.1%)
Psoriasis			
Not reported	144 (80.4%)	131 (74.0%)	275 (77.2%)
Yes	35 (19.6%)	46 (26.0%)	81 (22.8%)
Malignancy			
Not reported	160 (89.4%)	165 (93.2%)	325 (91.3%)
Yes	19 (10.6%)	12 (6.8%)	31 (8.7%)

Table 2i Clinical Characteristics at Index - All Eligible patients

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
Time from symptom onset(months), mean (SD)	140.98 (107.90) (n=182)	141.61 (106.88) (n=172)	107.26 (97.16) (n=267)	126.66 (104.33) (n=621)
Time from symptom onset(months), median (range)	110.44 (4.96, 614.60) (n=182)	113.31 (2.14, 481.03) (n=172)	72.22 (0.66, 592.74) (n=267)	94.44 (0.66, 614.60) (n=621)
Time since first seen(months), mean (SD)	66.53 (61.53) (n=139)	70.75 (72.15) (n=141)	46.36 (60.35) (n=202)	59.31 (65.17) (n=482)
Time since first seen(months), median	48.09 (0.00, 312.06) (n=139)	49.57 (0.00, 407.23) (n=141)	24.75 (0.00, 414.20) (n=202)	39.12 (0.00, 414.20) (n=482)

(range)				
DAS28CRP, mean (SD)	3.53 (1.38) (n=66)	3.45 (1.55) (n=80)	3.96 (1.56) (n=145)	3.72 (1.53) (n=291)
DAS28CRP, median (range)	3.40 (1.30, 6.40) (n=66)	3.25 (1.20, 8.10) (n=80)	3.80 (1.30, 7.40) (n=145)	3.60 (1.20, 8.10) (n=291)
DAS28CRP Category				
Remission	20 (4.9%)	26 (6.2%)	33 (5.0%)	79 (5.3%)
Low	9 (2.2%)	12 (2.9%)	13 (2.0%)	34 (2.3%)
Moderate	28 (6.9%)	32 (7.7%)	69 (10.4%)	129 (8.7%)
High	9 (2.2%)	10 (2.4%)	30 (4.5%)	49 (3.3%)
Missing	340 (83.7%)	336 (80.8%)	519 (78.2%)	1195 (80.4%)
DAS28CRP(3), mean (SD)	3.31 (1.39) (n=171)	3.50 (1.46) (n=174)	3.86 (1.47) (n=293)	3.62 (1.46) (n=638)
DAS28CRP(3), median (range)	3.17 (1.28, 7.59) (n=171)	3.25 (1.15, 7.58) (n=174)	3.83 (1.28, 7.10) (n=293)	3.47 (1.15, 7.59) (n=638)
DAS28CRP3 Category				
Remission	59 (14.5%)	54 (13.0%)	63 (9.5%)	176 (11.8%)
Low	29 (7.1%)	30 (7.2%)	39 (5.9%)	98 (6.6%)
Moderate	62 (15.3%)	64 (15.4%)	124 (18.7%)	250 (16.8%)
High	21 (5.2%)	26 (6.2%)	67 (10.1%)	114 (7.7%)
Missing	235 (57.9%)	242 (58.2%)	371 (55.9%)	848 (57.1%)
DAS28ESR, mean (SD)	3.34 (1.57) (n=65)	3.40 (1.81) (n=78)	3.78 (1.67) (n=144)	3.58 (1.70) (n=287)
DAS28ESR, median (range)	3.30 (0.50, 7.50) (n=65)	3.50 (0.00, 8.90) (n=78)	3.60 (0.10, 7.90) (n=144)	3.50 (0.00, 8.90) (n=287)

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
DAS28ESR Category				
Remission	22 (5.4%)	28 (6.7%)	39 (5.9%)	89 (6.0%)
Low	9 (2.2%)	9 (2.2%)	20 (3.0%)	38 (2.6%)
Moderate	25 (6.2%)	26 (6.2%)	50 (7.5%)	101 (6.8%)
High	9 (2.2%)	15 (3.6%)	35 (5.3%)	59 (4.0%)
Missing	341 (84.0%)	338 (81.2%)	520 (78.3%)	1199 (80.7%)
SDAI, mean (SD)	17.15 (12.91) (n=61)	16.93 (15.84) (n=78)	22.53 (17.47) (n=142)	19.81 (16.31) (n=281)
SDAI Category				
Remission	10 (2.5%)	13 (3.1%)	12 (1.8%)	35 (2.4%)
Low	13 (3.2%)	23 (5.5%)	27 (4.1%)	63 (4.2%)
Moderate	26 (6.4%)	25 (6.0%)	59 (8.9%)	110 (7.4%)
High	12 (3.0%)	17 (4.1%)	44 (6.6%)	73 (4.9%)
Missing	345 (85.0%)	338 (81.2%)	522 (78.6%)	1205 (81.1%)
CDAI, mean (SD)	16.48 (12.86) (n=61)	16.26 (15.09) (n=82)	21.64 (17.12) (n=146)	19.03 (15.91) (n=289)
CDAI Category				
Remission	9 (2.2%)	13 (3.1%)	14 (2.1%)	36 (2.4%)
Low	14 (3.4%)	24 (5.8%)	29 (4.4%)	67 (4.5%)
Moderate	22 (5.4%)	21 (5.0%)	43 (6.5%)	86 (5.8%)
High	16 (3.9%)	24 (5.8%)	60 (9.0%)	100 (6.7%)
Missing	345 (85.0%)	334 (80.3%)	518 (78.0%)	1197 (80.6%)

DAPSA, mean (SD)	29.16 (21.91) (n=61)	32.19 (34.35) (n=66)	41.80 (36.63) (n=128)	36.29 (33.44) (n=255)
DAPSA Category				
Remission	3 (0.7%)	3 (0.7%)	6 (0.9%)	12 (0.8%)
Low	17 (4.2%)	16 (3.8%)	20 (3.0%)	53 (3.6%)
High	13 (3.2%)	19 (4.6%)	35 (5.3%)	67 (4.5%)
Very High	28 (6.9%)	28 (6.7%)	67 (10.1%)	123 (8.3%)
Missing	345 (85.0%)	350 (84.1%)	536 (80.7%)	1231 (82.8%)
TJC28, mean (SD)	4.85 (6.24) (n=177)	5.60 (6.66) (n=183)	7.42 (7.78) (n=301)	6.23 (7.17) (n=661)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
TJC28, median (range)	2.00 (0.00, 25.00) (n=177)	2.00 (0.00, 25.00) (n=183)	4.00 (0.00, 28.00) (n=301)	4.00 (0.00, 28.00) (n=661)
TJC68, mean (SD)	7.94 (11.23) (n=177)	9.91 (12.00) (n=183)	13.38 (14.62) (n=301)	10.96 (13.26) (n=661)
TJC68, median (range)	4.00 (0.00, 57.00) (n=177)	5.00 (0.00, 58.00) (n=183)	8.00 (0.00, 61.00) (n=301)	6.00 (0.00, 61.00) (n=661)
SJC28, mean (SD)	4.22 (5.73) (n=177)	5.25 (6.45) (n=183)	6.82 (7.57) (n=301)	5.69 (6.89) (n=661)
SJC28, median (range)	2.00 (0.00, 25.00) (n=177)	2.00 (0.00, 25.00) (n=183)	4.00 (0.00, 28.00) (n=301)	3.00 (0.00, 28.00) (n=661)
SJC66, mean (SD)	6.15 (8.87) (n=177)	8.94 (11.50) (n=183)	11.47 (13.73) (n=301)	9.34 (12.16) (n=661)
SJC66, median (range)	3.00 (0.00, 56.00) (n=177)	4.00 (0.00, 58.00) (n=183)	6.00 (0.00, 60.00) (n=301)	5.00 (0.00, 60.00) (n=661)
CRP, mean (SD)	7.19 (10.63) (n=171)	6.84 (10.15) (n=174)	9.16 (24.35) (n=294)	8.00 (18.21) (n=639)
CRP, median (range)	4.00 (0.40, 99.00) (n=171)	4.20 (0.00, 96.00) (n=174)	4.00 (0.00, 353.00) (n=294)	4.00 (0.00, 353.00) (n=639)
Physician Skin Assessment, mean (SD)	12.36 (19.50) (n=55)	18.09 (20.37) (n=65)	16.32 (21.58) (n=139)	15.92 (20.87) (n=259)
Physician Skin	5.00 (0.00, 84.00) (n=55)	10.00 (0.00, 90.00) (n=65)	10.00 (0.00, 100.00)	10.00 (0.00, 100.00)

Assessment, median (range)			(n=139)	(n=259)
Patient Skin Assessment, mean (SD)	13.85 (20.95) (n=54)	23.72 (26.22) (n=58)	20.13 (24.82) (n=128)	19.59 (24.50) (n=240)
Patient Skin Assessment, median (range)	6.50 (0.00, 82.00) (n=54)	15.00 (0.00, 90.00) (n=58)	10.00 (0.00, 94.00) (n=128)	10.00 (0.00, 94.00) (n=240)
HAQDI13, mean (SD)	0.77 (0.58) (n=15)	0.92 (0.50) (n=14)	0.69 (0.61) (n=21)	0.78 (0.57) (n=50)
HAQDI13, median (range)	0.80 (0.00, 2.20) (n=15)	0.90 (0.30, 2.30) (n=14)	0.40 (0.00, 2.10) (n=21)	0.80 (0.00, 2.30) (n=50)
HCRU Q1 Dr/nurse visits?				
No	22 (5.4%)	18 (4.3%)	26 (3.9%)	66 (4.4%)
Yes	4 (1.0%)	2 (0.5%)	6 (0.9%)	12 (0.8%)
Missing	380 (93.6%)	396 (95.2%)	632 (95.2%)	1408 (94.8%)
HCRU Q2 seen in emergency?				
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
No	1 (0.2%)	5 (1.2%)	3 (0.5%)	9 (0.6%)
Yes	25 (6.2%)	15 (3.6%)	29 (4.4%)	69 (4.6%)
Missing	380 (93.6%)	396 (95.2%)	632 (95.2%)	1408 (94.8%)
HCRU Q3 hospitalised?				
No	2 (0.5%)	1 (0.2%)	1 (0.2%)	4 (0.3%)
Yes	24 (5.9%)	19 (4.6%)	31 (4.7%)	74 (5.0%)
Missing	380 (93.6%)	396 (95.2%)	632 (95.2%)	1408 (94.8%)

HCRU Q4 outpatients operations?				
No	4 (1.0%)	2 (0.5%)	7 (1.1%)	13 (0.9%)
Yes	22 (5.4%)	18 (4.3%)	25 (3.8%)	65 (4.4%)
Missing	380 (93.6%)	396 (95.2%)	632 (95.2%)	1408 (94.8%)
HCRU Q5 seen allied HPs?				
No	10 (2.5%)	3 (0.7%)	11 (1.7%)	24 (1.6%)
Yes	16 (3.9%)	17 (4.1%)	21 (3.2%)	54 (3.6%)
Missing	380 (93.6%)	396 (95.2%)	632 (95.2%)	1408 (94.8%)
HCRU Q6 seen alternative HPs?				
No	5 (1.2%)	1 (0.2%)	7 (1.1%)	13 (0.9%)
Yes	21 (5.2%)	19 (4.6%)	25 (3.8%)	65 (4.4%)
Missing	380 (93.6%)	396 (95.2%)	632 (95.2%)	1408 (94.8%)
FACIT Score, mean (SD)	29.74 (11.90) (n=27)	28.45 (12.74) (n=20)	31.71 (12.69) (n=35)	30.27 (12.37) (n=82)
FACIT Score, median (range)	29.00 (4.00, 48.00) (n=27)	26.00 (6.00, 47.00) (n=20)	34.00 (5.00, 50.00) (n=35)	31.50 (4.00, 50.00) (n=82)
NSAID				
No	219 (53.9%)	203 (48.8%)	366 (55.1%)	788 (53.0%)
Yes	187 (46.1%)	213 (51.2%)	298 (44.9%)	698 (47.0%)
corticosteroid				
No	207 (51.0%)	211 (50.7%)	307 (46.2%)	725 (48.8%)
Yes	199 (49.0%)	205 (49.3%)	357 (53.8%)	761 (51.2%)
Number of Prior biologics				

0	78 (19.2%)	174 (41.8%)	417 (62.8%)	669 (45.0%)
1	101 (24.9%)	119 (28.6%)	145 (21.8%)	365 (24.6%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	406	416	664	1486
2	91 (22.4%)	68 (16.3%)	64 (9.6%)	223 (15.0%)
3	71 (17.5%)	33 (7.9%)	23 (3.5%)	127 (8.5%)
>=4	65 (16.0%)	22 (5.3%)	15 (2.3%)	102 (6.9%)
Duration of prior bDMARD (total)				
>0 to <12 weeks	9 (2.2%)	0 (0.0%)	1 (0.2%)	10 (0.7%)
12 to <24 weeks	22 (5.4%)	8 (1.9%)	5 (0.8%)	35 (2.4%)
24 to <52 weeks	37 (9.1%)	9 (2.2%)	16 (2.4%)	62 (4.2%)
52 to <76 weeks	22 (5.4%)	12 (2.9%)	12 (1.8%)	46 (3.1%)
76 to <104 weeks	22 (5.4%)	21 (5.0%)	16 (2.4%)	59 (4.0%)
104 weeks or more	94 (23.2%)	75 (18.0%)	58 (8.7%)	227 (15.3%)
N/A (no prior bDMARD)	78 (19.2%)	174 (41.8%)	417 (62.8%)	669 (45.0%)
Missing	122 (30.0%)	117 (28.1%)	139 (20.9%)	378 (25.4%)
Number of Prior cDMARDs				
0	51 (12.6%)	74 (17.8%)	106 (16.0%)	231 (15.5%)
1	100 (24.6%)	140 (33.7%)	185 (27.9%)	425 (28.6%)
2	180 (44.3%)	157 (37.7%)	284 (42.8%)	621 (41.8%)
3	69 (17.0%)	39 (9.4%)	83 (12.5%)	191 (12.9%)

4	5 (1.2%)	6 (1.4%)	6 (0.9%)	17 (1.1%)
5	1 (0.2%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Prior Methotrexate dose, mean (SD)	3.29 (3.49) (n=286)	3.08 (2.88) (n=271)	3.04 (3.06) (n=421)	3.12 (3.14) (n=978)
Prior Sulfasalazine dose, mean (SD)	1887.60 (654.94) (n=40)	1546.60 (968.49) (n=43)	1731.30 (923.37) (n=106)	1722.36 (887.49) (n=189)
Combination information				
With Meth + other cDMARD	113 (27.8%)	124 (29.8%)	237 (35.7%)	474 (31.9%)
With Methotrexate only	97 (23.9%)	95 (22.8%)	147 (22.1%)	339 (22.8%)
With other cDMARD	57 (14.0%)	60 (14.4%)	105 (15.8%)	222 (14.9%)
bDMARD monotherapy	139 (34.2%)	137 (32.9%)	175 (26.4%)	451 (30.3%)

Note: Doses displayed are as captured in mgdoseperday field - dosing schedule may vary Note: insufficient information to summarise dose for previous cDMARDs other than Methotrexate and Sulfasalazine Note: HCRU information and FACIT scores only summarised where >5 patients in total have this information recorded Note: A window of -3 months to 1.5 months around the index date has been applied. Where there are multiple readings within this period, readings prior to Index are prioritised, followed by readings that are the closest to the Index date

Table 2ii Clinical Characteristics at Index - Matched Population: Tofacitinib/IL-17Ai groups

Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
Time from symptom onset(months), mean (SD)	139.38 (115.43) (n=127)	148.98 (101.54) (n=122)	144.09 (108.73) (n=249)
Time from symptom onset(months), median (range)	101.84 (4.96, 614.60) (n=127)	124.56 (13.45, 474.79) (n=122)	113.28 (4.96, 614.60) (n=249)
Time since first seen(months),	62.09 (69.65) (n=92)	77.99 (74.20) (n=102)	70.45 (72.33) (n=194)

mean (SD)			
Time since first seen(months), median (range)	37.84 (0.00, 312.06) (n=92)	52.83 (0.00, 407.23) (n=102)	45.17 (0.00, 407.23) (n=194)
DAS28CRP, mean (SD)	3.73 (1.29) (n=44)	3.32 (1.52) (n=60)	3.49 (1.44) (n=104)
DAS28CRP, median (range)	3.90 (1.30, 6.40) (n=44)	3.10 (1.20, 7.30) (n=60)	3.35 (1.20, 7.30) (n=104)
DAS28CRP Category			
Remission	9 (3.3%)	21 (7.8%)	30 (5.6%)
Low	7 (2.6%)	11 (4.1%)	18 (3.3%)
Moderate	22 (8.2%)	21 (7.8%)	43 (8.0%)
High	6 (2.2%)	7 (2.6%)	13 (2.4%)
Missing	225 (83.6%)	209 (77.7%)	434 (80.7%)
DAS28CRP(3), mean (SD)	3.54 (1.40) (n=112)	3.28 (1.41) (n=119)	3.41 (1.41) (n=231)
DAS28CRP(3), median (range)	3.41 (1.28, 7.59) (n=112)	3.03 (1.15, 7.06) (n=119)	3.17 (1.15, 7.59) (n=231)
DAS28CRP3 Category			
Remission	30 (11.2%)	45 (16.7%)	75 (13.9%)
Low	20 (7.4%)	23 (8.6%)	43 (8.0%)
Moderate	44 (16.4%)	37 (13.8%)	81 (15.1%)
High	18 (6.7%)	14 (5.2%)	32 (5.9%)
Missing	157 (58.4%)	150 (55.8%)	307 (57.1%)
DAS28ESR, mean (SD)	3.48 (1.42) (n=43)	3.27 (1.80) (n=58)	3.36 (1.64) (n=101)
DAS28ESR, median (range)	3.50 (0.50, 6.80) (n=43)	3.00 (0.00, 7.90) (n=58)	3.40 (0.00, 7.90) (n=101)
DAS28ESR Category			

Remission	10 (3.7%)	23 (8.6%)	33 (6.1%)
Low	7 (2.6%)	7 (2.6%)	14 (2.6%)
Moderate	21 (7.8%)	18 (6.7%)	39 (7.2%)
High	5 (1.9%)	10 (3.7%)	15 (2.8%)
Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
Missing	226 (84.0%)	211 (78.4%)	437 (81.2%)
SDAI, mean (SD)	19.40 (13.11) (n=42)	16.00 (15.19) (n=60)	17.40 (14.40) (n=102)
SDAI Category			
Remission	4 (1.5%)	10 (3.7%)	14 (2.6%)
Low	8 (3.0%)	20 (7.4%)	28 (5.2%)
Moderate	21 (7.8%)	18 (6.7%)	39 (7.2%)
High	9 (3.3%)	12 (4.5%)	21 (3.9%)
Missing	227 (84.4%)	209 (77.7%)	436 (81.0%)
CDAI, mean (SD)	18.70 (13.07) (n=42)	15.48 (14.78) (n=64)	16.76 (14.15) (n=106)
CDAI Category			
Remission	3 (1.1%)	10 (3.7%)	13 (2.4%)
Low	9 (3.3%)	22 (8.2%)	31 (5.8%)
Moderate	17 (6.3%)	15 (5.6%)	32 (5.9%)
High	13 (4.8%)	17 (6.3%)	30 (5.6%)
Missing	227 (84.4%)	205 (76.2%)	432 (80.3%)
DAPSA, mean (SD)	31.52 (22.34) (n=40)	29.73 (26.20) (n=48)	30.54 (24.40) (n=88)

DAPSA Category			
Remission	1 (0.4%)	3 (1.1%)	4 (0.7%)
Low	9 (3.3%)	10 (3.7%)	19 (3.5%)
High	10 (3.7%)	16 (5.9%)	26 (4.8%)
Very High	20 (7.4%)	19 (7.1%)	39 (7.2%)
Missing	229 (85.1%)	221 (82.2%)	450 (83.6%)
TJC28, mean (SD)	5.76 (6.72) (n=117)	4.68 (6.24) (n=127)	5.20 (6.49) (n=244)
TJC28, median (range)	4.00 (0.00, 25.00) (n=117)	2.00 (0.00, 24.00) (n=127)	2.00 (0.00, 25.00) (n=244)
TJC68, mean (SD)	9.45 (12.63) (n=117)	8.28 (10.95) (n=127)	8.84 (11.77) (n=244)
TJC68, median (range)	5.00 (0.00, 57.00) (n=117)	4.00 (0.00, 46.00) (n=127)	4.00 (0.00, 57.00) (n=244)
SJC28, mean (SD)	5.15 (6.21) (n=117)	4.31 (5.74) (n=127)	4.71 (5.98) (n=244)
SJC28, median (range)	3.00 (0.00, 25.00) (n=117)	2.00 (0.00, 24.00) (n=127)	2.00 (0.00, 25.00) (n=244)
Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
SJC66, mean (SD)	7.57 (9.84) (n=117)	7.20 (9.89) (n=127)	7.38 (9.85) (n=244)
SJC66, median (range)	4.00 (0.00, 56.00) (n=117)	3.00 (0.00, 45.00) (n=127)	4.00 (0.00, 56.00) (n=244)
CRP, mean (SD)	7.00 (11.44) (n=112)	6.83 (8.05) (n=119)	6.91 (9.82) (n=231)
CRP, median (range)	4.15 (0.40, 99.00) (n=112)	5.00 (0.00, 51.00) (n=119)	4.70 (0.00, 99.00) (n=231)
Physician Skin Assessment, mean (SD)	9.78 (13.05) (n=37)	13.37 (15.25) (n=49)	11.83 (14.37) (n=86)
Physician Skin Assessment, median (range)	7.00 (0.00, 54.00) (n=37)	10.00 (0.00, 58.00) (n=49)	8.00 (0.00, 58.00) (n=86)
Patient Skin Assessment, mean	10.94 (15.09) (n=35)	18.42 (20.91) (n=45)	15.15 (18.85) (n=80)

(SD)			
Patient Skin Assessment, median (range)	8.00 (0.00, 60.00) (n=35)	10.00 (0.00, 86.00) (n=45)	10.00 (0.00, 86.00) (n=80)
HAQDI13, mean (SD)	0.72 (0.43) (n=11)	0.88 (0.33) (n=9)	0.79 (0.39) (n=20)
HAQDI13, median (range)	0.80 (0.00, 1.30) (n=11)	1.10 (0.30, 1.20) (n=9)	0.80 (0.00, 1.30) (n=20)
HCRU Q1 Dr/nurse visits?			
No	14 (5.2%)	12 (4.5%)	26 (4.8%)
Yes	4 (1.5%)	2 (0.7%)	6 (1.1%)
Missing	251 (93.3%)	255 (94.8%)	506 (94.1%)
HCRU Q2 seen in emergency?			
No	0 (0.0%)	5 (1.9%)	5 (0.9%)
Yes	18 (6.7%)	9 (3.3%)	27 (5.0%)
Missing	251 (93.3%)	255 (94.8%)	506 (94.1%)
HCRU Q3 hospitalised?			
No	1 (0.4%)	1 (0.4%)	2 (0.4%)
Yes	17 (6.3%)	13 (4.8%)	30 (5.6%)
Missing	251 (93.3%)	255 (94.8%)	506 (94.1%)
HCRU Q4 outpatients operations?			
No	3 (1.1%)	1 (0.4%)	4 (0.7%)
Yes	15 (5.6%)	13 (4.8%)	28 (5.2%)
Missing	251 (93.3%)	255 (94.8%)	506 (94.1%)
HCRU Q5 seen allied HPs?			

No	6 (2.2%)	3 (1.1%)	9 (1.7%)
Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
Yes	12 (4.5%)	11 (4.1%)	23 (4.3%)
Missing	251 (93.3%)	255 (94.8%)	506 (94.1%)
HCRU Q6 seen alternative HPs?			
No	3 (1.1%)	1 (0.4%)	4 (0.7%)
Yes	15 (5.6%)	13 (4.8%)	28 (5.2%)
Missing	251 (93.3%)	255 (94.8%)	506 (94.1%)
FACIT Score, mean (SD)	29.19 (11.83) (n=19)	28.64 (12.19) (n=14)	28.96 (11.80) (n=33)
FACIT Score, median (range)	27.00 (15.00, 48.00) (n=19)	28.00 (6.00, 45.00) (n=14)	27.00 (6.00, 48.00) (n=33)
NSAID			
No	138 (51.3%)	132 (49.1%)	270 (50.2%)
Yes	131 (48.7%)	137 (50.9%)	268 (49.8%)
corticosteroid			
No	139 (51.7%)	140 (52.0%)	279 (51.9%)
Yes	130 (48.3%)	129 (48.0%)	259 (48.1%)
Number of Prior biologics			
0	77 (28.6%)	67 (24.9%)	144 (26.8%)
1	99 (36.8%)	79 (29.4%)	178 (33.1%)
2	36 (13.4%)	68 (25.3%)	104 (19.3%)
3	33 (12.3%)	33 (12.3%)	66 (12.3%)

>=4	24 (8.9%)	22 (8.2%)	46 (8.6%)
Duration of prior bDMARD (total)			
>0 to <12 weeks	7 (2.6%)	0 (0.0%)	7 (1.3%)
12 to <24 weeks	17 (6.3%)	7 (2.6%)	24 (4.5%)
24 to <52 weeks	24 (8.9%)	6 (2.2%)	30 (5.6%)
52 to <76 weeks	12 (4.5%)	11 (4.1%)	23 (4.3%)
76 to <104 weeks	14 (5.2%)	18 (6.7%)	32 (5.9%)
104 weeks or more	46 (17.1%)	63 (23.4%)	109 (20.3%)
N/A (no prior bDMARD)	77 (28.6%)	67 (24.9%)	144 (26.8%)
Missing	72 (26.8%)	97 (36.1%)	169 (31.4%)
Number of Prior cDMARDs			
Factor	Tofacitinib	IL-17Ai	All
N	269	269	538
0	43 (16.0%)	41 (15.2%)	84 (15.6%)
1	59 (21.9%)	88 (32.7%)	147 (27.3%)
2	120 (44.6%)	106 (39.4%)	226 (42.0%)
3	44 (16.4%)	28 (10.4%)	72 (13.4%)
4	2 (0.7%)	6 (2.2%)	8 (1.5%)
5	1 (0.4%)	0 (0.0%)	1 (0.2%)
Prior Methotrexate dose, mean (SD)	3.22 (3.17) (n=173)	3.27 (3.38) (n=191)	3.25 (3.28) (n=364)
Prior Sulfasalazine dose, mean (SD)	2018.00 (615.39) (n=28)	1553.71 (1012.10) (n=28)	1785.86 (862.34) (n=56)

Combination information			
With Meth + other cDMARD	70 (26.0%)	68 (25.3%)	138 (25.7%)
With Methotrexate only	63 (23.4%)	72 (26.8%)	135 (25.1%)
With other cDMARD	41 (15.2%)	38 (14.1%)	79 (14.7%)
bDMARD monotherapy	95 (35.3%)	91 (33.8%)	186 (34.6%)

Note: Doses displayed are as captured in mgdoseperday field - dosing schedule may vary Note: insufficient information to summarise dose for previous cDMARDs other than Methotrexate and Sulfasalazine Note: HCRU information and FACIT scores only summarised where >5 patients in total have this information recorded Note: A window of -3 months to 1.5 months around the index date has been applied. Where there are multiple readings within this period, readings prior to Index are prioritised, followed by readings that are the closest to the Index date

Table 2iii Clinical Characteristics at Index - Matched Population: Tofacitinib/TNFi groups

Factor	Tofacitinib	TNFi	All
N	256	256	512
Time from symptom onset(months), mean (SD)	137.71 (116.93) (n=122)	111.38 (85.83) (n=111)	125.17 (103.91) (n=233)
Time from symptom onset(months), median (range)	94.41 (4.96, 614.60) (n=122)	81.56 (0.66, 414.20) (n=111)	87.84 (0.66, 614.60) (n=233)
Time since first seen(months), mean (SD)	53.01 (58.84) (n=86)	54.25 (60.49) (n=86)	53.63 (59.50) (n=172)
Time since first seen(months), median (range)	36.69 (0.00, 280.64) (n=86)	31.28 (0.00, 414.20) (n=86)	35.52 (0.00, 414.20) (n=172)
DAS28CRP, mean (SD)	3.79 (1.26) (n=43)	3.52 (1.31) (n=58)	3.63 (1.29) (n=101)
DAS28CRP, median (range)	4.00 (1.50, 6.40) (n=43)	3.35 (1.60, 6.80) (n=58)	3.50 (1.50, 6.80) (n=101)

DAS28CRP Category			
Remission	8 (3.1%)	16 (6.2%)	24 (4.7%)
Low	7 (2.7%)	9 (3.5%)	16 (3.1%)
Moderate	22 (8.6%)	28 (10.9%)	50 (9.8%)
High	6 (2.3%)	5 (2.0%)	11 (2.1%)
Missing	213 (83.2%)	198 (77.3%)	411 (80.3%)
DAS28CRP(3), mean (SD)	3.52 (1.35) (n=106)	3.50 (1.39) (n=118)	3.51 (1.37) (n=224)
DAS28CRP(3), median (range)	3.43 (1.28, 6.61) (n=106)	3.26 (1.36, 7.10) (n=118)	3.35 (1.28, 7.10) (n=224)
DAS28CRP3 Category			
Remission	29 (11.3%)	36 (14.1%)	65 (12.7%)
Low	18 (7.0%)	22 (8.6%)	40 (7.8%)
Moderate	43 (16.8%)	42 (16.4%)	85 (16.6%)
High	16 (6.2%)	18 (7.0%)	34 (6.6%)
Missing	150 (58.6%)	138 (53.9%)	288 (56.2%)
DAS28ESR, mean (SD)	3.61 (1.40) (n=42)	3.29 (1.40) (n=57)	3.42 (1.40) (n=99)
DAS28ESR, median (range)	3.50 (0.50, 6.80) (n=42)	3.10 (0.50, 6.10) (n=57)	3.30 (0.50, 6.80) (n=99)
DAS28ESR Category			
Remission	9 (3.5%)	19 (7.4%)	28 (5.5%)
Low	7 (2.7%)	10 (3.9%)	17 (3.3%)
Moderate	20 (7.8%)	21 (8.2%)	41 (8.0%)
High	6 (2.3%)	7 (2.7%)	13 (2.5%)
Missing	214 (83.6%)	199 (77.7%)	413 (80.7%)

Factor	Tofacitinib	TNFi	All
N	256	256	512
SDAI, mean (SD)	19.96 (13.04) (n=41)	17.16 (13.70) (n=58)	18.32 (13.44) (n=99)
SDAI Category			
Remission	3 (1.2%)	5 (2.0%)	8 (1.6%)
Low	8 (3.1%)	16 (6.2%)	24 (4.7%)
Moderate	20 (7.8%)	26 (10.2%)	46 (9.0%)
High	10 (3.9%)	11 (4.3%)	21 (4.1%)
Missing	215 (84.0%)	198 (77.3%)	413 (80.7%)
CDAI, mean (SD)	19.25 (13.02) (n=41)	16.71 (13.60) (n=62)	17.72 (13.37) (n=103)
CDAI Category			
Remission	3 (1.2%)	8 (3.1%)	11 (2.1%)
Low	8 (3.1%)	15 (5.9%)	23 (4.5%)
Moderate	16 (6.2%)	20 (7.8%)	36 (7.0%)
High	14 (5.5%)	19 (7.4%)	33 (6.4%)
Missing	215 (84.0%)	194 (75.8%)	409 (79.9%)
DAPSA, mean (SD)	32.37 (22.41) (n=38)	28.71 (22.34) (n=50)	30.29 (22.31) (n=88)
DAPSA Category			
Remission	0 (0.0%)	1 (0.4%)	1 (0.2%)
Low	9 (3.5%)	10 (3.9%)	19 (3.7%)
High	10 (3.9%)	23 (9.0%)	33 (6.4%)
Very High	19 (7.4%)	16 (6.2%)	35 (6.8%)

Missing	218 (85.2%)	206 (80.5%)	424 (82.8%)
TJC28, mean (SD)	5.67 (6.43) (n=109)	5.89 (7.07) (n=123)	5.79 (6.76) (n=232)
TJC28, median (range)	4.00 (0.00, 24.00) (n=109)	3.00 (0.00, 26.00) (n=123)	3.00 (0.00, 26.00) (n=232)
TJC68, mean (SD)	9.16 (11.88) (n=109)	10.45 (12.85) (n=123)	9.84 (12.39) (n=232)
TJC68, median (range)	5.00 (0.00, 57.00) (n=109)	5.00 (0.00, 58.00) (n=123)	5.00 (0.00, 58.00) (n=232)
SJC28, mean (SD)	5.18 (6.10) (n=109)	5.33 (6.93) (n=123)	5.26 (6.53) (n=232)
SJC28, median (range)	3.00 (0.00, 24.00) (n=109)	2.00 (0.00, 26.00) (n=123)	2.50 (0.00, 26.00) (n=232)
SJC66, mean (SD)	7.64 (9.69) (n=109)	8.63 (11.84) (n=123)	8.16 (10.87) (n=232)
Factor	Tofacitinib	TNFi	All
N	256	256	512
SJC66, median (range)	4.00 (0.00, 56.00) (n=109)	4.00 (0.00, 58.00) (n=123)	4.00 (0.00, 58.00) (n=232)
CRP, mean (SD)	6.53 (7.88) (n=106)	7.37 (14.96) (n=119)	6.98 (12.13) (n=225)
CRP, median (range)	4.45 (0.40, 49.00) (n=106)	4.00 (0.30, 137.00) (n=119)	4.00 (0.30, 137.00) (n=225)
Physician Skin Assessment, mean (SD)	8.91 (11.37) (n=35)	13.00 (20.88) (n=55)	11.41 (17.83) (n=90)
Physician Skin Assessment, median (range)	7.00 (0.00, 54.00) (n=35)	6.00 (0.00, 87.00) (n=55)	6.00 (0.00, 87.00) (n=90)
Patient Skin Assessment, mean (SD)	10.09 (13.78) (n=33)	17.96 (24.33) (n=51)	14.87 (21.09) (n=84)
Patient Skin Assessment, median (range)	8.00 (0.00, 60.00) (n=33)	7.00 (0.00, 89.00) (n=51)	7.50 (0.00, 89.00) (n=84)
HAQDI13, mean (SD)	0.72 (0.43) (n=11)	0.79 (0.66) (n=9)	0.75 (0.53) (n=20)
HAQDI13, median (range)	0.80 (0.00, 1.30) (n=11)	0.50 (0.00, 2.10) (n=9)	0.65 (0.00, 2.10) (n=20)
HCRU Q1 Dr/nurse visits?			

No	15 (5.9%)	12 (4.7%)	27 (5.3%)
Yes	4 (1.6%)	3 (1.2%)	7 (1.4%)
Missing	237 (92.6%)	241 (94.1%)	478 (93.4%)
HCRU Q2 seen in emergency?			
No	0 (0.0%)	2 (0.8%)	2 (0.4%)
Yes	19 (7.4%)	13 (5.1%)	32 (6.2%)
Missing	237 (92.6%)	241 (94.1%)	478 (93.4%)
HCRU Q3 hospitalised?			
No	2 (0.8%)	1 (0.4%)	3 (0.6%)
Yes	17 (6.6%)	14 (5.5%)	31 (6.1%)
Missing	237 (92.6%)	241 (94.1%)	478 (93.4%)
HCRU Q4 outpatients operations?			
No	3 (1.2%)	3 (1.2%)	6 (1.2%)
Yes	16 (6.2%)	12 (4.7%)	28 (5.5%)
Missing	237 (92.6%)	241 (94.1%)	478 (93.4%)
HCRU Q5 seen allied HPs?			
No	6 (2.3%)	5 (2.0%)	11 (2.1%)
Yes	13 (5.1%)	10 (3.9%)	23 (4.5%)
Missing	237 (92.6%)	241 (94.1%)	478 (93.4%)
Factor	Tofacitinib	TNFi	All
N	256	256	512
HCRU Q6 seen alternative HPs?			

No	4 (1.6%)	3 (1.2%)	7 (1.4%)
Yes	15 (5.9%)	12 (4.7%)	27 (5.3%)
Missing	237 (92.6%)	241 (94.1%)	478 (93.4%)
FACIT Score, mean (SD)	29.58 (11.64) (n=20)	34.60 (13.73) (n=15)	31.73 (12.64) (n=35)
FACIT Score, median (range)	28.00 (15.00, 48.00) (n=20)	38.00 (5.00, 50.00) (n=15)	33.00 (5.00, 50.00) (n=35)
NSAID			
No	129 (50.4%)	146 (57.0%)	275 (53.7%)
Yes	127 (49.6%)	110 (43.0%)	237 (46.3%)
corticosteroid			
No	128 (50.0%)	126 (49.2%)	254 (49.6%)
Yes	128 (50.0%)	130 (50.8%)	258 (50.4%)
Number of Prior biologics			
0	77 (30.1%)	79 (30.9%)	156 (30.5%)
1	101 (39.5%)	82 (32.0%)	183 (35.7%)
2	28 (10.9%)	61 (23.8%)	89 (17.4%)
3	27 (10.5%)	20 (7.8%)	47 (9.2%)
>=4	23 (9.0%)	14 (5.5%)	37 (7.2%)
Duration of prior bDMARD (total)			
>0 to <12 weeks	5 (2.0%)	1 (0.4%)	6 (1.2%)
12 to <24 weeks	15 (5.9%)	4 (1.6%)	19 (3.7%)
24 to <52 weeks	23 (9.0%)	7 (2.7%)	30 (5.9%)
52 to <76 weeks	10 (3.9%)	11 (4.3%)	21 (4.1%)

76 to <104 weeks	10 (3.9%)	8 (3.1%)	18 (3.5%)
104 weeks or more	42 (16.4%)	49 (19.1%)	91 (17.8%)
N/A (no prior bDMARD)	77 (30.1%)	79 (30.9%)	156 (30.5%)
Missing	74 (28.9%)	97 (37.9%)	171 (33.4%)
Number of Prior cDMARDs			
0	39 (15.2%)	33 (12.9%)	72 (14.1%)
1	57 (22.3%)	75 (29.3%)	132 (25.8%)
Factor	Tofacitinib	TNFi	All
N	256	256	512
2	114 (44.5%)	109 (42.6%)	223 (43.6%)
3	42 (16.4%)	36 (14.1%)	78 (15.2%)
4	3 (1.2%)	3 (1.2%)	6 (1.2%)
5	1 (0.4%)	0 (0.0%)	1 (0.2%)
Prior Methotrexate dose, mean (SD)	3.40 (4.05) (n=170)	2.69 (1.56) (n=180)	3.04 (3.05) (n=350)
Prior Sulfasalazine dose, mean (SD)	2037.19 (516.89) (n=27)	1719.61 (993.86) (n=41)	1845.71 (847.29) (n=68)
Combination information			
With Meth + other cDMARD	76 (29.7%)	70 (27.3%)	146 (28.5%)
With Methotrexate only	59 (23.0%)	68 (26.6%)	127 (24.8%)
With other cDMARD	50 (19.5%)	47 (18.4%)	97 (18.9%)

bDMARD monotherapy	71 (27.7%)	71 (27.7%)	142 (27.7%)

Note: Doses displayed are as captured in mgdoseperday field - dosing schedule may vary Note: insufficient information to summarise dose for previous cDMARDs other than Methotrexate and Sulfasalazine Note: HCRU information and FACIT scores only summarised where >5 patients in total have this information recorded Note: A window of -3 months to 1.5 months around the index date has been applied. Where there are multiple readings within this period, readings prior to Index are prioritised, followed by readings that are the closest to the Index date

Table 2ai Clinical Characteristics at Index - All Eligible patients , Subgroup: Monotherapy

Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
Time from symptom onset(months), mean (SD)	144.37 (110.48) (n=74)	149.87 (101.51) (n=55)	123.40 (111.21) (n=74)	138.22 (108.47) (n=203)
Time from symptom onset(months), median (range)	115.06 (4.96, 444.44) (n=74)	133.14 (2.14, 437.51) (n=55)	84.04 (9.50, 592.74) (n=74)	111.24 (2.14, 592.74) (n=203)
Time since first seen(months), mean (SD)	73.80 (64.60) (n=57)	89.03 (76.41) (n=49)	45.57 (40.30) (n=49)	69.69 (64.45) (n=155)
Time since first seen(months), median (range)	61.31 (0.00, 312.06) (n=57)	65.35 (0.00, 271.43) (n=49)	32.94 (0.00, 159.89) (n=49)	48.36 (0.00, 312.06) (n=155)
DAS28CRP, mean (SD)	3.09 (1.39) (n=17)	3.45 (1.70) (n=22)	3.64 (1.70) (n=32)	3.45 (1.62) (n=71)
DAS28CRP, median (range)	3.10 (1.30, 5.80) (n=17)	3.00 (1.30, 7.30) (n=22)	3.45 (1.40, 6.80) (n=32)	3.10 (1.30, 7.30) (n=71)
DAS28CRP Category				
Remission	8 (5.8%)	8 (5.8%)	11 (6.3%)	27 (6.0%)

Low	2 (1.4%)	4 (2.9%)	4 (2.3%)	10 (2.2%)
Moderate	5 (3.6%)	6 (4.4%)	11 (6.3%)	22 (4.9%)
High	2 (1.4%)	4 (2.9%)	6 (3.4%)	12 (2.7%)
Missing	122 (87.8%)	115 (83.9%)	143 (81.7%)	380 (84.3%)
DAS28CRP(3), mean (SD)	2.99 (1.43) (n=59)	3.47 (1.65) (n=42)	3.60 (1.49) (n=74)	3.36 (1.52) (n=175)
DAS28CRP(3), median (range)	2.67 (1.28, 7.59) (n=59)	3.09 (1.15, 6.55) (n=42)	3.55 (1.28, 7.10) (n=74)	3.13 (1.15, 7.59) (n=175)
DAS28CRP3 Category				
Remission	27 (19.4%)	17 (12.4%)	22 (12.6%)	66 (14.6%)
Low	11 (7.9%)	5 (3.6%)	11 (6.3%)	27 (6.0%)
Moderate	14 (10.1%)	12 (8.8%)	29 (16.6%)	55 (12.2%)
High	7 (5.0%)	8 (5.8%)	12 (6.9%)	27 (6.0%)
Missing	80 (57.6%)	95 (69.3%)	101 (57.7%)	276 (61.2%)
DAS28ESR, mean (SD)	2.59 (1.49) (n=17)	3.49 (1.87) (n=22)	3.53 (1.84) (n=32)	3.29 (1.79) (n=71)
DAS28ESR, median (range)	2.60 (0.50, 5.50) (n=17)	3.00 (0.60, 6.60) (n=22)	3.75 (0.50, 7.20) (n=32)	2.90 (0.50, 7.20) (n=71)
DAS28ESR Category				
Remission	9 (6.5%)	9 (6.6%)	12 (6.9%)	30 (6.7%)
Low	3 (2.2%)	3 (2.2%)	3 (1.7%)	9 (2.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
Moderate	4 (2.9%)	4 (2.9%)	9 (5.1%)	17 (3.8%)

High	1 (0.7%)	6 (4.4%)	8 (4.6%)	15 (3.3%)
Missing	122 (87.8%)	115 (83.9%)	143 (81.7%)	380 (84.3%)
SDAI, mean (SD)	14.88 (13.10) (n=16)	18.25 (17.77) (n=22)	19.27 (18.60) (n=33)	17.96 (17.11) (n=71)
SDAI Category				
Remission	3 (2.2%)	2 (1.5%)	7 (4.0%)	12 (2.7%)
Low	5 (3.6%)	8 (5.8%)	7 (4.0%)	20 (4.4%)
Moderate	5 (3.6%)	6 (4.4%)	11 (6.3%)	22 (4.9%)
High	3 (2.2%)	6 (4.4%)	8 (4.6%)	17 (3.8%)
Missing	123 (88.5%)	115 (83.9%)	142 (81.1%)	380 (84.3%)
CDAI, mean (SD)	14.38 (12.98) (n=16)	18.18 (17.44) (n=23)	18.21 (18.32) (n=35)	17.37 (16.88) (n=74)
CDAI Category				
Remission	2 (1.4%)	2 (1.5%)	8 (4.6%)	12 (2.7%)
Low	6 (4.3%)	8 (5.8%)	8 (4.6%)	22 (4.9%)
Moderate	4 (2.9%)	5 (3.6%)	7 (4.0%)	16 (3.5%)
High	4 (2.9%)	8 (5.8%)	12 (6.9%)	24 (5.3%)
Missing	123 (88.5%)	114 (83.2%)	140 (80.0%)	377 (83.6%)
DAPSA, mean (SD)	22.82 (16.93) (n=17)	33.48 (29.28) (n=19)	33.48 (33.18) (n=29)	30.70 (28.58) (n=65)
DAPSA Category				
Remission	1 (0.7%)	0 (0.0%)	3 (1.7%)	4 (0.9%)
Low	6 (4.3%)	6 (4.4%)	10 (5.7%)	22 (4.9%)
High	4 (2.9%)	5 (3.6%)	3 (1.7%)	12 (2.7%)
Very High	6 (4.3%)	8 (5.8%)	13 (7.4%)	27 (6.0%)

Missing	122 (87.8%)	118 (86.1%)	146 (83.4%)	386 (85.6%)
TJC28, mean (SD)	3.86 (6.37) (n=64)	6.05 (7.66) (n=44)	6.36 (7.49) (n=78)	5.42 (7.22) (n=186)
TJC28, median (range)	2.00 (0.00, 25.00) (n=64)	2.00 (0.00, 24.00) (n=44)	4.00 (0.00, 26.00) (n=78)	2.00 (0.00, 26.00) (n=186)
TJC68, mean (SD)	6.62 (11.93) (n=64)	10.34 (14.17) (n=44)	10.37 (13.94) (n=78)	9.08 (13.39) (n=186)
TJC68, median (range)	2.00 (0.00, 56.00) (n=64)	4.00 (0.00, 54.00) (n=44)	6.00 (0.00, 60.00) (n=78)	4.00 (0.00, 60.00) (n=186)
SJC28, mean (SD)	3.41 (5.97) (n=64)	5.30 (7.48) (n=44)	5.94 (7.21) (n=78)	4.91 (6.93) (n=186)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
SJC28, median (range)	1.00 (0.00, 25.00) (n=64)	1.50 (0.00, 24.00) (n=44)	3.50 (0.00, 26.00) (n=78)	2.00 (0.00, 26.00) (n=186)
SJC66, mean (SD)	5.09 (9.98) (n=64)	8.70 (13.51) (n=44)	9.28 (12.78) (n=78)	7.70 (12.16) (n=186)
SJC66, median (range)	2.00 (0.00, 56.00) (n=64)	3.00 (0.00, 56.00) (n=44)	5.00 (0.00, 60.00) (n=78)	2.00 (0.00, 60.00) (n=186)
CRP, mean (SD)	7.24 (13.90) (n=59)	7.95 (9.57) (n=42)	6.72 (9.05) (n=74)	7.19 (10.98) (n=175)
CRP, median (range)	4.00 (0.40, 99.00) (n=59)	5.00 (0.00, 51.00) (n=42)	3.00 (0.30, 40.00) (n=74)	4.00 (0.00, 99.00) (n=175)
Physician Skin Assessment, mean (SD)	14.58 (23.87) (n=19)	14.05 (15.31) (n=19)	19.64 (25.48) (n=36)	16.91 (22.73) (n=74)
Physician Skin Assessment, median (range)	5.00 (0.00, 84.00) (n=19)	10.00 (0.00, 42.00) (n=19)	9.00 (0.00, 87.00) (n=36)	7.50 (0.00, 87.00) (n=74)
Patient Skin Assessment, mean (SD)	15.89 (25.05) (n=18)	17.47 (19.17) (n=15)	20.63 (26.74) (n=30)	18.52 (24.37) (n=63)
Patient Skin Assessment,	4.00 (0.00, 82.00)	10.00 (0.00, 50.00)	7.00 (0.00, 89.00)	5.00 (0.00, 89.00) (n=63)

median (range)	(n=18)	(n=15)	(n=30)	
HAQDI13, mean (SD)	. (.) (n=0)	0.90 (0.32) (n=4)	0.32 (0.02) (n=2)	0.71 (0.39) (n=6)
HAQDI13, median (range)	. (., .) (n=0)	0.95 (0.50, 1.20) (n=4)	0.32 (0.30, 0.33) (n=2)	0.65 (0.30, 1.20) (n=6)
HCRU Q1 Dr/nurse visits?				
No	0 (0.0%)	5 (3.6%)	5 (2.9%)	10 (2.2%)
Missing	139 (100.0%)	132 (96.4%)	170 (97.1%)	441 (97.8%)
HCRU Q2 seen in emergency?				
No	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.2%)
Yes	0 (0.0%)	4 (2.9%)	5 (2.9%)	9 (2.0%)
Missing	139 (100.0%)	132 (96.4%)	170 (97.1%)	441 (97.8%)
HCRU Q3 hospitalised?				
Yes	0 (0.0%)	5 (3.6%)	5 (2.9%)	10 (2.2%)
Missing	139 (100.0%)	132 (96.4%)	170 (97.1%)	441 (97.8%)
HCRU Q4 outpatients operations?				
No	0 (0.0%)	0 (0.0%)	2 (1.1%)	2 (0.4%)
Yes	0 (0.0%)	5 (3.6%)	3 (1.7%)	8 (1.8%)
Missing	139 (100.0%)	132 (96.4%)	170 (97.1%)	441 (97.8%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
HCRU Q5 seen allied HPs?				
No	0 (0.0%)	1 (0.7%)	1 (0.6%)	2 (0.4%)

Yes	0 (0.0%)	4 (2.9%)	4 (2.3%)	8 (1.8%)
Missing	139 (100.0%)	132 (96.4%)	170 (97.1%)	441 (97.8%)
HCRU Q6 seen alternative HPs?				
No	0 (0.0%)	1 (0.7%)	1 (0.6%)	2 (0.4%)
Yes	0 (0.0%)	4 (2.9%)	4 (2.3%)	8 (1.8%)
Missing	139 (100.0%)	132 (96.4%)	170 (97.1%)	441 (97.8%)
FACIT Score, mean (SD)	. (.) (n=0)	24.00 (12.57) (n=5)	34.64 (11.75) (n=6)	29.80 (12.77) (n=11)
FACIT Score, median (range)	. (., .) (n=0)	25.00 (6.00, 41.00) (n=5)	37.42 (14.00, 46.00) (n=6)	29.00 (6.00, 46.00) (n=11)
NSAID				
No	82 (59.0%)	72 (52.6%)	112 (64.0%)	266 (59.0%)
Yes	57 (41.0%)	65 (47.4%)	63 (36.0%)	185 (41.0%)
corticosteroid				
No	88 (63.3%)	90 (65.7%)	114 (65.1%)	292 (64.7%)
Yes	51 (36.7%)	47 (34.3%)	61 (34.9%)	159 (35.3%)
Number of Prior biologics				
0	15 (10.8%)	46 (33.6%)	97 (55.4%)	158 (35.0%)
1	33 (23.7%)	42 (30.7%)	40 (22.9%)	115 (25.5%)
2	37 (26.6%)	22 (16.1%)	18 (10.3%)	77 (17.1%)
3	25 (18.0%)	12 (8.8%)	9 (5.1%)	46 (10.2%)
>=4	29 (20.9%)	15 (10.9%)	11 (6.3%)	55 (12.2%)
Duration of prior bDMARD (total)				

>0 to <12 weeks	5 (3.6%)	0 (0.0%)	0 (0.0%)	5 (1.1%)
12 to <24 weeks	11 (7.9%)	4 (2.9%)	1 (0.6%)	16 (3.5%)
24 to <52 weeks	18 (12.9%)	5 (3.6%)	5 (2.9%)	28 (6.2%)
52 to <76 weeks	11 (7.9%)	6 (4.4%)	4 (2.3%)	21 (4.7%)
76 to <104 weeks	8 (5.8%)	8 (5.8%)	7 (4.0%)	23 (5.1%)
104 weeks or more	43 (30.9%)	42 (30.7%)	29 (16.6%)	114 (25.3%)
N/A (no prior bDMARD)	15 (10.8%)	46 (33.6%)	97 (55.4%)	158 (35.0%)
Factor	Tofacitinib	IL-17Ai	TNFi	All
N	139	137	175	451
Missing	28 (20.1%)	26 (19.0%)	32 (18.3%)	86 (19.1%)
Number of Prior cDMARDs				
0	36 (25.9%)	52 (38.0%)	63 (36.0%)	151 (33.5%)
1	26 (18.7%)	31 (22.6%)	32 (18.3%)	89 (19.7%)
2	52 (37.4%)	40 (29.2%)	55 (31.4%)	147 (32.6%)
3	23 (16.5%)	11 (8.0%)	25 (14.3%)	59 (13.1%)
4	2 (1.4%)	3 (2.2%)	0 (0.0%)	5 (1.1%)
Prior Methotrexate dose, mean (SD)	2.78 (0.63) (n=80)	2.62 (0.97) (n=67)	3.05 (2.82) (n=88)	2.84 (1.84) (n=235)
Prior Sulfasalazine dose, mean (SD)	1958.33 (689.48) (n=12)	875.00 (1246.42) (n=8)	1625.17 (1085.72) (n=24)	1579.64 (1067.04) (n=44)
Combination information				
bDMARD	139 (100.0%)	137 (100.0%)	175 (100.0%)	451 (100.0%)

monotherapy				

Note: Doses displayed are as captured in mgdoseperday field - dosing schedule may vary Note: insufficient information to summarise dose for previous cDMARDs other than Methotrexate and Sulfasalazine Note: HCRU information and FACIT scores only summarised where >5 patients in total have this information recorded Note: A window of -3 months to 1.5 months around the index date has been applied. Where there are multiple readings within this period, readings prior to Index are prioritised, followed by readings that are the closest to the Index date

Table 2aii Clinical Characteristics at Index - Matched Population: Tofacitinib/IL-17Ai groups , Subgroup: Monotherapy

Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
Time from symptom onset(months), mean (SD)	144.50 (117.64) (n=54)	167.31 (102.86) (n=38)	153.92 (111.75) (n=92)
Time from symptom onset(months), median (range)	115.06 (4.96, 444.44) (n=54)	155.33 (22.06, 437.51) (n=38)	127.35 (4.96, 444.44) (n=92)
Time since first seen(months), mean (SD)	72.54 (72.20) (n=40)	104.07 (79.52) (n=33)	86.79 (76.70) (n=73)
Time since first seen(months), median (range)	48.60 (0.00, 312.06) (n=40)	77.61 (0.00, 271.43) (n=33)	61.31 (0.00, 312.06) (n=73)
DAS28CRP, mean (SD)	3.04 (1.56) (n=10)	3.74 (1.71) (n=18)	3.49 (1.66) (n=28)
DAS28CRP, median (range)	2.80 (1.30, 5.80) (n=10)	3.35 (1.30, 7.30) (n=18)	3.10 (1.30, 7.30) (n=28)
DAS28CRP Category			
Remission	5 (5.3%)	5 (5.5%)	10 (5.4%)
Low	1 (1.1%)	4 (4.4%)	5 (2.7%)
Moderate	3 (3.2%)	5 (5.5%)	8 (4.3%)
High	1 (1.1%)	4 (4.4%)	5 (2.7%)
Missing	85 (89.5%)	73 (80.2%)	158 (84.9%)

DAS28CRP(3), mean (SD)	3.18 (1.57) (n=40)	3.40 (1.53) (n=30)	3.28 (1.54) (n=70)
DAS28CRP(3), median (range)	3.08 (1.28, 7.59) (n=40)	3.03 (1.15, 6.55) (n=30)	3.07 (1.15, 7.59) (n=70)
DAS28CRP3 Category			
Remission	16 (16.8%)	13 (14.3%)	29 (15.6%)
Low	9 (9.5%)	4 (4.4%)	13 (7.0%)
Moderate	8 (8.4%)	9 (9.9%)	17 (9.1%)
High	7 (7.4%)	4 (4.4%)	11 (5.9%)
Missing	55 (57.9%)	61 (67.0%)	116 (62.4%)
DAS28ESR, mean (SD)	2.66 (1.67) (n=10)	3.84 (1.84) (n=18)	3.42 (1.85) (n=28)
DAS28ESR, median (range)	2.65 (0.50, 5.50) (n=10)	3.75 (0.80, 6.60) (n=18)	3.00 (0.50, 6.60) (n=28)
DAS28ESR Category			
Remission	5 (5.3%)	6 (6.6%)	11 (5.9%)
Low	2 (2.1%)	2 (2.2%)	4 (2.2%)
Moderate	2 (2.1%)	4 (4.4%)	6 (3.2%)
High	1 (1.1%)	6 (6.6%)	7 (3.8%)
Missing	85 (89.5%)	73 (80.2%)	158 (84.9%)
Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
SDAI, mean (SD)	14.53 (14.87) (n=10)	20.98 (18.54) (n=18)	18.68 (17.32) (n=28)
SDAI Category			
Remission	2 (2.1%)	1 (1.1%)	3 (1.6%)
Low	4 (4.2%)	6 (6.6%)	10 (5.4%)

Moderate	2 (2.1%)	5 (5.5%)	7 (3.8%)
High	2 (2.1%)	6 (6.6%)	8 (4.3%)
Missing	85 (89.5%)	73 (80.2%)	158 (84.9%)
CDAI, mean (SD)	14.09 (14.73) (n=10)	20.85 (18.06) (n=19)	18.52 (17.03) (n=29)
CDAI Category			
Remission	1 (1.1%)	1 (1.1%)	2 (1.1%)
Low	5 (5.3%)	6 (6.6%)	11 (5.9%)
Moderate	1 (1.1%)	4 (4.4%)	5 (2.7%)
High	3 (3.2%)	8 (8.8%)	11 (5.9%)
Missing	85 (89.5%)	72 (79.1%)	157 (84.4%)
DAPSA, mean (SD)	20.79 (18.67) (n=10)	37.81 (30.03) (n=16)	31.26 (27.17) (n=26)
DAPSA Category			
Remission	1 (1.1%)	0 (0.0%)	1 (0.5%)
Low	4 (4.2%)	3 (3.3%)	7 (3.8%)
High	2 (2.1%)	5 (5.5%)	7 (3.8%)
Very High	3 (3.2%)	8 (8.8%)	11 (5.9%)
Missing	85 (89.5%)	75 (82.4%)	160 (86.0%)
TJC28, mean (SD)	4.86 (7.30) (n=44)	5.58 (7.25) (n=31)	5.16 (7.24) (n=75)
TJC28, median (range)	2.00 (0.00, 25.00) (n=44)	2.00 (0.00, 24.00) (n=31)	2.00 (0.00, 25.00) (n=75)
TJC68, mean (SD)	7.89 (13.72) (n=44)	9.42 (13.02) (n=31)	8.52 (13.37) (n=75)
TJC68, median (range)	2.00 (0.00, 56.00) (n=44)	4.00 (0.00, 45.00) (n=31)	3.00 (0.00, 56.00) (n=75)
SJC28, mean (SD)	4.50 (6.88) (n=44)	4.65 (6.63) (n=31)	4.56 (6.73) (n=75)

SJC28, median (range)	2.00 (0.00, 25.00) (n=44)	1.00 (0.00, 24.00) (n=31)	2.00 (0.00, 25.00) (n=75)
SJC66, mean (SD)	6.70 (11.65) (n=44)	7.35 (11.37) (n=31)	6.97 (11.46) (n=75)
SJC66, median (range)	2.00 (0.00, 56.00) (n=44)	3.00 (0.00, 45.00) (n=31)	2.00 (0.00, 56.00) (n=75)
CRP, mean (SD)	7.48 (15.98) (n=40)	8.76 (10.30) (n=30)	8.03 (13.76) (n=70)
CRP, median (range)	4.00 (0.40, 99.00) (n=40)	5.50 (0.00, 51.00) (n=30)	4.90 (0.00, 99.00) (n=70)
Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
Physician Skin Assessment, mean (SD)	9.83 (14.63) (n=12)	14.40 (15.81) (n=15)	12.37 (15.18) (n=27)
Physician Skin Assessment, median (range)	4.00 (0.00, 50.00) (n=12)	10.00 (0.00, 42.00) (n=15)	5.00 (0.00, 50.00) (n=27)
Patient Skin Assessment, mean (SD)	9.30 (15.79) (n=10)	20.17 (20.09) (n=12)	15.23 (18.68) (n=22)
Patient Skin Assessment, median (range)	1.50 (0.00, 50.00) (n=10)	17.50 (0.00, 50.00) (n=12)	6.50 (0.00, 50.00) (n=22)
HAQDI13, mean (SD)	. (.) (n=0)	1.03 (0.21) (n=3)	1.03 (0.21) (n=3)
HAQDI13, median (range)	. (., .) (n=0)	1.10 (0.80, 1.20) (n=3)	1.10 (0.80, 1.20) (n=3)
HCRU Q1 Dr/nurse visits?			
No	0 (0.0%)	4 (4.4%)	4 (2.2%)
Missing	95 (100.0%)	87 (95.6%)	182 (97.8%)
HCRU Q2 seen in emergency?			
No	0 (0.0%)	1 (1.1%)	1 (0.5%)
Yes	0 (0.0%)	3 (3.3%)	3 (1.6%)
Missing	95 (100.0%)	87 (95.6%)	182 (97.8%)

HCRU Q3 hospitalised?			
Yes	0 (0.0%)	4 (4.4%)	4 (2.2%)
Missing	95 (100.0%)	87 (95.6%)	182 (97.8%)
HCRU Q4 outpatients operations?			
Yes	0 (0.0%)	4 (4.4%)	4 (2.2%)
Missing	95 (100.0%)	87 (95.6%)	182 (97.8%)
HCRU Q5 seen allied HPs?			
No	0 (0.0%)	1 (1.1%)	1 (0.5%)
Yes	0 (0.0%)	3 (3.3%)	3 (1.6%)
Missing	95 (100.0%)	87 (95.6%)	182 (97.8%)
HCRU Q6 seen alternative HPs?			
No	0 (0.0%)	1 (1.1%)	1 (0.5%)
Yes	0 (0.0%)	3 (3.3%)	3 (1.6%)
Missing	95 (100.0%)	87 (95.6%)	182 (97.8%)
FACIT Score, mean (SD)	. (.) (n=0)	23.25 (14.38) (n=4)	23.25 (14.38) (n=4)
FACIT Score, median (range)	. (., .) (n=0)	23.00 (6.00, 41.00) (n=4)	23.00 (6.00, 41.00) (n=4)
NSAID			
No	57 (60.0%)	52 (57.1%)	109 (58.6%)
Factor	Tofacitinib	IL-17Ai	All
N	95	91	186
Yes	38 (40.0%)	39 (42.9%)	77 (41.4%)
corticosteroid			

No	62 (65.3%)	59 (64.8%)	121 (65.1%)
Yes	33 (34.7%)	32 (35.2%)	65 (34.9%)
Number of Prior biologics			
0	15 (15.8%)	15 (16.5%)	30 (16.1%)
1	33 (34.7%)	27 (29.7%)	60 (32.3%)
2	19 (20.0%)	22 (24.2%)	41 (22.0%)
3	13 (13.7%)	12 (13.2%)	25 (13.4%)
>=4	15 (15.8%)	15 (16.5%)	30 (16.1%)
Duration of prior bDMARD (total)			
>0 to <12 weeks	3 (3.2%)	0 (0.0%)	3 (1.6%)
12 to <24 weeks	9 (9.5%)	4 (4.4%)	13 (7.0%)
24 to <52 weeks	12 (12.6%)	3 (3.3%)	15 (8.1%)
52 to <76 weeks	5 (5.3%)	5 (5.5%)	10 (5.4%)
76 to <104 weeks	7 (7.4%)	6 (6.6%)	13 (7.0%)
104 weeks or more	24 (25.3%)	35 (38.5%)	59 (31.7%)
N/A (no prior bDMARD)	15 (15.8%)	15 (16.5%)	30 (16.1%)
Missing	20 (21.1%)	23 (25.3%)	43 (23.1%)
Number of Prior cDMARDs			
0	30 (31.6%)	28 (30.8%)	58 (31.2%)
1	14 (14.7%)	22 (24.2%)	36 (19.4%)
2	35 (36.8%)	30 (33.0%)	65 (34.9%)
3	15 (15.8%)	8 (8.8%)	23 (12.4%)

4	1 (1.1%)	3 (3.3%)	4 (2.2%)
Prior Methotrexate dose, mean (SD)	2.83 (0.66) (n=46)	2.63 (1.04) (n=51)	2.72 (0.88) (n=97)
Prior Sulfasalazine dose, mean (SD)	2055.56 (726.48) (n=9)	1250.00 (1500.00) (n=4)	1807.69 (1031.55) (n=13)
Combination information			
bDMARD monotherapy	95 (100.0%)	91 (100.0%)	186 (100.0%)

Note: Doses displayed are as captured in mgdoseperday field - dosing schedule may vary Note: insufficient information to summarise dose for previous cDMARDs other than Methotrexate and Sulfasalazine
Note: HCRU information and FACIT scores only summarised where >5 patients in total have this information recorded Note: A window of -3 months to 1.5 months around the index date has been applied. Where there are multiple readings within this period, readings prior to Index are prioritised, followed by readings that are the closest to the Index date

Table 2aiii Clinical Characteristics at Index - Matched Population: Tofacitinib/TNFi groups , Subgroup: Monotherapy

Factor	Tofacitinib	TNFi	All
N	71	71	142
Time from symptom onset(months), mean (SD)	136.38 (121.05) (n=43)	120.87 (76.04) (n=35)	129.42 (102.99) (n=78)
Time from symptom onset(months), median (range)	89.05 (4.96, 444.44) (n=43)	102.70 (10.95, 310.55) (n=35)	95.23 (4.96, 444.44) (n=78)
Time since first seen(months), mean (SD)	56.39 (58.45) (n=30)	65.27 (44.49) (n=20)	59.94 (52.99) (n=50)
Time since first seen(months), median (range)	29.90 (0.00, 202.47) (n=30)	48.96 (4.27, 159.89) (n=20)	42.54 (0.00, 202.47) (n=50)
DAS28CRP, mean (SD)	3.40 (1.54) (n=8)	3.32 (1.50) (n=13)	3.35 (1.47) (n=21)
DAS28CRP, median (range)	3.25 (1.50, 5.80) (n=8)	2.80 (1.60, 6.80) (n=13)	3.00 (1.50, 6.80) (n=21)

DAS28CRP Category			
Remission	3 (4.2%)	5 (7.0%)	8 (5.6%)
Low	1 (1.4%)	3 (4.2%)	4 (2.8%)
Moderate	3 (4.2%)	4 (5.6%)	7 (4.9%)
High	1 (1.4%)	1 (1.4%)	2 (1.4%)
Missing	63 (88.7%)	58 (81.7%)	121 (85.2%)
DAS28CRP(3), mean (SD)	3.13 (1.47) (n=29)	3.36 (1.42) (n=36)	3.26 (1.44) (n=65)
DAS28CRP(3), median (range)	3.09 (1.28, 6.04) (n=29)	3.07 (1.53, 7.10) (n=36)	3.09 (1.28, 7.10) (n=65)
DAS28CRP3 Category			
Remission	12 (16.9%)	13 (18.3%)	25 (17.6%)
Low	6 (8.5%)	8 (11.3%)	14 (9.9%)
Moderate	6 (8.5%)	12 (16.9%)	18 (12.7%)
High	5 (7.0%)	3 (4.2%)	8 (5.6%)
Missing	42 (59.2%)	35 (49.3%)	77 (54.2%)
DAS28ESR, mean (SD)	3.01 (1.70) (n=8)	2.91 (1.45) (n=13)	2.95 (1.51) (n=21)
DAS28ESR, median (range)	2.90 (0.50, 5.50) (n=8)	2.90 (0.50, 5.30) (n=13)	2.90 (0.50, 5.50) (n=21)
DAS28ESR Category			
Remission	3 (4.2%)	5 (7.0%)	8 (5.6%)
Low	2 (2.8%)	3 (4.2%)	5 (3.5%)
Moderate	2 (2.8%)	4 (5.6%)	6 (4.2%)
High	1 (1.4%)	1 (1.4%)	2 (1.4%)
Missing	63 (88.7%)	58 (81.7%)	121 (85.2%)

Factor	Tofacitinib	TNFi	All
N	71	71	142
SDAI, mean (SD)	17.08 (15.71) (n=8)	14.87 (15.53) (n=14)	15.68 (15.26) (n=22)
SDAI Category			
Remission	1 (1.4%)	2 (2.8%)	3 (2.1%)
Low	3 (4.2%)	5 (7.0%)	8 (5.6%)
Moderate	2 (2.8%)	5 (7.0%)	7 (4.9%)
High	2 (2.8%)	2 (2.8%)	4 (2.8%)
Missing	63 (88.7%)	57 (80.3%)	120 (84.5%)
CDAI, mean (SD)	16.55 (15.62) (n=8)	14.18 (15.29) (n=16)	14.97 (15.10) (n=24)
CDAI Category			
Remission	1 (1.4%)	4 (5.6%)	5 (3.5%)
Low	3 (4.2%)	5 (7.0%)	8 (5.6%)
Moderate	1 (1.4%)	3 (4.2%)	4 (2.8%)
High	3 (4.2%)	4 (5.6%)	7 (4.9%)
Missing	63 (88.7%)	55 (77.5%)	118 (83.1%)
DAPSA, mean (SD)	24.24 (19.38) (n=8)	26.68 (26.38) (n=12)	25.70 (23.30) (n=20)
DAPSA Category			
Low	3 (4.2%)	6 (8.5%)	9 (6.3%)
High	2 (2.8%)	2 (2.8%)	4 (2.8%)
Very High	3 (4.2%)	4 (5.6%)	7 (4.9%)
Missing	63 (88.7%)	59 (83.1%)	122 (85.9%)

TJC28, mean (SD)	4.71 (6.79) (n=31)	4.69 (5.96) (n=39)	4.70 (6.29) (n=70)
TJC28, median (range)	2.00 (0.00, 24.00) (n=31)	2.00 (0.00, 26.00) (n=39)	2.00 (0.00, 26.00) (n=70)
TJC68, mean (SD)	7.29 (12.28) (n=31)	7.18 (9.81) (n=39)	7.23 (10.89) (n=70)
TJC68, median (range)	2.00 (0.00, 56.00) (n=31)	3.00 (0.00, 38.00) (n=39)	2.50 (0.00, 56.00) (n=70)
SJC28, mean (SD)	4.94 (7.01) (n=31)	4.62 (6.04) (n=39)	4.76 (6.44) (n=70)
SJC28, median (range)	2.00 (0.00, 24.00) (n=31)	2.00 (0.00, 26.00) (n=39)	2.00 (0.00, 26.00) (n=70)
SJC66, mean (SD)	7.55 (12.32) (n=31)	6.97 (9.71) (n=39)	7.23 (10.87) (n=70)
SJC66, median (range)	2.00 (0.00, 56.00) (n=31)	2.00 (0.00, 36.00) (n=39)	2.00 (0.00, 56.00) (n=70)
CRP, mean (SD)	5.25 (6.49) (n=29)	6.34 (7.64) (n=36)	5.86 (7.12) (n=65)
CRP, median (range)	4.00 (0.40, 31.00) (n=29)	4.45 (0.30, 39.00) (n=36)	4.00 (0.30, 39.00) (n=65)
Physician Skin Assessment, mean (SD)	6.80 (7.84) (n=10)	24.35 (30.51) (n=17)	17.85 (25.86) (n=27)
Factor	Tofacitinib	TNFi	All
N	71	71	142
Physician Skin Assessment, median (range)	4.00 (0.00, 20.00) (n=10)	8.00 (0.00, 87.00) (n=17)	5.00 (0.00, 87.00) (n=27)
Patient Skin Assessment, mean (SD)	5.38 (7.35) (n=8)	31.79 (32.78) (n=14)	22.18 (29.19) (n=22)
Patient Skin Assessment, median (range)	1.50 (0.00, 20.00) (n=8)	23.00 (0.00, 89.00) (n=14)	7.50 (0.00, 89.00) (n=22)
HAQDI13, mean (SD)	. (.) (n=0)	0.33 (.) (n=1)	0.33 (.) (n=1)
HAQDI13, median (range)	. (., .) (n=0)	0.33 (0.33, 0.33) (n=1)	0.33 (0.33, 0.33) (n=1)
NSAID			
No	42 (59.2%)	50 (70.4%)	92 (64.8%)

Yes	29 (40.8%)	21 (29.6%)	50 (35.2%)
corticosteroid			
No	46 (64.8%)	47 (66.2%)	93 (65.5%)
Yes	25 (35.2%)	24 (33.8%)	49 (34.5%)
Number of Prior biologics			
0	15 (21.1%)	16 (22.5%)	31 (21.8%)
1	33 (46.5%)	23 (32.4%)	56 (39.4%)
2	8 (11.3%)	16 (22.5%)	24 (16.9%)
3	7 (9.9%)	6 (8.5%)	13 (9.2%)
>=4	8 (11.3%)	10 (14.1%)	18 (12.7%)
Duration of prior bDMARD (total)			
>0 to <12 weeks	1 (1.4%)	0 (0.0%)	1 (0.7%)
12 to <24 weeks	7 (9.9%)	1 (1.4%)	8 (5.6%)
24 to <52 weeks	10 (14.1%)	4 (5.6%)	14 (9.9%)
52 to <76 weeks	4 (5.6%)	3 (4.2%)	7 (4.9%)
76 to <104 weeks	3 (4.2%)	3 (4.2%)	6 (4.2%)
104 weeks or more	15 (21.1%)	25 (35.2%)	40 (28.2%)
N/A (no prior bDMARD)	15 (21.1%)	16 (22.5%)	31 (21.8%)
Missing	16 (22.5%)	19 (26.8%)	35 (24.6%)
Number of Prior cDMARDs			
0	25 (35.2%)	16 (22.5%)	41 (28.9%)
1	10 (14.1%)	13 (18.3%)	23 (16.2%)

2	25 (35.2%)	32 (45.1%)	57 (40.1%)
3	10 (14.1%)	10 (14.1%)	20 (14.1%)
Factor	Tofacitinib	TNFi	All
N	71	71	142
4	1 (1.4%)	0 (0.0%)	1 (0.7%)
Prior Methotrexate dose, mean (SD)	2.86 (0.63) (n=34)	2.94 (2.72) (n=45)	2.90 (2.08) (n=79)
Prior Sulfasalazine dose, mean (SD)	2142.86 (377.96) (n=7)	1889.33 (780.53) (n=9)	2000.25 (631.61) (n=16)
Combination information			
bDMARD monotherapy	71 (100.0%)	71 (100.0%)	142 (100.0%)

Note: Doses displayed are as captured in mgdoseperday field - dosing schedule may vary Note: insufficient information to summarise dose for previous cDMARDs other than Methotrexate and Sulfasalazine Note: HCRU information and FACIT scores only summarised where >5 patients in total have this information recorded Note: A window of -3 months to 1.5 months around the index date has been applied. Where there are multiple readings within this period, readings prior to Index are prioritised, followed by readings that are the closest to the Index date

* For additional Tables and Figures, reference the OPAL Final Analysis Report.

16.1. Other Analyses

As this study does not involve data subject to privacy laws, according to applicable legal requirements, obtaining informed consent from patients by Pfizer was not required.

16.2. Adverse Adverse Events/Adverse Reactions

Adverse events reported in more than 5% of patients in any treatment group were summarized.

17. DISCUSSION

17.1. CONCLUSIONS

18. REFERENCES

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19. LIST OF SOURCE TABLES AND FIGURES

20. LIST OF TABLES:

ANNEX 1. LIST OF STAND ALONE DOCUMENTS

Number	Document reference number	Date	Title
Number 1	Not applicable	19 July 2022	Abstract: *Real-world evaluation of effectiveness, persistence and usage patterns of tofacitinib in treatment of psoriatic arthritis in Australia.*

ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Not required.

ANNEX 3. ADDITIONAL INFORMATION

Not applicable.

Document Approval Record

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Signed By:	Date(GMT)	Signing Capacity
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Redacted	Redacted	Redacted