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Efficacy and safety of pharmacological treatment of psoriatic arthritis: a systematic literature research informing the 2023 update of the EULAR recommendations for the management of psoriatic arthritis

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ABSTRACT

Objectives To obtain an overview of recent evidence on efficacy and safety of pharmacological treatments in psoriatic arthritis (PsA).

Methods This systematic literature research (SLR) investigated the efficacy and safety of conventional synthetic (cs), biological (b) and targeted synthetic (ts) disease-modifying antirheumatic drugs (DMARDs) in patients with PsA. A systematic database search using Medline, EMBASE, Cochrane CENTRAL was conducted to identify relevant articles published since the previous update in 2019 until 28 December 2022. Efficacy was assessed in trials while for safety observational data were also considered. Adverse events of special interest were infections (including herpes zoster, influenza and tuberculosis), malignancies, major adverse cardiovascular events, venous thromboembolisms, liver disease, laboratory changes and psychiatric adverse events. No meta-analyses were performed.

Results For efficacy, of 3946 articles screened, 38 articles (30 trials) were analysed. The compounds investigated included csDMARDs (leflunomide, methotrexate), bDMARDs inhibiting IL17 (bimekizumab, brodalumab, ixekizumab, izokibep, secukinumab,), IL-23 (guselkumab, risankizumab, tildrakizumab), IL-12/23 (ustekinumab) as well as TNF (adalimumab, certolizumab-pegol, etanercept, infliximab, golimumab) and Janus Kinase inhibitors (JAKi) (brepocitinib, deucravacitinib, tofacitinib, upadacitinib). The compounds investigated were efficacious in improving signs and symptoms of PsA, improving physical functioning and quality of life. For safety, 2055 abstracts were screened, and 24 articles analysed: 15 observational studies and 9 long-term follow-ups of trials, assessing glucocorticoids, TNFi, IL-17i, JAKi, IL-12/23i and PDE4i (apremilast). Safety indicators were generally coherent with the previous SLR in 2019.

Conclusion The results of this SLR informed the task force responsible for the 2023 update of the European

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Many drugs have become available over the last years in psoriatic arthritis (PsA); trials of new drugs have consistently been positive in terms of the primary outcomes, but it is difficult to obtain an overview of the efficacy and safety of systemic therapies for PsA, including conventional synthetic, biological and targeted synthetic disease-modifying antirheumatic drugs (DMARDs).

WHAT THIS STUDY ADDS

This systematic literature research (SLR) provides an overview of the efficacy and safety results of:

⇒ Established DMARDs, trials investigating efficacy of DMARDs on specific domains of PsA (axial, dactylitis, synovitis).

⇒ Novel biological DMARDs, including inhibitors of IL23-p19 (risankizumab, guselkumab, tildrakizumab), IL17A (izokibep), IL17A/F (bimekizumab).

⇒ Novel Janus kinase inhibitors, including brepocitinib (JAK1/TYK2), deucravacitinib (TYK2) and upadacitinib (JAK1/JAK2).

⇒ Studies on treatment tapering and stopping.

Safety analyses of observational data investigating established DMARDs on adverse events of special interest (infections, malignancies, cardiovascular and thrombotic events).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This SLR informed the 2023 European Alliance of Associations for Rheumatology PsA management recommendations task force with the available evidence published since the previous update published in 2019.

Alliance of Associations for Rheumatology recommendations for pharmacological management of PsA.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease occurring in patients with psoriasis, leading to the typical clinical hallmarks of oligoarthritis or polyarthritis, enthesitis and dactylitis; if left untreated, radiographic damage and, although rare, potentially mutilating joint destruction may occur.[1] Axial disease in PsA was recognised already by Moll and Wright as an important musculoskeletal manifestation, however, many new insights were gained over the past decades,[1] differentiating axial PsA from the manifestations observed in radiographic and non-radiographic axial spondyloarthritis, including genetics, pathological findings, clinical symptoms, subsequent radiographic changes and also potential implications for treatment.[2]

In 2012, the first European Alliance of Associations for Rheumatology (EULAR) management recommendations on pharmacological therapies for PsA were developed,[3] with subsequent updates in 2015[4] and 2019 [5]. With an increasing depth of understanding immunological pathways of PsA, the body of evidence on the efficacy of new molecules targeting different modes of action (MOAs), such as inhibition of the p19 subunit of interleukin (IL)-23[6–8] and IL-17,[9] but also Janus Kinase (JAK) including the tyrosine kinase 2 (TYK2) pathway, has significantly increased in recent years.[10–12]

Besides the mere development of new MOAs using established composite endpoints, recent studies also provided evidence on the efficacy of established disease-modifying antirheumatic drugs (DMARDs) on specific musculoskeletal manifestations, including synovitis,[13] axial disease[14] and dactylitis.[15] Furthermore, head-to-head trials, comparing different MOAs,[16–18] as well as conventional synthetic (cs) DMARD regimens[19] and strategic trials, also on tapering strategies, were published.[20 21] Increasing emphasis on adverse events of DMARD therapies gained attention over the past years due to safety signals identified in patients with rheumatoid arthritis and cardiovascular risk factors receiving a JAKi, namely tofacitinib (TOFA).[22] This may also be important in PsA, given the high prevalence of comorbidities and risk factors, such as obesity, dyslipidaemia, metabolic syndrome, cardiovascular disease and smoking in patients with PsA.[23]

This systematic literature research (SLR) was conducted to summarise and update the evidence on pharmacological treatments in PsA since 2019,[24] to inform the EULAR task force developing the 2023 update of the PsA management recommendations.[25]

METHODS

This SLR was conducted according to the EULAR updated standard operating procedures and based on a protocol developed and approved by the task force.[26]

To update the evidence from the previous SLR with the data cut on 21 December 2018,[24] articles published in English language between 1 January 2018 and 28 December 2022 were searched by an experienced librarian (JWS) using Medline (PubMed), Embase (OVID version), the Cochrane CENTRAL Register of Controlled Trials (Central) and the abstract archives of the EULAR and American College of Rheumatology (ACR) annual meetings. To prevent missing important publications, we included the year 2018 in the literature search, as manuscripts which carry the date of a specific year might be published with some delay. Like in previous SLRs, conference abstracts from the last 3 years (from 2020 to 2022) were eligible for inclusion. In the case of articles being published after the data cut of the literature search but before the EULAR task force meeting (17 April 2023), fully published manuscripts were eligible to be included only if they had been covered as a conference abstract in the initial systematic search. The search strategies are provided in online supplemental appendix (Text S1.1-S1.6).

During the first steering committee meeting (21 November 2022), a research protocol was developed. In total, 10 research questions were defined. These research questions covered the areas of the efficacy and safety of already approved DMARDs, safety of JAK inhibitors (JAKi), the efficacy and safety of new molecules, drug–drug interactions, the efficacy of DMARDs on different disease manifestations of PsA, evidence on strategic trials as well as evidence on dose reduction and treatment discontinuation. Based on the research questions, detailed PICO definitions (population, intervention, control, outcome) were developed. Details on the research questions as well as the PICO definitions are shown in online supplemental table S1.10. For efficacy, only randomised controlled trials (RCTs) investigating non-steroidal anti-inflammatory drugs (NSAIDs), cs, biological (b) or targeted synthetic (ts) DMARDs in adult patients classified as having PsA were eligible for inclusion. Phase 2 studies were eligible for inclusion, if no phase 3 studies were available, as efficacy but also safety profiles of new molecules, targeting similar pathways as currently licensed drugs, might be informative. For safety, data of identified RCTs as well as long-term extensions studies of RCTs with adequately defined comparator arms (placebo (PBO) or active therapy) were eligible. In addition to RCT safety data (including long-term extensions with adequate comparator arms) also observational studies (including registry analyses, claims data, cohort studies and case–control studies) with adequately defined controls were eligible for inclusion.

Patient populations of interest were defined as patients classified as having PsA; patients could be either DMARD-naïve, or with intolerance and/or insufficient response (IR) to csDMARDs, patients who were bDMARD-IR and/or tsDMARD-IR or mixed populations with previous IR to cs-DMARDs or/and bDMARDs; in some studies patients with IR to NSAIDs were also eligible. All interventions of interest are listed in online supplemental table S1.7. Efficacy outcomes included composite measures of state (such as Disease Activity Index for Psoriatic Arthritis (DAPSA) or minimal disease activity (MDA)) and of improvement (such as ACR criteria), individual core-set measures of signs and symptoms, patient-reported outcomes (including fatigue, physical function). Safety outcomes included infections (serious infections, herpes zoster (HZ), opportunistic and fungal infections, tuberculosis (Tb)); malignancies; major adverse cardiovascular events (MACEs); venous thromboembolic events (VTE); liver disease; gastrointestinal side effects; incidence of inflammatory bowel disease (IBD), uveitis; depression, suicidal ideation and behaviour (online supplemental table S1.8 List S1.9).

10% of all titles and abstracts were screened by two researchers (AK and RJOF) with an agreement of 94%. All other titles and abstracts were screened and assessed by one researcher (AK). In the case of any uncertainties, these were discussed with the methodologist (LG).

The selected articles were then assessed in full detail for eligibility and data of finally eligible articles were extracted using standardised spreadsheet forms by one researcher (AK) and verified in detail for correctness by the co-methodologist (RJOF). Risk of

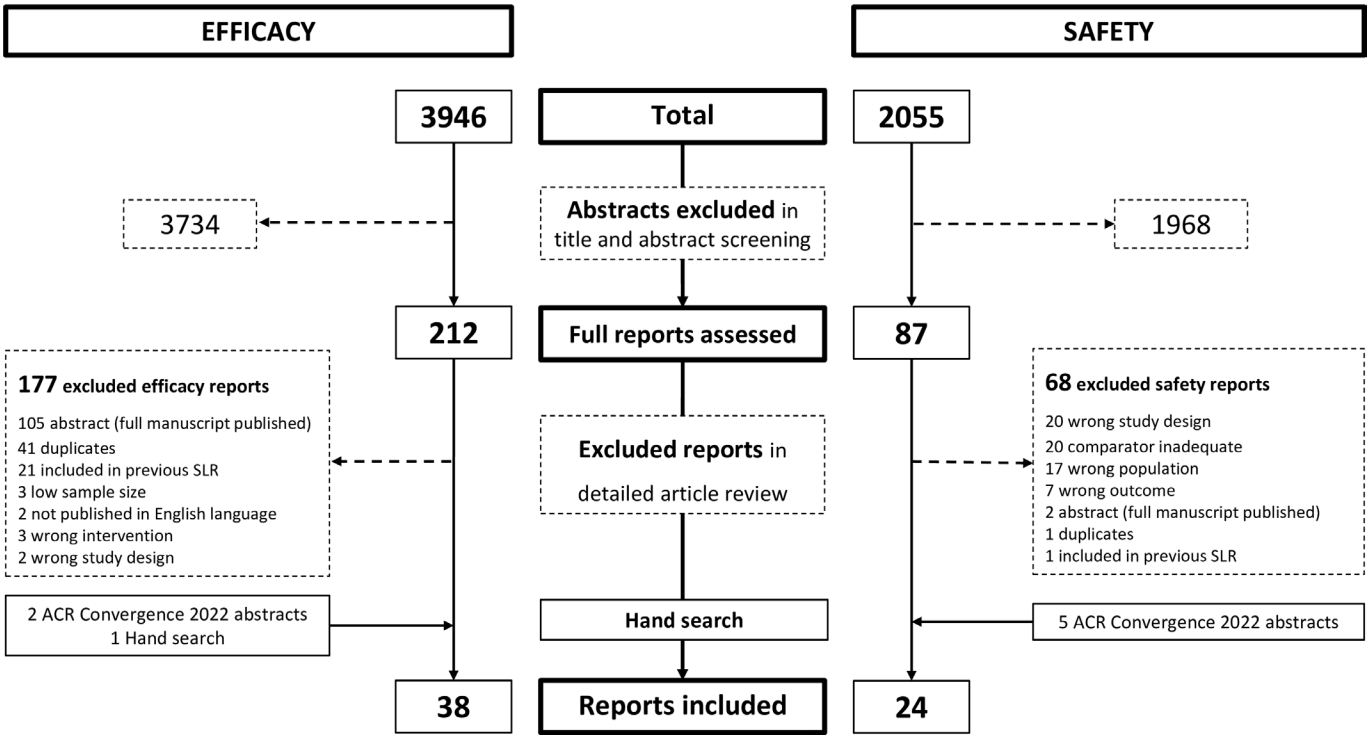

Figure 1 PRISMA flow chart of the efficacy and safety search of studies in PsA published 2018–2022. ACR, American College of Rheumatology; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PsA, psoriatic arthritis; SLR, systematic literature research.

bias (RoB) assessment was done using the Cochrane Collaborations RoB tool for RCTs (version 2), while the Newcastle-Ottawa scale was utilised for assessing RoB in cohort and case–control studies.[27] Conference abstracts were not assessed for RoB.[28] Due to the high heterogeneity of the finally selected studies, and for the purposes of recommendations, detailed information of each study rather than summary statistics was selected; thus, no meta-analyses were performed and results, including effect sizes derived from safety analyses were taken from the original articles and reported descriptively. Specific adverse events of special interest (AESI) occurring during the double-blind period are reported in detail, while summary estimates derived from long-term extension studies are reported directly following the respective sections on the double-blind period.

RESULTS

Search results

The efficacy search resulted in 3946 articles of which 212 references were selected to be assessed in the detailed article review, resulting in 38 articles describing 30 unique trials eligible for final inclusion in the SLR (figure 1). A detailed list of studies assessing the efficacy of DMARDs is shown in online supplemental table S2.1. Table 1 provides an overview of the drugs evaluated for efficacy and table 2 summarises the main reported efficacy outcomes of the studies included.

A total of 19 of the 30 trials (63.3%) were rated as having a low RoB; 7 of 30 trials (23.3%) received a rating of a high RoB—all due to an open-label or single-blinded trial design. Two trials (2/30, 6.6%) had an unclear RoB, both due to insufficient reporting of randomisation sequence generation and allocation concealment methods. One trial was published as a conference abstract only and was not assessed for RoB. All RoB assessments of efficacy studies are provided in online supplemental table S2.2, baseline characteristics are presented in online supplemental tables S2.3-S2.4, and detailed efficacy results are shown in online supplemental tables S2.5-S2.7.

For safety, beyond the adverse event profiles presented in the RCT publications already included in the efficacy search, further 2055 references were screened, and 87 articles assessed in detail with 24 studies finally included (figure 1). These 24 studies included 9 safety analyses of RCT data (long-term extensions and integrated safety analyses of AESI) as well as 15 observational studies: 8/24 (33.3%) with a low RoB, 1/24 (4.2%) with unclear and 10/24 (37.5%) with a high RoB (5 conference abstracts were not assessed for RoB). Investigations of AESI in RCTs were concerned with influenza, Tb, malignancies and thromboembolic events. Cohort studies investigated serious infections, Tb, solid and haematological malignancies, liver disease, MACEs as well as anxiety and depression (online supplemental table S3.1 provides a detailed list of safety studies included). RoB assessments of safety studies are shown in online supplemental table S3.2 and S3.3, population characteristics are presented in online supplemental table S3.4, with the main safety results shown in online supplemental tables S3.5.

Efficacy of csDMARDs

Only one RCT was available: the COMPLETE-PsA trial (low RoB).[19] Patients with a diagnosis of PsA and without concomitant DMARD therapy were randomised to methotrexate (MTX) + leflunomide (LEF) combination therapy (n=39) or MTX+PBO (n=39). MTX+LEF combination therapy was superior to MTX+PBO in achieving the primary outcome (mean change in Psoriatic Arthritis Disease Activity Score; PASDAS) at week 16 (3.1±1.4 vs 3.7±1.3, treatment difference: −0.6, 90% CI −1.0 to −0.1; p=0.025). Nausea and vomiting were more frequent in the MTX+LEF arm (44% vs 28%), as was alanine aminotransferase elevation (31% vs 18%) and altered bowel habits (26% vs 8%).[19]

Table 1 Summary of studies in psoriatic arthritis published 2018–2022 and included for evaluation of efficacy

Intervention	Number of articles/ abstracts	Therapeutic compound	Target	References
csDMARDs, csDMARD combination versus other csDMARDs or placebo	1	Methotrexate (MTX) + Leflunomide MTX + Placebo	Dihydrofolate reductase/adenosine metabolism (AICAR); dihydroorotate dehydrogenase	19
bDMARD ± csDMARDs versus placebo	4	Secukinumab	IL-17A	13 14 29 30
	3	Izokibep	IL-17A	43–45
	2	Bimekizumab	IL-17A/F	9 41
	1	Brodalumab	IL-17A receptor	42
	4	Guselkumab	IL-23p19	7 35–37
	4	Risankizumab	IL-23p19	8 38–40
	1	Tildrakizumab	IL-23p19	6
bDMARD + csDMARD (combination therapy) versus bDMARD + placebo (monotherapy)	1	Ustekinumab+MTX vs ustekinumab+placebo	IL-12/23; dihydrofolate reductase+purine metabolism (AICAR)	31
bDMARD + csDMARD (combination therapy) versus csDMARD + placebo (monotherapy)	1	Golimumab+MTX vs placebo+MTX	TNF; dihydrofolate reductase+purine metabolism (AICAR)	15
tsDMARDs ± csDMARDs versus placebo	1	Brepocitinib	JAK1, TYK2	10
	1	Deucravacitinib	TYK2	11
	1	Upadacitinib	JAK1, JAK2	12
bDMARDs versus other bDMARDs (head-to-head)	2	Secukinumab vs adalimumab	IL-17A vs TNF	16 33
	2	Ixekizumab vs adalimumab	IL-17A vs TNF	17 32
tsDMARDs versus bDMARDs (head-to-head)	2	Upadacitinib vs adalimumab	JAK1, JAK2 vs TNF	18 34
Strategic studies	3			20 48 49
csDMARD stopping	1	MTX	Dihydrofolate reductase+purine metabolim	52
bDMARD dose reduction and stopping	2	TNF	TNF	21 50
bDMARD stopping	1	Ixekizumab	IL-17A	51

AICAR, 5-aminoimidazole-4-carboxamide ribonucleotide; IL, interleukin; JAK, Janus Kinase; TNF, tumour necrosis factor alpha; TNFi, tumour necrosis factor alpha inhibitor.

Efficacy of established bDMARDs

In total, six placebo-controlled trials investigating approved bDMARDs (one golimumab (GOL), four secukinumab (SEC), one ustekinumab (UST)) with or without concomitant csDMARDs were included (four with low, two with unclear RoB).[13–15 29–31]

In GO-DACT (low RoB), MTX monotherapy was compared with MTX+GOL (TNFi) combination therapy in patients naïve to MTX and bDMARD with active dactylitis. An interim analysis at 50% of the planned recruitment suggested favourable results, which led to stopping of patient recruitment. A significantly higher median reduction in the dactylitis severity score at week 24 (primary endpoint) was observed for the MTX+GOL arm (n=21) compared with the MTX+PBO (n=23) arm (−5 vs −2, p=0.026). Assessment of dactylitis via Leeds Dactylitis Index (LDI) also showed significant differences between the arms (−69.4 vs 31.1, p=0.042), while dactylitis remission at week 24 was achieved in 6/20 (30%) vs 4/22 (18%, p=0.477) of patients receiving MTX+GOL vs MTX+PBO, respectively. MRI assessment of dactylitis (secondary exploratory endpoint) showed a significant difference in favour of the MTX+GOL arm (p=0.017). Outcomes assessing other domains besides dactylitis (enthesitis, tender joints, swollen joints, skin, physical function) showed a trend towards better efficacy for the combination therapy arm, without significant differences between the arms.[15]

Four trials (two with low RoB, two with unclear RoB) investigated SEC (anti-IL-17A) treatment. CHOICE (unclear RoB) demonstrated superior efficacy of SEC 300 mg (but not SEC 150 mg) every 4 weeks vs PBO (ACR20 at week 16: 51.5% vs 36.9% vs 23.1% for SEC 300 mg (p<0.001), SEC 150 mg (p=0.10) and PBO respectively) in a biological naïve PsA population.[29] The ULTIMATE trial investigated the change of ultrasound synovitis in biological naïve patients treated with SEC 300 mg every 4 weeks, 150 mg every 4 weeks or PBO. The primary endpoint (the ultrasound Global EULAR and OMERACT Synovitis Score mean change from baseline to week 12) was met with higher response rates in SEC (150 mg/300 mg combined group) treated patients vs PBO (−9±0.9 vs −6±0.9; difference: −3 (−6 to −1); one-sided p=0.004).[13] Baraliakos *et al.* conducted the first RCT investigating DMARD therapy in an axial PsA population. MAXIMISE (low RoB) demonstrated superior efficacy of SEC 300 mg or 150 mg every 4 weeks when compared with PBO, meeting the study's primary endpoint, ASAS20 response at week 12 (63% vs 66% vs 31%, respectively; p<0.001), as well as demonstrating improvement in MRI imaging (least squares mean difference vs PBO in total Berlin MRI score at week 12 for the entire spine: SEC 300 mg: −0.4±0.1, p<0.01; SEC 150 mg: −0.4±0.1, p<0.05; for the sacroiliac joints: SEC 300 mg −0.5±0.2, p<0.01; SEC 150 mg −0.5±0.2, p<0.01).[14] FUTURE-4 compared SEC 150 mg every 4 weeks with and without loading (ie, SEC 150 mg at weeks 0, 1, 2 and 3) to PBO. Both regimens showed superior

Table 2 Summary of efficacy outcomes of studies in psoriatic arthritis published 2018–2022 and included for evaluation of efficacy

Disease domain	Abbreviation	Full form
Composite scores	ACR response	American College of Rheumatology response definition
	DAPSA	Disease Activity Index for Psoriatic Arthritis
	DAS28-ESR/CRP	Disease Activity Score-28 (with ESR/CRP)
	MDA/VLDA	Minimal Disease Activity / Very Low Disease Activity criteria
	PASDAS	Psoriatic Arthritis Disease Activity Score
	PsARC	Psoriatic Arthritis Response Criteria
Peripheral arthritis	SJC66	Swollen Joint Count 66
	TJC68	Tender Joint Count 68
Patient-reported outcomes and Health-related quality of life	EGA	Evaluator global assessment of disease activity
	EQ5D	Euro Quality of Life five dimensions
	FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue
	Pain	Patient global assessment of pain
	PGA/PtGA	Patient global assessment of disease activity
	PSAID	Psoriatic Arthritis Impact of Disease
	SF36-MCS	Short Form 36 Mental Component Score
	WPAI	Work Productivity and Activity Impairment
Physical function	HAQ-DI	Health Assessment Questionnaire Disability Index
	SF36-PCS	Short Form 36 Physical Component Score
Skin/nails	BSA	Body surface area
	IGA	Investigator's Global Assessment Scale
	NAPSI	Nail Psoriasis Severity Index
	PASI	Psoriasis Area and Severity Index
Enthesitis	LEI	Leeds Enthesitis Index
	MASES	Maastrich Ankylosing Spondylitis Enthesitis Score
	SPARCC	Spondyloarthritis Research Consortium of Canada Index
	–	Resolution of Enthesitis
Dactylitis	DSS	Dactylitis Severity Score
	LDI	Leeds Dactylitis Index
	–	Resolution of Dactylitis
Axial disease	ASAS response	Assessment of SpondyloArthritis International Society response criteria
	ASDAS	Ankylosing Spondylitis Disease Activity Score
	BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
	BASFI	Bath Ankylosing Spondylitis Function Index
	BASMI	Bath Ankylosing Spondylitis Metrology Index
Imaging	GLOESS	Global EULAR and OMERACT Synovitis Score
	mSvDHS	modified Sharp van der Heijde Score
	–	Berlin MRI Score

CRP, C reactive protein; ESR, erythrocyte sedimentation rate.

efficacy compared with PBO and no meaningful differences between the active treatment arms.[30]

The MUST trial (low RoB) was an investigator initiated, non-inferiority trial, comparing UST (IL-12/23i) + MTX combination therapy (n=88) to UST+PBO (n=85) in PsA patients naïve to UST. While patients received open-label UST treatment, concomitant therapy with either MTX or PBO was masked. At week 24, non-inferiority was observed for the primary outcome (mean DAS28-ESR), further no meaningful differences in secondary outcomes were observed between the groups.[31]

Efficacy of targeted synthetic DMARDs

Three trials investigating the efficacy of tsDMARDs were included (all low RoB).[10–12]

Inhibition of JAK 1 and 2 via upadacitinib (UPA; 15 mg or 30 mg once daily) was compared with PBO treatment in patients with prior IR to biological DMARDs in SELECT PsA 2 (low RoB). The trial met the primary endpoint, ACR20 at week 12, with significantly higher response rates in UPA-treated patients (UPA 15 mg once daily: 120/211, 56.9%, p<0.001); UPA 30 mg once daily: 139/218, 63.8%; PBO: 51/212, 24.1%, p<0.001). Further, all secondary endpoints were met.[12]

Deucravacitinib (DEUC), a selective, oral TYK2 inhibitor, was investigated in a phase 2 double-blind RCT (low RoB) in patients with IR to ≥1 previous NSAID or DMARD therapy. The ACR 20 response at week 16 (primary endpoint) was demonstrated to be significantly higher in DEUC 6 mg once daily (37/70, 52.9%, p=0.013) and DEUC 12 mg once daily (42/67, 62.7%, p<0.001) treated patients compared with PBO (21/66, 31.8%). Higher response rates in improvement of physical function, skin disease as well as enthesitis and dactylitis resolution were observed.[11]

Another phase 2 RCT (low RoB) investigated brepocitinib (BREP), an inhibitor of TYK2 and JAK1 with active disease despite previous NSAID or DMARD treatment. BREP 30 mg once daily as well as 60 mg once daily, but not BREP 10 mg once daily, met the primary endpoint (ACR20 at week 16) when compared with PBO treatment (PBO: 29/67, 43.3%; BREP 10 mg once daily: 20/31, 43.4%, p=not significant; BREP 30 mg once daily: 40/60, 66.7%, p=0.0197; BREP 60 mg once daily: 44/59, 74.6%, p=0.0006). Significant differences compared with placebo were also observed in PASI 75/90% responses for BREP 30 mg and 60 mg once daily. Exploratory analyses also showed benefit for BREP-treated patients in achieving MDA and improvement of enthesitis (only for BREP 60 mg once daily) and dactylitis outcomes (only for BREP 10 mg and 60 mg once daily), as well as physical function and fatigue.[10]

Head-to-head studies

Three head-to-head trials were included (RoB; table 3).[16 18 32–34]

SPIRIT H2H (high RoB), an assessor-blinded, head-to-head trial compared open-label ixekizumab (IXE, IL17Ai) to adalimumab (ADA, TNFi) in bDMARD naïve patients with IR to csDMARDs. The primary endpoint was defined as simultaneous achievement of ACR50 and PASI100 response—assessed for superiority of IXE versus ADA at week 24. Significantly more patients achieved the primary outcome in the IXE group (102/283, 36%, p=0.036) vs ADA (79/283, 27.9%). No significant difference was found between the arms when comparing ACR (20/50/70) response rates, Health Assessment Questionnaire Disability (HAQ-DI) or dactylitis remission (LDI=0). However, comparing PASI75/90/100 results, these showed significantly higher response rates in IXE-treated patients compared with ADA. Other secondary endpoints such as DAPSA remission, MDA, VLDA were also in favour of IXE treatment.[17] The results were maintained until week 54, with a significantly higher proportion of patients achieving a simultaneous ACR50+PASI 100 response (39% vs 26%, p<0.001).[32]

In the EXCEED trial (low RoB), bDMARD naïve patients were randomised to SEC 300 mg every 4 weeks or ADA 40 mg every 2 weeks monotherapy in a double-blind manner. The study was powered to show superiority of SEC over ADA in achieving an

Table 3 Efficacy outcomes of head-to-head studies comparing JAK inhibitors to biological DMARDs

Population	Study	RoB	Treatment	n	Primary endpoint	Result (%)	Head-to-head comparison	Endpoints at week 24						
								ACR 20 (%)	ACR 50 (%)	ACR 70 (%)	PASI90 (%)	MDA (%)	LEI=0 n/N (%)	LDI-B=0 n/N (%)	ΔHAQ-DI
csDMARD-IR; bDMARD naive	Mease 2020/Smolen 2020 (SPIRIT-H2H)[17 32]	High (assessor blinded)	IXE 80 mg Q4W ± csDMARD	283	ACR50 + PASI100 at week 24	36.0	S (met)	68.9	50.5	31.8	71.7	47.7	95/159 (59.7)	37/42 (88.1)	NR
			ADA 40 mg Q2W ± csDMARD	283		27.9	Reference	72.1	46.6	25.8	55.8	35.3	81/147 (55.1)	54/58 (93.1)	NR
csDMARD-IR; bDMARD naive	McInnes 2020 (EXCEED)[16]	Low	SEC 300 mg Q4W (mono)	426	ACR20 at week 52	67	S (not met)	71	43	NR	63	NR	119/234 (51)	NR	−0.54
			ADA 40 mg Q2W (mono)	427		62	Reference	64	40	NR	42	NR	116/264 (44)	NR	−0.51
csDMARD-IR; bDMARD naive	McInnes 2021 (SELECT PsA 1)[18]	Low	UPA 15 mg OD±csDMARD	429	ACR 20 at week 12	70.6	NI (met) S (not met)	73.4	52.4	28.7	41.6	36.6	145/270 (53.7)	104/136 (76.5)	−0.51
			UPA 30 mg OD ± csDMARD	423		78.5	NI (met) S (met)	78.5	60.5	36.4	48.1	45.4	154/267 (57.7)	101/127 (79.5)	−0.51
			ADA 40 mg Q2W ± csDMARD	429		65.0	Reference	67.1	44.3	22.6	45.0	33.3	125/265 (47.2)	94/127 (74.0)	−0.39
			PBO ± csDMARD	423		36.2	–	45.2	18.9	5.2	16.6	12.3	78/241 (32.4)	50/126 (39.7)	−0.19

Results of secondary efficacy outcomes are shown at the timepoint of the primary endpoint.
ACR, American College of Rheumatology; ADA, adalimumab; bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic DMARD; HAQ-DI, health assessment questionnaire-disability Index; IR, insufficient response; IXE, ixekizumab; JAK, Janus Kinase; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; NI, non-inferiority; NR, not reported; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; RoB, risk of bias; S, superiority; SEC, secukinumab; UPA, upadacitinib.

ACR20% response at week 52. The primary endpoint was not met, with an ACR20 response of 67% vs 62% (p=0.072) for SEC and ADA, respectively. Similar responses were observed between both treatment arms, with the exception of skin outcomes (PASI 75/100) showing higher responses in the SEC arm.[16 33]

Another double-blind head-to-head trial (SELECT-PsA 1, low RoB) compared UPA 15 mg once daily and 30 mg once daily to ADA 40 mg every 2 weeks and PBO treatment in patients with IR to csDMARDs. With ACR 20 response rates at week 12 of 303/429 (70.6%), 332/423 (78.5%), 279/429 (65.0%) and 153/423 (36.2%) for UPA 15 mg once daily, UPA 30 mg once daily, ADA 40 mg every 2 weeks and PBO, all active treatment arms showed superiority compared with placebo (p<0.001). Further, non-inferiority (margin 15%) of both UPA dosages was demonstrated when compared with ADA, while testing for superiority (vs ADA) was only shown for UPA 30 mg once daily (p<0.001) and not for UPA 15 mg once daily (hierarchical testing failed, no p value reported). Radiographic progression at week 24 was low in all active treatment arms.[18 34]

A summary of the trial results is shown in table 3.

Efficacy of novel biological DMARDs targeting the p19 subunit of IL23

In total six trials (five with low RoB, one with unclear RoB) were included.[6–8 35–40]

Three trials investigated guselkumab (GUS) an IL23-p19 inhibitor. DISCOVER-1 (low RoB) was a phase 3, double-blind RCT investigating patients with and without prior TNFi exposure. The ACR 20% response at week 24 (primary endpoint) was significantly higher in GUS-treated patients compared with placebo (GUS 100 mg every 4 weeks: 76/128, 59%; p<0.001; GUS 100 mg every 8 weeks: 66/127, 52%, p<0.001; PBO: 28/126, 22%). Results in favour of GUS versus PBO, with a trend towards better efficacy in the every 4 weeks arm, were observed also for more stringent outcomes (ACR70 response for GUS 100 mg every 4 weeks: 26/128, 20%; GUS 100 mg every 8 weeks: 15/127, 12%; PBO: 7/126, 6%), physical function, extra articular manifestations like dactylitis, enthesitis and skin disease. Consistent results (not multiplicity corrected) were also shown for patients with or without previous TNFi therapy.[35] In DISCOVER-2 (low RoB) only patients who were naïve to bDMARDs were included. GUS treatment was superior to PBO for ACR20 (GUS 100 mg every 4 weeks: 156/245, 64%, p<0.001; GUS 100 mg every 8 weeks: 159/248, 64%, p<0.001; PBO: 81/246, 33%), however, no clear difference in other outcomes between the two GUS regimens was observed in this study except for radiographic damage progression, with only GUS 100 mg every 4 weeks but not GUS 100 mg every 8 weeks being significantly different versus PBO (Δmodified Sharp van der Heijde Score, mSvDHS: PBO: 0.95; 95% CI: 0.61 to 1.29; GUS 100 mg every 4 weeks: 0.29, −0.05 to 0.63, p=0.011; GUS 100 mg every 8 weeks: 0.52, 0.18 to 0.86, p=0.072).[7] Assessing patients with axial involvement (as defined by the investigator) and evidence of sacroiliitis (MRI or pelvic radiograph as reviewed locally by the respective investigator) showed improvement in GUS-treated patients compared with PBO when assessing axial involvement with the Bath Ankylosing Spondylitis Disease Activity Index (GUS 100 mg every 4 weeks, n=95: −2.7, −3.2 to −2.2; GUS 100 mg every 8 weeks, n=83: −2.7, −3.2 to −2.2; PBO: −1.3, −1.8 to −0.9) and the Ankylosing Spondylitis Disease Activity Score (GUS 100 mg every 4 weeks: −1.4, −1.7 to −1.2; GUS 100 mg every 8 weeks: −1.4, −1.7 to −1.2; PBO: −0.7, −0.9 to −0.5) in a pooled post hoc analysis.[36]

COSMOS (unclear RoB) investigated GUS 100 mg every 8 weeks compared with PBO in patients who were TNFi-IR, demonstrating superior efficacy of GUS over PBO in achieving the primary endpoint (ACR 20 at week 24: GUS 100 mg every 8 weeks: 84/189, 44.4%, p<0.001; PBO: 19/96, 19.8%) as well as all other secondary endpoints (MDA, DAPSA, physical function, skin disease, enthesitis, dactylitis and fatigue).[37]

The efficacy and safety of risankizumab (RIS), another inhibitor of the IL23-p19 subunit, was investigated in two RCTs (both low RoB).[38–40] In patients with IR to csDMARDs (KEEPsAKE 1), patients were randomised to RIS 150 mg (s.c. at weeks 0, 4 and 16). At week 24 the primary (ACR 20: RIS 150 mg: 277/482, 57.3%, p<0.001; PBO: 161/481, 33.5%) and most secondary endpoints (including MDA, PASI90, enthesitis, dactylitis, fatigue and physical function) except the secondary endpoint of radiographic damage progression (ΔmSvDHS at week 24: RIS 150 mg: 0.23, 0.02 to 0.44; PBO: 0.32, 0.11 to 0.53, p=0.50) were met.[8] Half of the patients included in KEEPsAKE 2 (low RoB) had received bDMARD therapy before the study. Also, this study met its primary (ACR 20 at week 24: RZB 150 mg: 115/224, 51.3%, p<0.001; PBO: 58/219, 26.5%) and all secondary endpoints.[38] Further, improvements in patient-reported outcomes, work productivity and health-related quality of life could be observed in patients treated with RIS.[39 40] A phase 2b study (low RoB) investigated tildrakizumab (TIL; IL23-p19i) 200 mg every 4 weeks or every 12 weeks, 100 mg every 12 weeks and 20 mg every 12 weeks in patients with previous iR to NSAIDs or DMARDs. The primary endpoint was met by all TIL arms compared with PBO (ACR 20 at week 24: TIL response rates ranging from 71%–80%; PBO: 51%), with no clear dose response.[6]

Efficacy of novel bDMARDs targeting IL-17

Five trials on novel molecules targeting IL-17 were included (four with low RoB, one conference abstract).[9 41–44]

Bimekizumab (BKZ), a selective inhibitor of IL17-A and IL17-F was investigated in two placebo-controlled RCTs. BE OPTIMAL (low RoB) investigated patients naïve to bDMARDs against PBO and active control and showed superior efficacy of BKZ 160 mg every 4 weeks over PBO in achieving the primary endpoint (ACR50% response at week 16: BKZ: 189/431, 44%, p<0.001; PBO: 28/281, 10%, reference; ADA: 64/140, 46%, no formal comparison) as well as in reduction of signs and symptoms of other manifestations like skin disease, enthesitis, dactylitis and radiographic damage progression.[9] Similarly, BE COMPLETE showed superior efficacy of BKZ versus PBO in patients with IR to TNFi.[41]

Brodalumab (BRO; IL-17-A receptor) was investigated in csDMARD IR patients in AMVISION 1 and 2. After randomisation of 962 patients, both trials were terminated early due to the sponsors' decision based on observed events of suicidal ideation and behaviour. The primary endpoint (ACR 20 at week 16) was met in both studies, with significantly higher response rates in achieving ACR50/70, PASI responses and resolution of dactylitis/enthesitis.[42]

Izokibep (IZO) is an antibody mimetic, a protein with a small molecular size that can inhibit IL17A and is thus a biological DMARD, but not an antibody. It is administered every other week. A 16-week phase 2 study (conference abstract, RoB not assessed) comparing IZO and PBO showed significant results compared with placebo and a slight dose–response relationship (ACR50 at week 16: IZO 40mg every 2 weeks: 20/42, 48%, p<0.001; IZO 80mg every 2 weeks: 24/46, 52%, p<0.001; PBO: 6/43, 13%).[43 44] Clinically relevant treatment benefits were also observed in enthesitis, dactylitis and nail disease.[45]

Figure 2 summarises and updates the evidence on established and new therapies based on the data presented and previous SLRs.[24 46 47]

Strategic trials

Three strategic trials were included in this SLR (all with high RoB due to their open-label design).[20 48 49]

The NOR-DRUM trial investigated therapeutic infliximab (IFX) dosed based on therapeutic drug monitoring (TDM) versus IFX therapy without TDM. In total 411 patients with inflammatory immune-mediated diseases were included in the induction part of the trial, with 42 patients diagnosed with PsA. The primary outcome was the achievement of remission (defined as DAS28-ESR<2.6 for PsA) at week 30, with no difference comparing TDM to standard dosing in the overall analysis, and looking at the PsA subgroup, numerically but not statistically better results for the standard dosing arm (Disease Activity Score 28-ESR<2.6 at week 30: TDM: 5/20, 25%; standard IFX dosing: 12/22, 54.5%; adjusted difference 29.4%, −0.2% to 59.0%).[49] The second part of this trial investigated the sustainment of response in patients who achieved DAS28<2.6 receiving IFX therapy, again comparing TDM to standard dosing. The PsA subgroup showed no clinically meaningful difference in the number of patients with sustained DAS28-ESR<2.6 from weeks 30 to 52 (TDM: 19/28, 67.9%; standard IFX dosing: 16/25, 64.0%; adjusted difference 6.2%, −19.5% to 31.9%).[48]

CONTROL was a strategic open-label study consisting of two parts: in part 1, patients with IR to MTX 15 mg/week were either randomised to dose escalation of MTX (20–25 mg/week) or additional treatment with adalimumab 40 mg every 2 weeks in combination with MTX 15 mg/week. The primary endpoint (MDA at week 16) was met, with significantly more patients in the ADA+MTX 15 mg/week arm (51/123, 41%) vs the MTX 20–25 mg/week dose escalation arm (16/122, 13%, p<0.001) achieving MDA. In part 2, patients who achieved MDA at week 16 received therapy modification (ADA 40 mg every 2 weeks+MTX 15 mg/week: ADA 40 mg every 2 weeks monotherapy) or continuation (MTX 20–25 mg/weekly) with most patients maintaining MDA at week 32 (41/51, 80% for ADA 40 mg every 2 weeks monotherapy vs 10/15, 67% for patients continuing MTX 20–25 mg/week monotherapy). Patients with IR were re-randomised at week 16 to treatment intensification: non-responders to ADA 40 mg every 2 weeks+MTX 15 mg/week were escalated to ADA 40 mg weekly+MTX 15 mg/week while those receiving MTX 20–25 mg/week received additional treatment with ADA 40 mg every 2 weeks. 17/57 (30%) of patients escalated from ADA 40 mg every 2 weeks (+MTX) to ADA 40 mg weekly+MTX 15 mg/week achieved MDA after 32 weeks, while 50/91 (55%) of patients with initial MTX non-response who received add-on ADA 40 mg every 2 weeks achieved MDA.[20]

Tapering and withdrawal

Four trials investigated treatment tapering and/or stopping (two with high, two with low RoB).[21 50–52]

Michielsens *et al.* conducted an open-label non-inferiority TNFi withdrawal trial (high RoB), using a treat-to-target (using PASDAS≤3.2 as target) dose-reduction and withdrawal strategy (n=42) compared with T2T treatment continuation without tapering (n=22) in patients with sustained PASDAS≤3.2. After 12 months, T2T tapering was shown to be non-inferior to a T2T

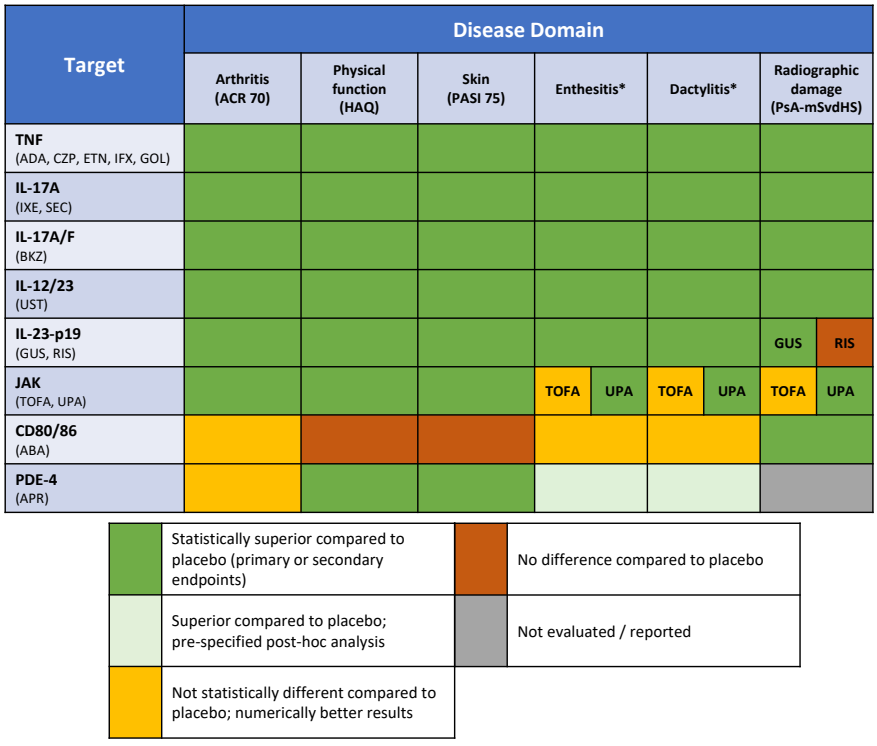

Figure 2 Efficacy results of randomised controlled trials stratified by mode of action and disease domain. Data from previous systematic literature research are also accounted for in this figure. *Different instruments used in studies. ABA, abatacept; ACR, American College of Rheumatology Response; ADA, adalimumab; APR, apremilast; BKZ, bimekizumab; CD, cluster of differentiation; CZP, certolizumab-pegol; ETN, etanercept; GOL, golimumab; GUS, guselkumab; HAQ, Health Assessment Questionnaire Disability Index; IL, interleukin; IFX, infliximab; IXE, ixekizumab; JAK, Janus kinases; PDE4, phosphodiesterase-4; PsA-mSvdHS, Psoriatic Arthritis modified Sharp van der Heijde Score; RIS, risankizumab; SEC, secukinumab; TNF, tumour necrosis factor; TOFA, tofacitinib; UPA, upadacitinib; UST, ustekinumab.

strategy without tapering. Rates of patients in PASDAS LDA were comparable (71% vs 73%) with 24% (T2T with tapering) vs 77% (T2T without tapering) of patients receiving 100% of their daily defined dose and 36% (T2T tapering) vs 0% (no tapering) had stopped any DMARD use.[21]

Another open-label study (high RoB) investigated interval prolongation (ie, doubling the dosing interval) and subsequent stopping (after 6 months) of etanercept (ETN) treatment versus ETN continuation. After 6 months, 57% (vs 70%) of PsA patients could double their ETN interval while still remaining in MDA after 6 months.[50]

SPIRIT-P3 was a double-blind RCT, in which patients achieving MDA after receiving (open-label) ixekizumab for 36 weeks (158/394, 40%) were randomised to either undergo blinded withdrawal (receiving placebo) or continuation of ixekizumab treatment. The primary endpoint of time to relapse (ie, loss of MDA) until week 64 occurred more rapidly in patients who withdrew ixekizumab (median 22.3 weeks; 16.1 to 28.3, p<0.001). From week 24 to week 104, 67/79 patients (85%) experienced a relapse in the withdrawal group, compared with 30/79 (38%; p<0.001) in the continuation group. After re-treatment, almost all patients reachieved MDA (64/67, 95.5%) with a median time to re-achievement of MDA of 4.1 weeks (95% CI 4.1 to 4.3) in the ixekizumab withdrawal group.[51]

A withdrawal substudy (low RoB) of the long-term extension study of TOFA (OPAL Balance) investigated MTX withdrawal in patients receiving TOFA 5 mg BID (two times per day) for at least 24 months as well as MTX (7.5–20 mg/week) for at least 4 weeks. All patients received open-label TOFA and were randomised to either PBO (ie, MTX withdrawal; n=90) or continued MTX background therapy (n=89). After 6 months, no difference was observed in the co-primary endpoints PASDAS (difference 0.09, −0.13 to 0.31) and HAQ-DI (difference 0.03, −0.05 to 0.10).[52]

Table 4 summarises the main results of studies investigating dose reduction and withdrawal.

Safety

Of the 24 additional reports included in the safety analysis (RoB: 8 low, 1 unclear, 10 high, 5 conference abstracts - not assessed), 9 were derived from long-term extension studies of RCTs, 12 were cohort studies including registry and claims analyses, 2 case–control studies and one prospective phase 4 observational study. Moreover, all trials included in the efficacy analysis were also assessed for safety. Detailed event rates of adverse events of interest are shown in online supplemental tables S3.4.1-S3.4.6. A summary of AESI of trials investigating tsDMARDs is shown in table 5.

Infections and infestations

Randomised controlled trials and long-term extension studies

In EXCEED comparison of SEC with ADA showed similar rates of serious infections (SEC: 7/426, 1,6%; ADA: 6/427, 1.4%), however, candida infections occurred numerically more frequently in SEC-treated patients (SEC 16/426, 4%; ADA: 7/427, 2%).[16] Two cases of candida skin infection were observed in TIL-treated patients (compared with none in the PBO arm).[6] Candida and other fungal infections were also more frequent in BKZ-treated patients compared with PBO (BE COMPLETE:

Table 4 Primary outcomes of studies investigating DMARD dose reduction and withdrawal

Study	RoB	Primary outcome(s) (unit)	Week	Treatment arm	n	Result	Difference/ 95% CI / p-value
bDMARD dose reduction and stopping							
Michielsens 2022[21]	High (open-label)	PASDAS≤3.2 Stopped DMARD usage (n/%)	52	T2T TNFi with tapering	42	30 (71%) 15 (36%)*	Difference: 8% (–14% to 30%)
				T2T TNFi without tapering	22	16 (73%) 0 (0%)*	
Ruwaard 2023[50]	High (open-label)	Sustained MDA (n/%)	24	ETN interval prolongation	21	12 (57%)	Not reported
				ETN continuation	20	14 (70%)	
bDMARD stopping							
Coates 2021 (SPIRIT-P3)[51]	Low	Time to relapse (loss of MDA) (weeks)	36 to 104	PBO (IXE withdrawal)	79	22.3	95% CI 16.1 to 28.3 <0.001
				IXE continuation	79	NE†	
csDMARD stopping							
Nash 2021 (OPAL Balance)[52]	Low	Change from baseline in PASDAS and HAQ-DI (LSM±SE)	24	PBO + TOFA 5 mg BID (MTX stopping)	90	0.23±0.08 0.04±0.03	Difference PASDAS: 0.09 (95% CI –0.13 to 0.31) HAQ-DI: 0.03 (95% CI –0.05 to 0.10)
				TOFA 5 mg BID + MTX (MTX continuation)	89	0.14±0.08 0.02±0.03	

*Secondary outcome.
†Not estimable, as <50% of patients experienced a relapse by the end of the study period.
BID, two times per day; DMARD, disease-modifying antirheumatic drug; ETN, etanercept; HAQ-DI, Health Assessment Questionnaire Disability Index; IXE, ixekizumab; LSM, least squares mean; MDA, minimal disease activity; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; RoB, risk of bias; SE, standard error; TNFi, tumour necrosis factor alpha inhibitor; TOFA, tofacitinib; T2T, treat-to-target.

BKZ: 7/267, 3%; PBO: 0, 0%; BE OPTIMAL: BKZ 20/431, 5%; PBO: 4/281, 1%; ADA: 1/140, <1%) with no systemic fungal infections observed.[9 41] No serious infection, HZ or opportunistic infection was observed in the DEUC phase 2 trial until week 16.[11] Also, in the GUS trials, no signal for increased rates of serious infections was observed.[7 35 37]

Rates of candida and fungal infections were very low in studies investigating IL23-p19 inhibitors, with few cases of local skin candidiasis.[6–8 35 38]

In integrated safety analyses of GUS, three cases of opportunistic infections were observed in the DISCOVER-2 trial (after week 52), with an otherwise consistent safety profile compared with the placebo-controlled period and no cases of active Tb.[53]

Long-term safety of PsA patients in the UPA trial programme (comparing UPA 15 mg once daily (n=907) to ADA 40 mg every 2 weeks (n=429) treated patients, data for UPA 30 mg once daily not reported; low RoB) showed higher rates for UPA for serious infections (exposure adjusted event rate, EAER, 95% CI: UPA 15mg once daily: 3.9, 3.1 to 4.9; ADA: 1.4, 0.8 to 2.5), opportunistic infections (UPA 15mg once daily: 0.5, 0.2 to 0.9; ADA: 0) and HZ rates (UPA 15mg once daily: 3.6, 2.8 to 4.6; ADA: 0.4, 0.1 to 1.1). Of note, 29 of 93 (31.2%) COVID-19 infections occurring in UPA-treated patients were serious (ADA: 4/37, 10.8%) with 6 (6.5%) fatal cases for UPA-treated versus none in ADA-treated patients. No cases of active Tb occurred in both groups.[54]

An analysis of influenza occurrence in the TOFA trial programme (low RoB) showed numerically increased rates of influenza infections in TOFA 5 mg BID (5/347, 196.2 patient years (PY), incidence rate, 95% CI: 2.51, 0.81 to 5.85) and TOFA 10 mg BID treated patients (5/344, 192.2 PY, incidence rate, 95% CI: 2.56, 0.83 to 5.97) compared with ADA 40 mg every other week (no event).[55]

Observational studies

Investigation of incidence of Tb (Tb activation, Tb development or Tb reactivation) in the secukinumab trial database (low RoB) on 2523 PsA patients with in total 4943 PY did not find cases of active Tb during the programme.[56] A Slovenian cohort study (low RoB) found similar Tb incidence rates in PsA patients receiving TNF treatment compared with the general population of non-endemic countries with 2 cases occurring in 413 patients (1849 PY; standardised incidence rate, SIR, 95% CI: 5.8, 0.3 to 112).[57]

An observational study (low RoB) of PsA and SpA patients in four Nordic registers (DANBIO, ROB-FIN, NOR-DMARD and ARTIS/SRQ) compared TNFi to SEC-treated patients to assess the differences in risk of hospitalised infections. Although not powered to investigate the PsA subpopulation separately, a trend towards a higher risk for hospitalised infections in SEC-treated patients (incidence rate, 95% CI: 5.6, 4.1 to 7.5; reference) compared with TNFi (adjusted Hazard Ratio, aHR: ADA: 0.59, 0.34 to 1.03; ETN: 0.59, 0.28 to 1.20; GOL: 0.57, 0.28 to 1.20; IFX: 0.88, 0.54 to 1.42) was observed.[58]

A claims database study (high RoB) also compared the risk of hospitalised infections in Pso and PsA patients receiving DMARD therapy, comparing UST to TNFi and IL17i as well as apremilast (APR). Lower rates of hospitalisations due to infection were observed for UST (reference) treated patients compared with the other therapies in the overall comparison, with a similar trend found in the sensitivity analysis investigating PsA patients only (aHR, 95% CI: ADA: 1.67 (0.55 to 5.07); APR: 1.72 (0.68 to 4.30); CZP: 1.28 (0.74 to 2.20), ETN: 1.41 (0.40 to 4.98), GOL: 1.62 (0.18 to 14.41), IFX: 2.89 (1.26 to 6.63), IXE: 15.05 (4.27 to 53.04) and SEC: 1.93 (0.97 to 3.87)).[59] Another claims database study (high RoB) compared the risk for infections requiring hospitalisation between TNF, IL17 or IL12/23 inhibition in PsA and Pso patients. No statistical difference was observed in serious infection for PsA patients between the different MOA (aHR (95% CI): IL-17 vs TNF: 0.73 (0.36 to 1.45); IL-12/23 vs TNF: 0.59 (0.38 to 0.92); IL-17 vs IL12/23: 1.01 (0.53 to 1.92)).[60]

A matched case–control study from the DANBIO registry (unclear RoB) compared the risk for serious infections in patients starting bDMARD treatment. Controls were randomly selected (matched by sex, age and postal code) from the general population without PsA. In 12 months 89/2429 (3.7%; HR, 95% CI: 3.4, 2.7 to 4.3) of PsA patients experienced a serious

Table 5 Safety outcomes (adverse events of special interest) of RCTs investigating targeted synthetic DMARDs

Population	Study	Risk of bias	Treatment	n	Safety endpoint (week)	Serious adverse event	Serious infectious event	Opportunistic infection	Herpes zoster	Malignancy (other than NMSC)	Major adverse cardiovascular event	Venous thromboembolism
csDMARD-IR; bDMARD naive	McInnes 2021 (SELECT PsA 1)[18]	Low	UPA 15 mg OD ± csDMARD	429	24	14 (3.3)	5 (1.2)	1 (0.2)	4 (0.9)	1 (0.2)	0	0
			UPA 30 mg OD ± csDMARD	423		13 (3.1)	4 (0.9)	0	3 (0.7)	1 (0.2)	0	1 (0.2)
			ADA 40 mg Q2W ± csDMARD	429		16 (3.7)	3 (0.7)	0	0	3 (0.7)	2 (0.5)	2 (0.5)
			PBO ± csDMARD	423		26 (6.1)	11 (2.6)	2 (0.5)	5 (1.2)	0	1 (0.2)	1 (0.2)
bDMARD-IR	Mease 2021 (SELECT PsA 2)[12]	low	UPA 15 mg OD ± csDMARD	211	24	12 (5.7)	1 (0.5)	0	3 (1.4)	2 (0.9)	1 (0.5)	1 (0.5)
			UPA 30 mg OD ± csDMARD	218		18 (8.3)	6 (2.8)	2 (0.9)	8 (3.7)	2 (0.9)	0	0
			PBO ± csDMARD	212		4 (1.9)	1 (0.5)	0	2 (0.9)	0	0	0
Mixed (NSAID/ csDMARD/bDMARD-IR)	Mease 2022 (DEUC Phase 2)[11]	low	DEUC 6 mg OD ± csDMARD	70	16	0	0	0	0	0	NR	0
			DEUC 12 mg OD ± csDMARD	67		0	0	0	0	0	NR	0
			PBO ± csDMARD	66		1 (1.5)	0	0	0	0	NR	1 (1.5)
Mixed (NSAID/ csDMARD/bDMARD-IR)	Mease 2023 (BREP Phase 2)[10]	low	PBO ± csDMARD	67	16	1 (1.5)	0	0	0	0	0	0
			BREP 10 mg OD ± csDMARD	31		0	0	0	1 (3.2)	0	0	0
			BREP 30 mg OD ± csDMARD	60		3 (5.0)	2 (3.3)	0	1 (1.7)	0	0	0
			BREP 60 mg OD ± csDMARD	59		1 (1.7)	0	0	0	2 (3.3)	0	0

ADA, adalimumab; bDMARD, biological disease-modifying antirheumatic drug; BREP, brepocitinib; csDMARD, conventional synthetic DMARD; DEUC, deucravacitinib; IR, insufficient response; NMSC, non-melanoma skin cancer; NR, not reported; NSAID, non-steroidal anti-inflammatory drug; OD, once daily; RCT, randomised controlled trial; UPA, upadacitinib.

infection vs 262/24288 (1.1%) of matched controls (reference). Patients with comorbidities were at higher risk (HR, 95% CI: one comorbidity: 5.3, 3.4 to 8.2; two or more comorbidities: 4.9, 2.5 to 9.6; without comorbidities: 2.5, 1.8 to 3.5), as well as patients receiving glucocorticoid (GC) treatment (GC use: 5.3, 3.3 to 8.5; no GC use: 2.9, 2.2 to 3.9).[61]

The PsABio study was an observational postmarketing surveillance study (high RoB), investigating UST (n=494) and TNFi (n=557) treatment in patients receiving these treatments as first-line, second-line or third-line therapy. The choice of the bDMARD was made by the treating rheumatologist. UST users showed numerically lower numbers of serious adverse events (UST: 31/494, 6.3%, (4.3% to 8.8%); TNFi: 40/557, 7.2% (5.2% to 9.7%)). Exposure-adjusted incidence rates (EAIR) showed a higher risk for the occurrence of infections in TNFi versus UST-treated patients (EAIR not reported). Rates of serious or opportunistic infections were similar (UST: 6/494, 1.2% (0.4% to 2.6%); TNFi: 5/557, 0.9% (0.3% to 2.1%)).[62]

MACEs and arterial thrombotic events

Randomised controlled trials and long-term extension studies

During the placebo controlled period of the SELECT PsA trials, in SELECT PsA 1, no MACE occurred in the UPA treatment arms, one in the PBO and two in the ADA arm.[18] In SELECT PsA 2, one MACE occurred in UPA 15 mg OD treated patients (compared with none in the PBO and UPA 30 mg OD arm).[12] No MACE was seen in either the DEUC or the BREP phase 2 trial.[10 11]

During the long-term safety period comparing UPA 15 mg OD (n=907) to ADA 40 mg every 2 weeks (n=429) rates of (adjudicated) MACE were similar between both groups (EAER, 95% CI: UPA 15mg OD: 0.3, 0.1 to 0.6; ADA: 0.3, 0.1 to 1.0).[54 63]

Analysis of the long-term safety data of PsA patients treated with TOFA (high RoB) showed 1/347 cases of arterial thromboembolisms in the TOFA 5 mg BID arm (IR: 0.5, 95% CI: 0.01 to 2.78), and 2/106 in the ADA arm (IR 2.16, 95% CI: 0.26 to 7.82) and no event in the TOFA 10 mg BID arm.[64]

No signal for MACE was identified in KEEPsAKE 1 and 2, investigating RIS[8 38] and in the integrated safety analyses of GUS.[53]

Observational studies

Two investigations of claims data (high RoB) found no increased risk of myocardial infarction or MACE in patients receiving bDMARD therapy compared with patients receiving csDMARDs, GC or APR.[65 66] A cohort study using the French health insurance and hospital discharge database found an increased risk of MACE in bDMARD naïve patients without previous cardiovascular disease initiating IL12/23i therapy (aHR, 95% CI: 2.0, 1.3 to 3.0) or IL17i therapy (1.9, 1.2 to 3.0) compared with TNFi (reference). No increased risk was found when comparing TNFi to APR (1.3, 0.8 to 2.2), while JAKis were not studied.[65] A study from Hong Kong (conference abstract, RoB not assessed) did not find bDMARD treatment to be associated with occurrence of MACE, but it was associated with elevated acute-phase reactants over time (aHR, 95% CI: 1.16, 1.11 to 1,21; p<0.001), as well as with GC usage (1.93, 1.04 to 3.57; p=0.036).[66]

In the UST arm of the PsABio study (see details above), two myocardial infarctions and one cardiac arrest occurred, compared with three myocardial infarctions in the TNFi arm.[62]

Venous thromboembolisms

Comparing UPA 15 mg OD (n=907) to ADA 40 mg every 2 weeks (n=429) rates of (adjudicated) VTE were similar for both groups (VTE: UPA 15mg OD: 0.2, 0.1 to 0.5); ADA: 0.2, 0 to 0.8) in patients receiving UPA.[54 63] No VTE was observed in the DEUC and BREP phase 2 trial.[10 11]

Analysis of the long-term safety data of PsA patients treated with TOFA 5 mg BID or 10 mg BID (high RoB) showed low event rates, with one VTE (deep vein thrombosis, incidence rate, 95% CI: 0.51, 0.01 to 2.83) occurring in the TOFA 10 mg BID arm (1/344, 197.2 PY) vs none in the ADA arm (92.6 PY) and none in the TOFA 5 mg BID arm (201.1 PY) during the active-controlled period. VTEs were experienced by patients who had baseline cardiovascular or VTE risk factors [64]

Malignancies

Randomised controlled trials and long-term extension studies

During the placebo-controlled period of SELECT-PsA 1, five malignancies (excluding non-melanoma skin cancer) were observed: one in the UPA 15 mg OD arm (neuroendocrine carcinoma), one in the UPA 30 mg OD arm (malignant lung neoplasm) and three in the ADA 40 mg every 2 weeks arm (colon cancer, ovarian cancer, uterine cancer), with none in the PBO arm.[18] In the PBO controlled period of the SELECT-PsA 2 trial, malignancies observed in each of the UPA arms were: one prostate cancer, one rectal cancer in UPA 15 mg OD (n=2); one rectal adenocarcinoma and one ovarian/endometrial cancer in the UPA 30 mg OD arm (n=2), compared with none in the PBO arm.[12] In the UPA long-term extension, rates of malignancies (excluding non-melanoma skin cancer) were similar (UPA 15 mg OD: 0.6, 0.3 to 1.1; ADA: 0.4, 0.1 to 1.1), with higher age (HR, 95% CI: 3.1, 1.7 to 5.8) and body mass index (1.1, 1.003 to 1.15), being significant predictors for development of malignancies in patients receiving UPA 15 mg OD.[54 67] Rates of non-melanoma skin cancer were numerically higher (UPA: 0.8, 0.4 to 1.3; ADA: 0.2, 0 to 0.8) for UPA-treated patients. One basal cell carcinoma occurred in the BREP 60 mg once daily arm compared with no events in the other arms.[10]

In the phase 2 trial investigating BREP, one malignancy was observed (uterine leiomyoma) in the BREP 60 mg OD arm compared with no events in the other treatment arms.[10] No malignancy occurred during the 16 weeks of the DEUC phase 2 trial.[11]

An analysis of malignancy occurrence during SEC treatment in the SEC trial database showed a cumulative incidence of 51/4902 malignancies in PsA patients (EAIR per 100 patient years, 95% CI: 1.04, 0.77 to 1.37), with non-melanoma skin cancer (basal cell carcinoma, n=15; squamous cell carcinoma, n=2) being the most prevalent. The incidence rate was in line with the expected rate of the general population (SEER database, standardised incidence rate, 95% CI: 1.16, 0.80 to 1.62).[68] No signal for an increased risk for malignancies was found in the integrated safety analysis of GUS.[53]

Observational studies

No difference in the occurrence of malignancies between UST and TNFi-treated patients was observed in the PsABio study.[62]

In a British cohort study (high RoB) the incidence of cancer was found to be comparable in PsA patients receiving TNFi treatment compared with the general population (SIR, 95% CI: 0.94, 0.65 to 1.34), however, an increased risk for non-melanoma skin cancer was observed (2.12, 1.19 to 3.50). Also, increased all-cause mortality (standardised mortality rate, 95% CI: 1.56,

1.12 to 2.11) and increased risk of death from coronary heart disease (2.42, 1.11 to 4.59) were found.[69] No increased risk for development of solid cancer was found in a large Nordic cohort study (unclear RoB) comparing PsA patients exposed to TNFi treatment with bDMARD naïve PsA patients (aHR, 95% CI: Nordic clinical rheumatology registers: 1.0, 0.9 to 1.2; and national patient registers: 0.8, 0.7 to 1.0).[70] A similar analysis (low RoB) investigating haematological malignancies did not find an increased risk for PsA patients receiving TNFi therapy compared with bDMARD naïve patients (incidence rate ratio, 95% CI: TNFi: 0.96, 0.68 to 1.35; bDMARD naive: 0.84, 0.64 to 1.10). However, an increased risk of haematological malignancies compared with the general population was observed (incidence rate ratio, 95% CI: 1.35, 1.17 to 1.55).[71]

Adverse events of special interest

Randomised controlled trials and long-term extension studies

In EXCEED, new cases of IBD were more frequent in the SEC arm compared with ADA (two cases vs none).[16]

In the PBO-controlled period (until week 16) of the phase 2 trial investigating DEUC, acne was reported in 2/70 (2.9%) patients receiving DEUC 6 mg once daily and 1/67 (1.5%) in the 12 mg once daily arm—compared with none in the PBO group. Also, acneiform dermatitis was reported in 2/70 (2.9%), 2/67 (3%) in DEUC 6 mg/12 mg once daily treated patients compared with none in the PBO arm.[11]

In the DISCOVER-1 and DISCOVER-2 trials, similar rates of suicidal ideation in GUS-treated patients, compared with PBO were observed, with no events occurring in the studies investigating BKZ and TIL.[6–9 35 37 38 41] In COSMOS, one patient in the GUS arm experienced two events of conversion disorder, which resolved after discontinuation of GUS. Another patient with a previous history of a suicidal attempt did report depressive symptoms after receiving GUS—the study drug was discontinued, and no further follow-up occurred.[37] Trials investigating BRO (AMVISION 1 and 2) were terminated early following a sponsor's decision due to events of suicidal ideation and behaviour observed in the study programme.[42]

In the integrated safety analyses of GUS, no cases of IBD or anaphylactic reactions were observed.[53] No risk for MACE or malignancies was observed in the PBO and long-term extension period for APR-treated patients.[72] Also, investigation of long-term safety from the UST PsA trial database did not reveal any new signal regarding the safety of MACE, malignancies or Tb.[73]

Observational studies

A US claims database analysis (high RoB, n=30 426, 60 497 PY) investigating the incidence of anxiety and depression disorder found especially users of GC (as an adjunctive therapy) to be at higher risk for depression (aHR, 95% CI: 1.5, 1.1 to 2.0) and a trend regarding anxiety (1.3, 0.9 to 1.9) with no signal for other DMARDs including bDMARDs and apremilast investigated.[72]

Another US claims database study (high RoB) investigated the impact of TNFi treatment on development of liver disease (cirrhosis or non-alcoholic fatty liver disease) and found a higher risk in the overall cohort (including patients with rheumatoid arthritis, ankylosing spondylitis and IBD), with a trend towards higher rates of liver disease also in the PsA subcohort (TNFi vs no TNFi use: aHR, 95% CI: 1.25, 0.88 to 1.76).[74]

DISCUSSION

The aim of this SLR was to summarise the evidence regarding efficacy and safety of pharmacological therapies of PsA since the elaboration of the 2019 EULAR PsA management recommendations.

Similar to other SLRs, also this SLR has strengths and limitations. Data of trials included were not pooled through meta-analyses, due to high heterogeneity of the trials. Instead, the data were reported descriptively, avoiding (indirect) meta-analytical comparisons between drugs. On the other hand, the literature was fully searched in a systematic manner using predefined criteria. Though 10% of articles were screened in duplicate, each article was analysed for RoB and quality; and the data synthesis was descriptive which avoids overinterpretation.

Evidence on the efficacy of csDMARDs and especially MTX was confirmed with clinically meaningful improvements of disease activity observed in the COMPLETE-PsA and GO-DACT trials but is still based on comparisons to other treatment regimens and not to placebo. Combination of MTX with leflunomide provided significantly better efficacy results than MTX monotherapy, however, with substantially higher rates of adverse events.[19]

The efficacy of other meanwhile well-established therapies was confirmed and furthermore expanded with trials investigating the efficacy of IL-17 inhibition on specific musculoskeletal domains which showed significant differences compared with placebo treatment for axial disease (MAXIMISE),[14] and synovitis (ULTIMATE),[13] as well as the efficacy of golimumab in combination with MTX (vs MTX monotherapy) on dactylitis (GO-DACT).[15] Several recent trials used more stringent and clinically meaningful efficacy outcomes than the commonly used ACR20% response as a (co)primary efficacy endpoint (ACR50% response at week 16/24).[9 17 32 41] Non-inferiority of ustekinumab monotherapy compared with ustekinumab+MTX combination therapy was shown in the MUST study.[31] Head-to-head comparisons of IL-17i (secukinumab (EXCEED), ixekizumab (SPIRIT-H2H)) compared with TNFi (adalimumab) showed comparable ACR response rates, but better skin responses in IL-17i-treated patients.[16 32] Two observational studies found higher rates of hospitalised infections in IL-17i-treated patients (compared with TNFi)[58 59], while another study did not show an increased risk.[60] No benefit of therapeutic drug monitoring was seen in infliximab-treated PsA patients.[48 49] Studies investigating molecules targeting the p19 subunit of IL-23 (guselkumab, risankizumab, tildrakizumab) as well as new molecules inhibiting IL-17A (izokibep) and IL-17A/F (bimekizumab),[9 41 43–45] showed superior efficacy when compared with placebo across many disease domains (including arthritis, enthesitis, dactylitis, skin and nail disease) as well as improvement of physical function,[6–8 37 39 40] Fungal infections occurred more frequently in patients receiving IL-17i compared with placebo and TNFi treatment. Only very few cases of fungal infections were observed in IL23-p19i-treated patients.[6–8 35 38]

RCTs on novel targeted synthetic DMARDs (brepocitinib (JAK1/TYK2) deucravacitinib (TYK2), upadacitinib (JAK1/2)) showed significantly higher response rates compared with placebo treatment,[10–12] as well as superiority of UPA 30 mg (but not 15 mg) compared with adalimumab 40 mg every 2 weeks on the expense of more adverse events.[18 34]

In regard to safety, higher event rates in upadactinib-treated patients of serious infections (including serious and fatal COVID-19 infections), opportunistic infections, and HZ rates were observed, compared with adalimumab, while rates of MACE and VTEs were similar.[54] Also, decreases of haemoglobin levels were higher in upadactinib-treated patients, while they increased on adalimumab.[12] Increased rates of acne and acneiform rashes were reported in deucravacitinib-treated patients.[11]

No trial investigating the efficacy of glucocorticoids was identified, however, observational studies provided evidence of increased adverse event rates (MACE, serious infections, anxiety and depression) in patients treated with systemic glucocorticoids.[66 75]

Trials on strategic tapering (using a T2T approach) were reassuring, showing the potential of successful treatment withdrawal while maintaining disease control,[21] but abrupt treatment cessation led to an elevated risk of disease flares.[51]

Results of the safety analysis also highlighted the importance of comorbidities in PsA patients, with higher risks of serious infections especially in patients with one or more comorbidities compared with patients without comorbidities,[61] a higher risk for VTEs in patients with cardiovascular or VTE risk factors.[64] While not associated with any DMARD therapy, an increased risk for non-melanoma skin cancer in PsA patients was observed, as well as an increased all-cause mortality and death from coronary heart disease.[69]

This SLR provided the task force with the evolved evidence since 2018 for the 2023 update of the EULAR recommendations on pharmacological management of PsA.

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Supplementary appendix

Kerschbaumer A, *et al. Ann Rheum Dis* 2024;0:1–15. doi: 10.1136/ard-2024-225534

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Section 1: Search strategy and PICOs

Text S1.1: Efficacy: MEDLINE Search strategy

(("Arthritis, Psoriatic"[Mesh] OR "Psoriatic Arthritis"[tw] OR "Arthritic Psoriasis"[tw] OR "Psoriatic Arthritis"[tw] OR "Psoriasis Arthropathica"[tw] OR "Psoriatic Arthropathy"[tw] OR "Psoriatic Arthropathies"[tw]) NOT (("Infant"[mesh] OR "infant"[ti] OR "infants"[ti] OR "Child"[mesh] OR "child"[ti] OR "children"[ti] OR "pediatric"[ti] OR "paediatric"[ti] OR "pediatrics"[ti] OR "paediatrics"[ti] OR "Adolescent"[mesh] OR "adolescent"[ti] OR "adolescents"[ti]) NOT ("Adult"[mesh] OR "adult"[ti] OR "adults"[ti] OR "middle aged"[ti] OR "elderly"[ti])) AND ("biological therapy"[mesh] OR "antibodies, monoclonal"[mesh] OR "monokines"[mesh] OR "receptors, interleukin-1"[mesh] OR "receptors, interleukin-6"[mesh] OR "immunoglobulin g"[mesh] OR "immunoconjugates"[mesh] OR "polyethylene glycols"[mesh] OR "immunoglobulin fab fragments"[mesh] OR "t-lymphocytes"[mesh] OR "biologic*"[tw] OR "bDMARD"[tw] OR "biosimilar"[tw] OR "abatacept"[tw] OR "actemra"[tw] OR "adalimumab"[tw] OR "anakinra"[tw] OR "Arzerra"[tw] OR "Brodalumab"[tw] OR "Certolizumab"[tw] OR "cimzia"[tw] OR "Clazakizumab"[tw] OR "enbrel"[tw] OR "Etanercept"[tw] OR "Golimumab"[tw] OR "Guselkumab"[tw] OR "humira"[tw] OR "infliximab"[tw] OR "Ixekizumab"[tw] OR "kineret"[tw] OR "mabthera"[tw] OR "mavrilimumab"[tw] OR "Ocrelizumab"[tw] OR "Ofatumumab"[tw] OR "Olokizumab"[tw] OR "orencia"[tw] OR "Pateclizumab"[tw] OR "remicade"[tw] OR "rituxan"[tw] OR "rituximab"[tw] OR "RoActemra"[tw] OR "Sarilumab"[tw] OR "Siliq"[tw] OR "simponi"[tw] OR "Sirukumab"[tw] OR "Stelara"[tw] OR "Tabalumab"[tw] OR "Taltz"[tw] OR "Tocilizumab"[tw] OR "trudexa"[tw] OR "Ustekinumab"[tw] OR "bDMARD*"[tw] OR "biosimilar*"[tw] OR "abatacept*"[tw] OR "actemra*"[tw] OR "adalimumab*"[tw] OR "anakinra*"[tw] OR "Arzerra*"[tw] OR "Brodalumab*"[tw] OR "Certolizumab*"[tw] OR "cimzia*"[tw] OR "Clazakizumab*"[tw] OR "enbrel*"[tw] OR "Etanercept*"[tw] OR "Golimumab*"[tw] OR "Guselkumab*"[tw] OR "humira*"[tw] OR "infliximab*"[tw] OR "Ixekizumab*"[tw] OR "kineret*"[tw] OR "mabthera*"[tw] OR "mavrilimumab*"[tw] OR "Ocrelizumab*"[tw] OR "Ofatumumab*"[tw] OR "Olokizumab*"[tw] OR "orencia*"[tw] OR "Pateclizumab*"[tw] OR "remicade*"[tw] OR "rituxan*"[tw] OR "rituximab*"[tw] OR "RoActemra*"[tw] OR "Sarilumab*"[tw] OR "Siliq*"[tw] OR "simponi*"[tw] OR "Sirukumab*"[tw] OR "Stelara*"[tw] OR "Tabalumab*"[tw] OR "Taltz*"[tw] OR "Tocilizumab*"[tw] OR "trudexa*"[tw] OR "Ustekinumab*"[tw] OR "Antirheumatic Agents"[mesh] OR "Antirheumatic Agents"[pharmacological action] OR "Antirheumatic*"[tw] OR "dmard*"[tw] OR "sdmard*"[tw] OR "Methotrexate"[mesh] OR "Methotrexate"[tw] OR "Abitrexate"[tw] OR "ametopterin*"[tw] OR "amethopterin*"[tw] OR "Abitrexate"[tw] OR "A Metopterin*"[tw] OR "A Methopterin*"[tw] OR "Antifolan"[tw] OR "Emtexate"[tw] OR "Emthexate"[tw] OR "Enthexate"[tw] OR "Farmitrexate"[tw] OR "Folex"[tw] OR "Ledertrexate"[tw] OR "Methoblastin"[tw] OR "Methohexate"[tw] OR "Methotrate"[tw] OR "Methylaminopterin"[tw] OR "Metotrexat*"[tw] OR "mtx"[tw] OR "Novatrex"[tw] OR "Rheumatrex"[tw] OR "Isoxazoles"[mesh] OR "isoxazole*"[tw] OR "leflunomide*"[tw] OR "Afiancen"[tw] OR "Arabloc"[tw] OR "Arava"[tw] OR "Artrilab"[tw] OR "Artrimod"[tw] OR "Filartros"[tw] OR "Inmunoartro"[tw] OR "Lefluar"[tw] OR "Leflucross"[tw] OR "Lefno"[tw] OR "Lefra"[tw] OR "Lefumide"[tw] OR "Lisifen"[tw] OR "Molagar"[tw] OR "Repso"[tw] OR "Rumalef"[tw] OR "Sulfasalazine"[mesh] OR "sulfasalazine"[tw] OR "Salazosulfapyridine"[tw] OR "sulfasalazine"[tw] OR "Sulfosalazine"[tw] OR "Sulfasalzine"[tw] OR "Salazopyridin*"[tw] OR "asulfidine"[tw] OR "azulfdine"[tw] OR "Hydroxychloroquine"[mesh] OR "Hydroxychloro*"[tw] OR "Axokineor"[tw] OR "Dolquine"[tw] OR "Ercoquin"[tw] OR "Evoquin"[tw] OR "HCQS"[tw] OR "HQT"[tw] OR "Hydrocad"[tw] OR "Hydroquin"[tw] OR "Ilinol"[tw] OR "Immard"[tw] OR "Metirel"[tw] OR "Narbon"[tw] OR "Oxcq"[tw] OR "Oxiklorin"[tw] OR "Oxy-Q"[tw] OR "Plaquen*"[tw] OR "Polirreuminor"[tw] OR "Quensyl"[tw] OR "Reuquinol"[tw] OR "Gold Compounds"[mesh] OR "Organogold Compounds"[mesh] OR "gold"[tw] OR "Chloroquine"[mesh] OR "chloroquine*"[tw] OR "aralen"[tw] OR "arechine"[tw] OR "arequin"[tw] OR "chingamin"[tw] OR "chlorochin"[tw] OR "khingamin"[tw] OR "nivaquine"[tw] OR "oxychloroquine"[tw] OR "oxychlorochin"[tw] OR

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"efalizumab"[Supplementary Concept] OR "efalizumab"[tw] OR "raptiva"[tw] OR "secukinumab"[Supplementary Concept] OR "secukinumab"[tw] OR "cosentyx"[tw] OR "human recombinant IL 10"[tw] OR "human recombinant Interleukin 10"[tw] OR "human rIL 10"[tw] OR "recombinant IL 10"[tw] OR "recombinant Interleukin 10"[tw] OR "rIL 10"[tw] OR "rIL10"[tw] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[tw] OR "deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[tw] OR "sonelokimab"[Supplementary Concept] OR "sonelokimab"[tw] OR "izokibep"[tw] OR "apremilast"[Supplementary Concept] OR "apremilast"[tw] OR "otezla"[tw] OR "Glucocorticoids"[Mesh] OR "Glucocorticoids"[Pharmacological Action] OR "glucocorticoids"[tw] OR "glucocorticoid"[tw] OR "glucocorticoid*"[tw] OR "alclometasone dipropionate"[tw] OR "amcinonide"[tw] OR "Beclomethasone"[tw] OR "Betamethasone"[tw] OR "betamethasone acetate"[tw] OR "betamethasone benzoate"[tw] OR "betamethasone dipropionate, betamethasone sodium phosphate drug combination"[tw] OR "betamethasone sodium phosphate"[tw] OR "Betamethasone Valerate"[tw] OR "Budesonide"[tw] OR "ciclesonide"[tw] OR "Clobetasol"[tw] OR "clobetasone butyrate"[tw] OR "clocortolone"[tw] OR "clocortolone pivalate"[tw] OR "Desoximetasone"[tw] OR "Dexamethasone"[tw] OR "dexamethasone 21-phosphate"[tw] OR "Dexamethasone Isonicotinate"[tw] OR "dichlorisone acetate"[tw] OR "diflorasone"[tw] OR "Diflucortolone"[tw] OR "difluprednate"[tw] OR "drocinonide phosphate potassium"[tw] OR "Flumethasone"[tw] OR "flumethasone pivalate"[tw] OR "Fluocinolone Acetonide"[tw] OR "Fluocinonide"[tw] OR "fluocortin butyl ester"[tw] OR "Fluocortolone"[tw] OR "Fluorometholone"[tw] OR "fluperolone acetate"[tw] OR "fluprednidene acetate"[tw] OR "Fluprednisolone"[tw] OR "Flurandrenolone"[tw] OR "Fluticasone-Salmeterol Drug Combination"[tw] OR "FX006"[tw] OR "halometasone"[tw] OR "medrysone"[tw] OR "Melengestrol Acetate"[tw] OR "Methylprednisolone"[tw] OR "Methylprednisolone Hemisuccinate"[tw] OR "Paramethasone"[tw] OR "prednicarbate"[tw] OR "Prednisolone"[tw] OR "prednisolone hemisuccinate"[tw] OR "prednisolone phosphate"[tw] OR "Prednisone"[tw] OR "rimexolone"[tw] OR "terofenamate"[tw] OR "Tobramycin, Dexamethasone Drug Combination"[tw] OR "Triamcinolone"[tw] OR "Triamcinolone Acetonide"[tw] OR "triamcinolone benetonide"[tw] OR "Anti-Inflammatory Agents, Non-Steroidal"[Mesh] OR "Anti-Inflammatory Agents, Non-Steroidal"[Pharmacological Action] OR "Nonsteroidal Anti Inflammatory"[tw] OR "Nonsteroidal Antiinflammatory"[tw] OR "Non-Steroidal Anti-Inflammatory "[tw] OR "Non-Steroidal Antiinflammatory "[tw] OR "NSAIDs"[tw] OR "NSAID"[tw] OR "((E)-(5)-(3,5-di-tert-butyl-4-hydroxybenzylidene)- 2-ethyl-1,2-isothiazolidine-1,1-dioxide)"[tw] OR "1-((4,5-bis(4-methoxyphenyl)-2-thiazoyl)carbonyl)-4-methylpiperazine"[tw] OR "1-((4-methylsulfonyl)phenyl)-3-trifluoromethyl-5-(4-fluorophenyl)pyrazole"[tw] OR "1-(4-chlorobenzoyl)-3-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-methoxy-2-methyl-1H-indole"[tw] OR "2-(4-(quinolin-2-yl-methoxy)phenyl)-2-cyclopentylacetic acid"[tw] OR "2-(4-acetoxyphenyl)-2-chloro-N-methylethylamine"[tw] OR "2-aminomethyl-4-t-butyl-6-iodophenol"[tw] OR "2-diethylaminoethanol"[tw] OR "2-hydroxymethyl-4-(5-(4-methoxyphenyl)-3-trifluoromethyl-1H-1-pyrazolyl)-1-benzenesulfonamide"[tw] OR "4,5-Dihydro-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-3-amine"[tw] OR "4-(5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide"[tw] OR "4-bromo-2,7-dimethoxy-3H-phenothiazin-3-one"[tw] OR "6-(4-fluorophenyl)-2,3-dihydro-5-(4-pyridinyl)imidazo(2,1-b)thiazole"[tw] OR "6-acetylaminocaproic acid"[tw] OR "6-ethoxy-3-(4-methanesulfonylphenyl)-4-phenylpyran-2-one"[tw] OR "7-methoxy-alpha-methyl-2-naphthaleneacetic acid"[tw] OR "aceclofenac"[tw] OR "acemetacin"[tw] OR "acetaminophen, aspirin, caffeine drug combination"[tw] OR "acetaminophen, butalbital, caffeine drug combination"[tw] OR "acetaminophen, hydrocodone drug combination"[tw] OR "acetosyringone"[tw] OR "acetovanillone"[tw] OR "acetylsalicylic acid lysinate"[tw] OR "Adapalene"[tw] OR "Adapalene, Benzoyl Peroxide Drug Combination"[tw] OR "alclofenac"[tw] OR "alminoprofen"[tw] OR "alpha-pentyl-3-(2-quinolinylmethoxy)benzenemethanol"[tw] OR "amiprilose"[tw] OR "Ampyrone"[tw] OR "amylase, phosphates, proteases drug combinations"[tw] OR "andrographolide"[tw] OR "anisodamine"[tw] OR "anisodine"[tw] OR "antiflammin P2"[tw] OR "Antipyrine"[tw] OR "Apazone"[tw] OR "apremilast"[tw] OR "Arteparon"[tw] OR "Arthrotec"[tw] OR "Aspirin"[tw] OR "aspirin, aluminum hydroxide, magnesium hydroxide drug combination"[tw] OR "aspirin, butalbital and caffeine drug

combination"[tw] OR "aspirin, meprobamate drug combination"[tw] OR "atrinositol"[tw] OR "azulene"[tw] OR "baicalin"[tw] OR "balsalazide"[tw] OR "bendazac"[tw] OR "bendazac lysine"[tw] OR "benorilate"[tw] OR "benoxaprofen"[tw] OR "benzobarbital"[tw] OR "berbamine"[tw] OR "bevonium"[tw] OR "BI 607812 BS"[tw] OR "biphenylylacetic acid"[tw] OR "boldine"[tw] OR "boswellic acid"[tw] OR "bromfenac"[tw] OR "bucillamine"[tw] OR "Bufexamac"[tw] OR "bumadizone"[tw] OR "butibufen"[tw] OR "carbaspirin calcium"[tw] OR "carprofen"[tw] OR "caryophyllene"[tw] OR "castanospermine"[tw] OR "CDP 571"[tw] OR "Celecoxib"[tw] OR "cepharanthine"[tw] OR "chloroquine diphosphate"[tw] OR "choline magnesium trisalicylate"[tw] OR "chrysarobin"[tw] OR "Clonixin"[tw] OR "CP 96345"[tw] OR "Curcumin"[tw] OR "CX 659S"[tw] OR "dauricine"[tw] OR "dexketoprofen trometamol"[tw] OR "Diclofenac"[tw] OR "diclofenac hydroxyethylpyrrolidine"[tw] OR "difenpiramide"[tw] OR "Diflunisal"[tw] OR "dimephosphon"[tw] OR "Dipyrone"[tw] OR "diucifon"[tw] OR "droxicam"[tw] OR "dual inhibitor PTUPB"[tw] OR "DuP 697"[tw] OR "ebselen"[tw] OR "ecallantide"[tw] OR "eltenac"[tw] OR "enfenamic acid"[tw] OR "enkephalin-Leu, Ala(2)-Arg(6)-"[tw] OR "Epirizole"[tw] OR "Etanercept"[tw] OR "ethenzamide"[tw] OR "Ethonium"[tw] OR "Etodolac"[tw] OR "etofenamate"[tw] OR "Etoricoxib"[tw] OR "evening primrose oil"[tw] OR "fenamic acid"[tw] OR "fenbufen"[tw] OR "fenclofenac"[tw] OR "fenflumizole"[tw] OR "Fenoprofen"[tw] OR "fentiazac"[tw] OR "fepradinol"[tw] OR "Feprazone"[tw] OR "ferulic acid"[tw] OR "floctafenine"[tw] OR "flosulide"[tw] OR "flunixin"[tw] OR "flunixin meglumine"[tw] OR "flunoxaprofen"[tw] OR "fluproquazone"[tw] OR "Flurbiprofen"[tw] OR "flurbiprofen axetil"[tw] OR "FR 167653"[tw] OR "FR 173657"[tw] OR "glucametacin"[tw] OR "guacetisal"[tw] OR "helenalin"[tw] OR "heliodermin"[tw] OR "hemodes"[tw] OR "higenamine"[tw] OR "Ibuprofen"[tw] OR "ibuproxam"[tw] OR "icatibant"[tw] OR "IH 764-3"[tw] OR "imidazole-2-hydroxybenzoate"[tw] OR "indobufen"[tw] OR "Indomethacin"[tw] OR "Indoprofen"[tw] OR "iodoantipyrine"[tw] OR "isoxicam"[tw] OR "kebuzone"[tw] OR "Ketoprofen"[tw] OR "ketoprofen lysine"[tw] OR "Ketorolac"[tw] OR "Ketorolac Tromethamine"[tw] OR "L 745337"[tw] OR "L 778736"[tw] OR "licofelone"[tw] OR "lipoxin A4"[tw] OR "lipoxin B4"[tw] OR "lisofylline"[tw] OR "lobenzarit"[tw] OR "lonazolac"[tw] OR "lornoxicam"[tw] OR "loxoprofen"[tw] OR "LQFM-091"[tw] OR "lumiracoxib"[tw] OR "Magnesium Salicylate"[tw] OR "magnolol"[tw] OR "manoalide"[tw] OR "Masoprocol"[tw] OR "Meclofenamic Acid"[tw] OR "Mefenamic Acid"[tw] OR "Meloxicam"[tw] OR "Mesalamine"[tw] OR "mirikizumab"[tw] OR "mizoribine"[tw] OR "mofebutazone"[tw] OR "mofezolac"[tw] OR "muricarpone B"[tw] OR "N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide"[tw] OR "N-(9H-(2,7-dimethylfluoren-9-ylmethoxy)carbonyl)leucine"[tw] OR "N-succinimidyl-1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetate"[tw] OR "NAAA inhibitor F215"[tw] OR "Nabumetone"[tw] OR "nafamostat"[tw] OR "Naproxen"[tw] OR "Nebacetin"[tw] OR "nepafenac"[tw] OR "nifenazone"[tw] OR "Niflumic Acid"[tw] OR "nimesulide"[tw] OR "nitroaspirin"[tw] OR "Olopatadine Hydrochloride"[tw] OR "olsalazine"[tw] OR "olvanil"[tw] OR "oren gedoku to"[tw] OR "orgotein"[tw] OR "Oxaprozin"[tw] OR "Oxyphenbutazone"[tw] OR "palmidrol"[tw] OR "parecoxib"[tw] OR "parthenolide"[tw] OR "peoniflorin"[tw] OR "phenidone"[tw] OR "Phenylbutazone"[tw] OR "pimecrolimus"[tw] OR "pirfenidone"[tw] OR "Piroxicam"[tw] OR "piroxicam-beta-cyclodextrin"[tw] OR "pirprofen"[tw] OR "proglumetacin"[tw] OR "propacetamol"[tw] OR "propionylcarnitine"[tw] OR "propyphenazone"[tw] OR "proquazone"[tw] OR "pyranoprofen"[tw] OR "pyrazolone"[tw] OR "pyrogenal"[tw] OR "RNS60"[tw] OR "rofecoxib"[tw] OR "rosmarinic acid"[tw] OR "Rumalon"[tw] OR "saiko-keishi-to"[tw] OR "saikosaponin D"[tw] OR "salicin"[tw] OR "salicylamide"[tw] OR "Salicylates"[tw] OR "salicylsalicylic acid"[tw] OR "SB 203580"[tw] OR "SC 299"[tw] OR "SC 41930"[tw] OR "SC 560"[tw] OR "semapimod"[tw] OR "seratrodast"[tw] OR "serratiopeptidase"[tw] OR "shikonin"[tw] OR "sinapaldehyde"[tw] OR "SK^ and F 105685"[tw] OR "Sodium Salicylate"[tw] OR "ST 679"[tw] OR "Sul-121"[tw] OR "Sulfasalazine"[tw] OR "Sulindac"[tw] OR "sulindac sulfide"[tw] OR "sulindac sulfone"[tw] OR "Suprofen"[tw] OR "suxibuzone"[tw] OR "tanshinone"[tw] OR "taxifolin"[tw] OR "tenidap"[tw] OR "tenoxicam"[tw] OR "tepoxalin"[tw] OR "teriflunomide"[tw] OR "tiaprofenic acid"[tw] OR "tiaramide"[tw] OR "tinoridine"[tw] OR "tolfenamic acid"[tw] OR "Tolmetin"[tw] OR "tramadol, dexketoprofen drug combination"[tw] OR "tranilast"[tw] OR "tribenoside"[tw] OR "ursolic acid"[tw] OR "valdecoxib"[tw] OR "zileuton"[tw] OR "zomepirac"[tw]) AND ((randomized controlled

trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "RCT"[ti] OR (("randomized"[ti] OR "randomised"[ti]) AND "trial"[ti]) NOT ("animals"[mesh] NOT "humans"[mesh]))) AND ("2018/01/01"[PDAT] : "3000/12/31"[PDAT]))

Text S1.2: Efficacy: EMBASE Search strategy

((exp *"Psoriatic Arthritis"/ OR "Psoriatic Arthritis".ti,ab OR "Arthritic Psoriasis".ti,ab OR "Psoriatic Arthritis".ti,ab OR "Psoriasis Arthropathica".ti,ab OR "Psoriatic Arthropathy".ti,ab OR "Psoriatic Arthropathies".ti,ab) NOT ((exp "Infant"/ OR "infant".ti OR "infants".ti OR exp "Child"/ OR "child".ti OR "children".ti OR "pediatric".ti OR "paediatric".ti OR "pediatrics".ti OR "paediatrics".ti OR exp "Adolescent"/ OR "adolescent".ti OR "adolescents".ti) NOT (exp "Adult"/ OR "adult".ti OR "adults".ti OR "middle aged".ti OR "elderly".ti)) AND (exp *"biological therapy"/ OR exp *"monoclonal antibody"/ OR exp *"monokine"/ OR exp *"interleukin 1 receptor"/ OR exp *"interleukin 1 receptor accessory protein"/ OR exp *"interleukin 1 receptor like 1 protein"/ OR exp *"interleukin 1 receptor type I"/ OR exp *"interleukin 1 receptor type II"/ OR exp *"interleukin 6 receptor"/ OR exp *"interleukin 6 receptor alpha"/ OR exp *"immunoglobulin g"/ OR exp *"antibody conjugate"/ OR exp *"macrogol derivative"/ OR exp *"immunoglobulin F(ab) fragment"/ OR exp *"T lymphocyte"/ OR "biologic*".ti,ab OR "bDMARD".ti,ab OR "biosimilar".ti,ab OR "abatacept".ti,ab OR "actemra".ti,ab OR "adalimumab".ti,ab OR "anakinra".ti,ab OR "Arzerra".ti,ab OR "Brodalumab".ti,ab OR "Certolizumab".ti,ab OR "cimzia".ti,ab OR "Clazakizumab".ti,ab OR "enbrel".ti,ab OR "Etanercept".ti,ab OR "Golimumab".ti,ab OR "Guselkumab".ti,ab OR "humira".ti,ab OR "infliximab".ti,ab OR "Ixekizumab".ti,ab OR "kineret".ti,ab OR "mabthera".ti,ab OR "mavrilimumab".ti,ab OR "Ocrelizumab".ti,ab OR "Ofatumumab".ti,ab OR "Olokizumab".ti,ab OR "orencia".ti,ab OR "Pateclizumab".ti,ab OR "remicade".ti,ab OR "rituxan".ti,ab OR "rituximab".ti,ab OR "RoActemra".ti,ab OR "Sarilumab".ti,ab OR "Siliq".ti,ab OR "simponi".ti,ab OR "Sirukumab".ti,ab OR "Stelara".ti,ab OR "Tabalumab".ti,ab OR "Taltz".ti,ab OR "Tocilizumab".ti,ab OR "trudexa".ti,ab OR "Ustekinumab".ti,ab OR "bDMARD*".ti,ab OR "biosimilar*".ti,ab OR "abatacept*".ti,ab OR "actemra*".ti,ab OR "adalimumab*".ti,ab OR "anakinra*".ti,ab OR "Arzerra*".ti,ab OR "Brodalumab*".ti,ab OR "Certolizumab*".ti,ab OR "cimzia*".ti,ab OR "Clazakizumab*".ti,ab OR "enbrel*".ti,ab OR "Etanercept*".ti,ab OR "Golimumab*".ti,ab OR "Guselkumab*".ti,ab OR "humira*".ti,ab OR "infliximab*".ti,ab OR "Ixekizumab*".ti,ab OR "kineret*".ti,ab OR "mabthera*".ti,ab OR "mavrilimumab*".ti,ab OR "Ocrelizumab*".ti,ab OR "Ofatumumab*".ti,ab OR "Olokizumab*".ti,ab OR "orencia*".ti,ab OR "Pateclizumab*".ti,ab OR "remicade*".ti,ab OR "rituxan*".ti,ab OR "rituximab*".ti,ab OR "RoActemra*".ti,ab OR "Sarilumab*".ti,ab OR "Siliq*".ti,ab OR "simponi*".ti,ab OR "Sirukumab*".ti,ab OR "Stelara*".ti,ab OR "Tabalumab*".ti,ab OR "Taltz*".ti,ab OR "Tocilizumab*".ti,ab OR "trudexa*".ti,ab OR "Ustekinumab*".ti,ab OR exp *"Antirheumatic Agent"/ OR "Antirheumatic*".ti,ab OR "dmard*".ti,ab OR "sdmard*".ti,ab OR exp *"Methotrexate"/ OR "Methotrexate".ti,ab OR "Abitrexate".ti,ab OR "ametopterin*".ti,ab OR "amethopterin*".ti,ab OR "Abitrexate".ti,ab OR "A Metopterin*".ti,ab OR "A Methopterin*".ti,ab OR "Antifolan".ti,ab OR "Emtexate".ti,ab OR "Emthexate".ti,ab OR "Enthexate".ti,ab OR "Farmitrexate".ti,ab OR "Folex".ti,ab OR "Ledertrexate".ti,ab OR "Methoblastin".ti,ab OR "Methohexate".ti,ab OR "Methotrate".ti,ab OR "Methylaminopterin".ti,ab OR "Metotrexat*".ti,ab OR "mtx".ti,ab OR "Novatrex".ti,ab OR "Rheumatrex".ti,ab OR exp *"Isoxazole"/ OR "isoxazole*".ti,ab OR "leflunomide*".ti,ab OR "Afiancen".ti,ab OR "Arabloc".ti,ab OR "Arava".ti,ab OR "Artrilab".ti,ab OR "Artrimod".ti,ab OR "Filartros".ti,ab OR "Inmunoartro".ti,ab OR "Lefluar".ti,ab OR "Leflucross".ti,ab OR "Lefno".ti,ab OR "Lefra".ti,ab OR "Lefumide".ti,ab OR "Lisifen".ti,ab OR "Molagar".ti,ab OR "Repso".ti,ab OR "Rumalef".ti,ab OR exp *"salazosulfapyridine"/ OR "sulfasalazine".ti,ab OR "Salazosulfapyridine".ti,ab OR "sulfasalazine".ti,ab OR "Sulfosalazine".ti,ab OR "Sulfasalzine".ti,ab OR "Salazopyridin*".ti,ab OR "asulfidine".ti,ab OR "azulfdine".ti,ab OR exp *"Hydroxychloroquine"/ OR "Hydroxychloro*".ti,ab OR "Axokineor".ti,ab OR "Dolquine".ti,ab OR "Ercoquin".ti,ab OR "Evoquin".ti,ab OR "HCQS".ti,ab OR "HQT".ti,ab OR "Hydrocad".ti,ab OR "Hydroquin".ti,ab OR "Ilinol".ti,ab OR "Immard".ti,ab OR "Metirel".ti,ab OR "Narbon".ti,ab OR "Oxcq".ti,ab OR

"Oxiklorin".ti,ab OR "Oxy-Q".ti,ab OR "Plaquen*".ti,ab OR "Polirreuminor".ti,ab OR "Quensyl".ti,ab OR "Reuquinol".ti,ab OR exp *"Gold Derivative"/ OR exp *"Organogold Compound"/ OR exp *"Gold"/ OR "gold".ti,ab OR exp *"Chloroquine"/ OR "chloroquine*".ti,ab OR "aralen".ti,ab OR "arechine".ti,ab OR "arequin".ti,ab OR "chingamin".ti,ab OR "chlorochin".ti,ab OR "khingamin".ti,ab OR "nivaquine".ti,ab OR "oxychloroquine".ti,ab OR "oxychlorochin".ti,ab OR "plaquinol".ti,ab OR "plaquinil".ti,ab OR "quensy".ti,ab OR "anoclor".ti,ab OR "arthrabas".ti,ab OR "avloclor".ti,ab OR "cidanchin".ti,ab OR "clopirim".ti,ab OR "collagenan".ti,ab OR "daraclor".ti,ab OR "daramal".ti,ab OR "dichinalex".ti,ab OR "difosquin".ti,ab OR "diroquine".ti,ab OR "genocin".ti,ab OR "heliopar".ti,ab OR "klorokin".ti,ab OR "malarex".ti,ab OR "malaviron".ti,ab OR "mirquin".ti,ab OR "nivaquine".ti,ab OR "novo-chloroquine".ti,ab OR "novochloroquine".ti,ab OR "paluken".ti,ab OR "palux".ti,ab OR "pharmaquinine".ti,ab OR "plasmoquine".ti,ab OR "promal".ti,ab OR "p-roquine".ti,ab OR "resoquin*".ti,ab OR "savarine".ti,ab OR "syncoquin".ti,ab OR "weimerquin".ti,ab OR exp *"Azathioprine"/ OR "azathioprine".ti,ab OR "Aseroprim".ti,ab OR "Aseroprin".ti,ab OR "Azaallen".ti,ab OR "Azadus".ti,ab OR "Azafalk".ti,ab OR "Azafor".ti,ab OR "Azafrine".ti,ab OR "Azaglax".ti,ab OR "Azahexal".ti,ab OR "Azamun*".ti,ab OR "Azamedac".ti,ab OR "Azap".ti,ab OR "Azapin*".ti,ab OR "Azapress".ti,ab OR "Aza-Q".ti,ab OR "Azarek".ti,ab OR "Azasan".ti,ab OR "Azathiodura".ti,ab OR "Azathiodura".ti,ab OR "Azathioregio".ti,ab OR "Azatrilem".ti,ab OR "Azimune".ti,ab OR "Azopin*".ti,ab OR "Azoran".ti,ab OR "Berkaprine".ti,ab OR "Colinsan".ti,ab OR "Glaxoprin".ti,ab OR "Immunoprin".ti,ab OR "Imuger".ti,ab OR "Imunen".ti,ab OR "Imuprin*".ti,ab OR "Imuran".ti,ab OR "Imureor Imuzat".ti,ab OR "Oprisine".ti,ab OR "Satedon".ti,ab OR "Thioprine".ti,ab OR "Tiosalprin".ti,ab OR "Transimune".ti,ab OR "Zaprine".ti,ab OR "Zytrim".ti,ab OR exp *"Cyclosporine"/ OR "ciclosporin*".ti,ab OR "cyclosporin*".ti,ab OR "neoral".ti,ab OR "gengraf".ti,ab OR "restasis".ti,ab OR "sandimmun*".ti,ab OR "sangcya".ti,ab OR exp *"Penicillamine"/ OR "Penicillamine".ti,ab OR "Adalkenor".ti,ab OR "Artamin".ti,ab OR "Atamir".ti,ab OR "Byanodine".ti,ab OR "Cilamin".ti,ab OR "Cuprenil".ti,ab OR "Cuprimine".ti,ab OR "Cupripen".ti,ab OR "Depen".ti,ab OR "Distamin*".ti,ab OR "D-Penamine".ti,ab OR "Gerodyl".ti,ab OR "Kelatin*".ti,ab OR "Mercaptyl".ti,ab OR "Metalcaptase".ti,ab OR "Pendramine".ti,ab OR "Rhumantin".ti,ab OR "Sufortan*".ti,ab OR "Trisorcin".ti,ab OR "Trolovol".ti,ab OR exp *"Cyclophosphamide"/ OR "cyclophosph*".ti,ab OR "cytophosphan".ti,ab OR "Cytoxan".ti,ab OR "sendoxan".ti,ab OR "endoxan".ti,ab OR "neosar".ti,ab OR "nsc-26271".ti,ab OR "procytox".ti,ab OR "b-518".ti,ab OR "ifosfamide".ti,ab OR "isophosphamide".ti,ab OR "iphosphamide".ti,ab OR "isofosfamide".ti,ab OR "holoxan".ti,ab OR "nsc-109*".ti,ab OR "asta z 4942".ti,ab OR "cfx".ti,ab OR "phosphoramide mustard*".ti,ab OR exp *"Mycophenolic Acid"/ OR "mycophenolate".ti,ab OR "Arzip".ti,ab OR "Baxmune".ti,ab OR "CellCept".ti,ab OR "Cellmune".ti,ab OR "Celprot".ti,ab OR "Ceptolate".ti,ab OR "Imulate".ti,ab OR "Imuxgen".ti,ab OR "Lanfetil".ti,ab OR "Limfocept".ti,ab OR "Metocris".ti,ab OR "Micocept".ti,ab OR "MMF".ti,ab OR "Mofecept".ti,ab OR "Mofetyl".ti,ab OR "Mofilet".ti,ab OR "Mofimutral".ti,ab OR "Mometil".ti,ab OR "Mophecen".ti,ab OR "Munotras".ti,ab OR "Myaccord".ti,ab OR "Mycept".ti,ab OR "Myclausenor".ti,ab OR "Mycofenor".ti,ab OR "Mycolat".ti,ab OR "Mycoldosa".ti,ab OR "Mycophen".ti,ab OR "Myfenax Myfetil".ti,ab OR "Mygref".ti,ab OR "Myotec".ti,ab OR "Mysept".ti,ab OR "Presumin".ti,ab OR "Refrat".ti,ab OR "Renocell".ti,ab OR "Supresta".ti,ab OR "Tevacept".ti,ab OR "Trixin".ti,ab OR exp *"Chlorambucil"/ OR "chlorambucil".ti,ab OR "Amboclorin".ti,ab OR "Clokeran".ti,ab OR "Leukeran".ti,ab OR "Linfolysin".ti,ab OR "Lympholysin".ti,ab OR exp *"Minocycline"/ OR "minocyclin*".ti,ab OR "Acneclin".ti,ab OR "Akamin".ti,ab OR "Aknemin".ti,ab OR "Akne-Puren".ti,ab OR "Aknereduct".ti,ab OR "Aknin-Mino".ti,ab OR "Aknin-N".ti,ab OR "Aknoral".ti,ab OR "Aknosan".ti,ab OR "Apominolin".ti,ab OR "Arestinor".ti,ab OR "Auramin".ti,ab OR "Blemix".ti,ab OR "Borymycin".ti,ab OR "Cipancin".ti,ab OR "Cyclimycin".ti,ab OR "Dentomycin*".ti,ab OR "durakne".ti,ab OR "Dynacin".ti,ab OR "Enca".ti,ab OR "Icht-Oralor".ti,ab OR "Klinoc".ti,ab OR "Klinomycin".ti,ab OR "Klinotab".ti,ab OR "Lederderm".ti,ab OR "Logryx".ti,ab OR "Meibi".ti,ab OR "Mestacine".ti,ab OR "Micromycin".ti,ab OR "Minac 50".ti,ab OR "Minakne".ti,ab OR "Minaxen".ti,ab

OR "Mino-50".ti,ab OR "Minocin".ti,ab OR "Minoclin".ti,ab OR "Minodene".ti,ab OR "Minoderm".ti,ab OR "Minogalen".ti,ab OR "Minolis".ti,ab OR "Minomax".ti,ab OR "Minomycin".ti,ab OR "Minoplus".ti,ab OR "Minosil".ti,ab OR "Minostad".ti,ab OR "Minotab*".ti,ab OR "Minotekor".ti,ab OR "Minotrex".ti,ab OR "Minotyrol".ti,ab OR "Mino-Wolff".ti,ab OR "Minox".ti,ab OR "Mynocine".ti,ab OR "Myrac".ti,ab OR "Oracyclin".ti,ab OR "Parocline".ti,ab OR "Periocline".ti,ab OR "Peritrol".ti,ab OR "Ranmino".ti,ab OR "Romin".ti,ab OR "Seboclear".ti,ab OR "Sebomin".ti,ab OR "Sebren".ti,ab OR "Skid".ti,ab OR "Skinocyclin".ti,ab OR "Solodyn".ti,ab OR "Spicline".ti,ab OR "Triomin".ti,ab OR "Udima".ti,ab OR "Vectrin".ti,ab OR "Yelnac".ti,ab OR "Zacnan".ti,ab OR exp *"Pyrrole"/ OR "tofacitinib".ti,ab OR "Xeljanz".ti,ab OR "baricitinib".ti,ab OR "peficitinib".ti,ab OR "filgotinib".ti,ab OR "upadacitinib".ti,ab OR "fostamatinib".ti,ab OR exp *"Alefacept"/ OR "alefacept".ti,ab OR "Amevive".ti,ab OR exp *"efalizumab"/ OR "efalizumab".ti,ab OR "raptiva".ti,ab OR exp *"secukinumab"/ OR "secukinumab".ti,ab OR "cosentyx".ti,ab OR exp *"recombinant interleukin 10"/ OR "human recombinant IL 10".ti,ab OR "human recombinant Interleukin 10".ti,ab OR "human rIL 10".ti,ab OR "recombinant IL 10".ti,ab OR "recombinant Interleukin 10".ti,ab OR "rIL 10".ti,ab OR "rIL10".ti,ab OR exp *"bimekizumab"/ OR "bimekizumab".ti,ab OR exp *"deucravacitinib"/ OR "deucravacitinib".ti,ab OR exp *"sonelokimab"/ OR "sonelokimab".ti,ab OR "izokibep".ti,ab OR exp *"apremilast"/ OR "apremilast".ti,ab OR "otezla".ti,ab OR exp *"Glucocorticoid"/ OR "glucocorticoids".ti,ab OR "glucocorticoid".ti,ab OR "glucocorticoid*".ti,ab OR "alclometasone dipropionate".ti,ab OR "amcinonide".ti,ab OR "Beclomethasone".ti,ab OR "Betamethasone".ti,ab OR "betamethasone acetate".ti,ab OR "betamethasone benzoate".ti,ab OR "betamethasone dipropionate, betamethasone sodium phosphate drug combination".ti,ab OR "betamethasone sodium phosphate".ti,ab OR "Betamethasone Valerate".ti,ab OR "Budesonide".ti,ab OR "ciclesonide".ti,ab OR "Clobetasol".ti,ab OR "clobetasone butyrate".ti,ab OR "clocortolone".ti,ab OR "clocortolone pivalate".ti,ab OR "Desoximetasone".ti,ab OR "Dexamethasone".ti,ab OR "dexamethasone 21-phosphate".ti,ab OR "Dexamethasone Isonicotinate".ti,ab OR "dichlorisone acetate".ti,ab OR "diflorasone".ti,ab OR "Diflucortolone".ti,ab OR "difluprednate".ti,ab OR "drocinonide phosphate potassium".ti,ab OR "Flumethasone".ti,ab OR "flumethasone pivalate".ti,ab OR "Fluocinolone Acetonide".ti,ab OR "Fluocinonide".ti,ab OR "fluocortin butyl ester".ti,ab OR "Fluocortolone".ti,ab OR "Fluorometholone".ti,ab OR "fluperolone acetate".ti,ab OR "fluprednidene acetate".ti,ab OR "Fluprednisolone".ti,ab OR "Flurandrenolone".ti,ab OR "Fluticasone-Salmeterol Drug Combination".ti,ab OR "FX006".ti,ab OR "halometasone".ti,ab OR "medrysone".ti,ab OR "Melengestrol Acetate".ti,ab OR "Methylprednisolone".ti,ab OR "Methylprednisolone Hemisuccinate".ti,ab OR "Paramethasone".ti,ab OR "prednicarbate".ti,ab OR "Prednisolone".ti,ab OR "prednisolone hemisuccinate".ti,ab OR "prednisolone phosphate".ti,ab OR "Prednisone".ti,ab OR "rimexolone".ti,ab OR "terofenamate".ti,ab OR "Tobramycin, Dexamethasone Drug Combination".ti,ab OR "Triamcinolone".ti,ab OR "Triamcinolone Acetonide".ti,ab OR "triamcinolone benetonide".ti,ab OR exp *"nonsteroid antiinflammatory agent"/ OR "Nonsteroidal Anti Inflammatory".ti,ab OR "Nonsteroidal Antiinflammatory".ti,ab OR "Non-Steroidal Anti-Inflammatory ".ti,ab OR "Non-Steroidal Antiinflammatory ".ti,ab OR "NSAIDs".ti,ab OR "NSAID".ti,ab OR "((E)-(5)-(3,5-di-tert-butyl-4-hydroxybenzylidene)- 2-ethyl-1,2-isothiazolidine-1,1-dioxide)".ti,ab OR "1-((4,5-bis(4-methoxyphenyl)-2-thiazoyl)carbonyl)-4-methylpiperazine".ti,ab OR "1-((4-methylsulfonyl)phenyl)-3-trifluoromethyl-5-(4-fluorophenyl)pyrazole".ti,ab OR "1-(4-chlorobenzoyl)-3-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-methoxy-2-methyl-1H-indole".ti,ab OR "2-(4-(quinolin-2-yl-methoxy)phenyl)-2-cyclopentylacetic acid".ti,ab OR "2-(4-acetoxyphenyl)-2-chloro-N-methylethylamine".ti,ab OR "2-aminomethyl-4-t-butyl-6-iodophenol".ti,ab OR "2-diethylaminoethanol".ti,ab OR "2-hydroxymethyl-4-(5-(4-methoxyphenyl)-3-trifluoromethyl-1H-1-pyrazolyl)-1-benzenesulfonamide".ti,ab OR "4,5-Dihydro-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-3-amine".ti,ab OR "4-(5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide".ti,ab OR "4-bromo-2,7-dimethoxy-3H-phenothiazin-3-one".ti,ab OR "6-(4-

fluorophenyl)-2,3-dihydro-5-(4-pyridinyl)imidazo(2,1-b)thiazole".ti,ab OR "6-acetylaminocaproic acid".ti,ab OR "6-ethoxy-3-(4-methanesulfonylphenyl)-4-phenylpyran-2-one".ti,ab OR "7-methoxy-alpha-methyl-2-naphthaleneacetic acid".ti,ab OR "aceclofenac".ti,ab OR "acemetacin".ti,ab OR "acetaminophen, aspirin, caffeine drug combination".ti,ab OR "acetaminophen, butalbital, caffeine drug combination".ti,ab OR "acetaminophen, hydrocodone drug combination".ti,ab OR "acetosyringone".ti,ab OR "acetovanillone".ti,ab OR "acetylsalicylic acid lysinate".ti,ab OR "Adapalene".ti,ab OR "Adapalene, Benzoyl Peroxide Drug Combination".ti,ab OR "alclofenac".ti,ab OR "alminoprofen".ti,ab OR "alpha-pentyl-3-(2-quinolinylmethoxy)benzenemethanol".ti,ab OR "amiprilose".ti,ab OR "Ampyrone".ti,ab OR "amylase, phosphates, proteases drug combinations".ti,ab OR "andrographolide".ti,ab OR "anisodamine".ti,ab OR "anisodine".ti,ab OR "antiflammin P2".ti,ab OR "Antipyrine".ti,ab OR "Apazone".ti,ab OR "apremilast".ti,ab OR "Arteparon".ti,ab OR "Arthrotec".ti,ab OR "Aspirin".ti,ab OR "aspirin, aluminum hydroxide, magnesium hydroxide drug combination".ti,ab OR "aspirin, butalbital and caffeine drug combination".ti,ab OR "aspirin, meprobamate drug combination".ti,ab OR "atrinositol".ti,ab OR "azulene".ti,ab OR "baicalin".ti,ab OR "balsalazide".ti,ab OR "bendazac".ti,ab OR "bendazac lysine".ti,ab OR "benorilate".ti,ab OR "benoxaprofen".ti,ab OR "benzobarbital".ti,ab OR "berbamine".ti,ab OR "bevonium".ti,ab OR "BI 607812 BS".ti,ab OR "biphenylylacetic acid".ti,ab OR "boldine".ti,ab OR "boswellic acid".ti,ab OR "bromfenac".ti,ab OR "bucillamine".ti,ab OR "Bufexamac".ti,ab OR "bumadizone".ti,ab OR "butibufen".ti,ab OR "carbaspirin calcium".ti,ab OR "carprofen".ti,ab OR "caryophyllene".ti,ab OR "castanospermine".ti,ab OR "CDP 571".ti,ab OR "Celecoxib".ti,ab OR "cepharanthine".ti,ab OR "chloroquine diphosphate".ti,ab OR "choline magnesium trisalicylate".ti,ab OR "chrysarobin".ti,ab OR "Clonixin".ti,ab OR "CP 96345".ti,ab OR "Curcumin".ti,ab OR "CX 659S".ti,ab OR "dauricine".ti,ab OR "dexketoprofen trometamol".ti,ab OR "Diclofenac".ti,ab OR "diclofenac hydroxyethylpyrrolidine".ti,ab OR "difenpiramide".ti,ab OR "Diflunisal".ti,ab OR "dimephosphon".ti,ab OR "Dipyrone".ti,ab OR "diucifon".ti,ab OR "droxicam".ti,ab OR "dual inhibitor PTUPB".ti,ab OR "DuP 697".ti,ab OR "ebselen".ti,ab OR "ecallantide".ti,ab OR "eltenac".ti,ab OR "enfenamic acid".ti,ab OR "enkephalin-Leu, Ala(2)-Arg(6)-".ti,ab OR "Epirizole".ti,ab OR "Etanercept".ti,ab OR "ethenzamide".ti,ab OR "Ethonium".ti,ab OR "Etodolac".ti,ab OR "etofenamate".ti,ab OR "Etoricoxib".ti,ab OR "evening primrose oil".ti,ab OR "fenamic acid".ti,ab OR "fenbufen".ti,ab OR "fenclofenac".ti,ab OR "fenflumizole".ti,ab OR "Fenoprofen".ti,ab OR "fentiazac".ti,ab OR "fepradinol".ti,ab OR "Feprazone".ti,ab OR "ferulic acid".ti,ab OR "floctafenine".ti,ab OR "flosulide".ti,ab OR "flunixin".ti,ab OR "flunixin meglumine".ti,ab OR "flunoxaprofen".ti,ab OR "fluproquazone".ti,ab OR "Flurbiprofen".ti,ab OR "flurbiprofen axetil".ti,ab OR "FR 167653".ti,ab OR "FR 173657".ti,ab OR "glucametacin".ti,ab OR "guacetisal".ti,ab OR "helenalin".ti,ab OR "heliodermin".ti,ab OR "hemodes".ti,ab OR "higenamine".ti,ab OR "Ibuprofen".ti,ab OR "ibuproxam".ti,ab OR "icatibant".ti,ab OR "IH 764-3".ti,ab OR "imidazole-2-hydroxybenzoate".ti,ab OR "indobufen".ti,ab OR "Indomethacin".ti,ab OR "Indoprofen".ti,ab OR "iodoantipyrine".ti,ab OR "isoxicam".ti,ab OR "kebuzone".ti,ab OR "Ketoprofen".ti,ab OR "ketoprofen lysine".ti,ab OR "Ketorolac".ti,ab OR "Ketorolac Tromethamine".ti,ab OR "L 745337".ti,ab OR "L 778736".ti,ab OR "licofelone".ti,ab OR "lipoxin A4".ti,ab OR "lipoxin B4".ti,ab OR "lisofylline".ti,ab OR "lobenzarit".ti,ab OR "lonazolac".ti,ab OR "lornoxicam".ti,ab OR "loxoprofen".ti,ab OR "LQFM-091".ti,ab OR "lumiracoxib".ti,ab OR "Magnesium Salicylate".ti,ab OR "magnolol".ti,ab OR "manoalide".ti,ab OR "Masoprocol".ti,ab OR "Meclofenamic Acid".ti,ab OR "Mefenamic Acid".ti,ab OR "Meloxicam".ti,ab OR "Mesalamine".ti,ab OR "mirikizumab".ti,ab OR "mizoribine".ti,ab OR "mofebutazone".ti,ab OR "mofezolac".ti,ab OR "muricarpone B".ti,ab OR "N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide".ti,ab OR "N-(9H-(2,7-dimethylfluoren-9-ylmethoxy)carbonyl)leucine".ti,ab OR "N-succinimidyl-1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetate".ti,ab OR "NAAA inhibitor F215".ti,ab OR "Nabumetone".ti,ab OR "nafamostat".ti,ab OR "Naproxen".ti,ab OR "Nebacetin".ti,ab OR "nepafenac".ti,ab OR

"nifenazone".ti,ab OR "Niflumic Acid".ti,ab OR "nimesulide".ti,ab OR "nitroaspirin".ti,ab OR "Olopatadine Hydrochloride".ti,ab OR "olsalazine".ti,ab OR "olvanil".ti,ab OR "oren gedoku to".ti,ab OR "orgotein".ti,ab OR "Oxaprozin".ti,ab OR "Oxyphenbutazone".ti,ab OR "palmidrol".ti,ab OR "parecoxib".ti,ab OR "parthenolide".ti,ab OR "peoniflorin".ti,ab OR "phenidone".ti,ab OR "Phenylbutazone".ti,ab OR "pimecrolimus".ti,ab OR "pirfenidone".ti,ab OR "Piroxicam".ti,ab OR "piroxicam-beta-cyclodextrin".ti,ab OR "pirprofen".ti,ab OR "proglumetacin".ti,ab OR "propacetamol".ti,ab OR "propionylcarnitine".ti,ab OR "propyphenazone".ti,ab OR "proquazone".ti,ab OR "pyranoprofen".ti,ab OR "pyrazolone".ti,ab OR "pyrogenal".ti,ab OR "RNS60".ti,ab OR "rofecoxib".ti,ab OR "rosmarinic acid".ti,ab OR "Rumalon".ti,ab OR "saiko-keishi-to".ti,ab OR "saikosaponin D".ti,ab OR "salicin".ti,ab OR "salicylamide".ti,ab OR "Salicylates".ti,ab OR "salicylsalicylic acid".ti,ab OR "SB 203580".ti,ab OR "SC 299".ti,ab OR "SC 41930".ti,ab OR "SC 560".ti,ab OR "semapimod".ti,ab OR "seratrodast".ti,ab OR "serratiopeptidase".ti,ab OR "shikonin".ti,ab OR "sinapaldehyde".ti,ab OR "SK^ and F 105685".ti,ab OR "Sodium Salicylate".ti,ab OR "ST 679".ti,ab OR "Sul-121".ti,ab OR "Sulfasalazine".ti,ab OR "Sulindac".ti,ab OR "sulindac sulfide".ti,ab OR "sulindac sulfone".ti,ab OR "Suprofen".ti,ab OR "suxibuzone".ti,ab OR "tanshinone".ti,ab OR "taxifolin".ti,ab OR "tenidap".ti,ab OR "tenoxicam".ti,ab OR "tepoxalin".ti,ab OR "teriflunomide".ti,ab OR "tiaprofenic acid".ti,ab OR "tiaramide".ti,ab OR "tinoridine".ti,ab OR "tolfenamic acid".ti,ab OR "Tolmetin".ti,ab OR "tramadol, dexketoprofen drug combination".ti,ab OR "tranilast".ti,ab OR "tribenoside".ti,ab OR "ursolic acid".ti,ab OR "valdecoxib".ti,ab OR "zileuton".ti,ab OR "zomepirac".ti,ab) AND (exp "randomized controlled trial"/ OR exp "controlled clinical trial"/ OR randomized.ti,ab OR placebo.ti,ab OR "dt".fs OR randomly.ti,ab OR trial.ti,ab OR groups.ti,ab OR "RCT".ti OR (("randomized".ti OR "randomised".ti) AND "trial".ti)) NOT (exp "animals"/ NOT exp "humans"/) AND 2018:2023.(sa_year))

Text S1.3: Efficacy: Cochrane Library Search strategy

(("Psoriatic Arthritis" OR "Psoriatic Arthritis" OR "Arthritic Psoriasis" OR "Psoriatic Arthritis" OR "Psoriasis Arthropathica" OR "Psoriatic Arthropathy" OR "Psoriatic Arthropathies"):ti,ab,kw NOT ((exp "Infant" OR "infant" OR "infants" OR exp "Child" OR "child" OR "children" OR "pediatric" OR "paediatric" OR "pediatrics" OR "paediatrics" OR exp "Adolescent" OR "adolescent" OR "adolescents") NOT (exp "Adult" OR "adult" OR "adults" OR "middle aged" OR "elderly")):ti AND ("biological therapy" OR "monoclonal antibody" OR "monokine" OR "interleukin 1 receptor" OR "interleukin 1 receptor accessory protein" OR "interleukin 1 receptor like 1 protein" OR "interleukin 1 receptor type I" OR "interleukin 1 receptor type II" OR "interleukin 6 receptor" OR "interleukin 6 receptor alpha" OR "immunoglobulin g" OR "antibody conjugate" OR "macrogol derivative" OR "immunoglobulin F(ab) fragment" OR "T lymphocyte" OR "biologic*" OR "bDMARD" OR "biosimilar" OR "abatacept" OR "actemra" OR "adalimumab" OR "anakinra" OR "Arzerra" OR "Brodalumab" OR "Certolizumab" OR "cimzia" OR "Clazakizumab" OR "enbrel" OR "Etanercept" OR "Golimumab" OR "Guselkumab" OR "humira" OR "infliximab" OR "Ixekizumab" OR "kineret" OR "mabthera" OR "mavrilimumab" OR "Ocrelizumab" OR "Ofatumumab" OR "Olokizumab" OR "orencia" OR "Pateclizumab" OR "remicade" OR "rituxan" OR "rituximab" OR "RoActemra" OR "Sarilumab" OR "Siliq" OR "simponi" OR "Sirukumab" OR "Stelara" OR "Tabalumab" OR "Taltz" OR "Tocilizumab" OR "trudexa" OR "Ustekinumab" OR "bDMARD*" OR "biosimilar*" OR "abatacept*" OR "actemra*" OR "adalimumab*" OR "anakinra*" OR "Arzerra*" OR "Brodalumab*" OR "Certolizumab*" OR "cimzia*" OR "Clazakizumab*" OR "enbrel*" OR "Etanercept*" OR "Golimumab*" OR "Guselkumab*" OR "humira*" OR "infliximab*" OR "Ixekizumab*" OR "kineret*" OR "mabthera*" OR "mavrilimumab*" OR "Ocrelizumab*" OR "Ofatumumab*" OR "Olokizumab*" OR "orencia*" OR "Pateclizumab*" OR "remicade*" OR "rituxan*" OR "rituximab*" OR "RoActemra*" OR "Sarilumab*" OR "Siliq*" OR "simponi*" OR "Sirukumab*" OR "Stelara*" OR "Tabalumab*" OR "Taltz*" OR "Tocilizumab*" OR "trudexa*" OR "Ustekinumab*" OR "Antirheumatic Agent" OR "Antirheumatic*" OR "dmard*" OR "sdmard*" OR "Methotrexate" OR "Methotrexate" OR "Abitrexate" OR "ametopterin*" OR "amethopterin*" OR "Abitrexate" OR "A Metopterin*" OR "A Methopterin*" OR "Antifolan" OR "Emtexate" OR "Emthexate" OR "Enthexate" OR "Farmitrexate" OR "Folex" OR "Ledertrexate" OR "Methoblastin" OR "Methohexate" OR "Methotrate" OR "Methylaminopterin" OR "Metotrexat*" OR "mtx" OR "Novatrex" OR "Rheumatrex" OR "Isoxazole" OR "isoxazole*" OR "leflunomide*" OR "Afiancen" OR "Arabloc" OR "Arava" OR "Artrilab" OR "Artrimod" OR "Filartros" OR "Inmunoartro" OR "Lefluar" OR "Leflucross" OR "Lefno" OR "Lefra" OR "Lefumide" OR "Lisifen" OR "Molagar" OR "Repso" OR "Rumalef" OR "salazosulfapyridine" OR "sulfasalazine" OR "Salazosulfapyridine" OR "sulfasalazine" OR "Sulfosalazine" OR "Sulfasalzine" OR "Salazopyridin*" OR "asulfidine" OR "azulfdine" OR "Hydroxychloroquine" OR "Hydroxychloro*" OR "Axokineor" OR "Dolquine" OR "Ercoquin" OR "Evoquin" OR "HCQS" OR "HQT" OR "Hydrocad" OR "Hydroquin" OR "Ilinol" OR "Immard" OR "Metirel" OR "Narbon" OR "Oxcq" OR "Oxiklorin" OR "Oxy Q" OR "Plaquen*" OR "Polirreuminor" OR "Quensyl" OR "Reuquinol" OR "Gold Derivative" OR "Organogold Compound" OR "Gold" OR "gold" OR "Chloroquine" OR "chloroquine*" OR "aralen" OR "arechine" OR "arequin" OR "chingamin" OR "chlorochin" OR "khingamin" OR "nivaquine" OR "oxychloroquine" OR "oxychlorochin" OR "plaquinol" OR "plaquinil" OR "quensy" OR "anoclor" OR "arthrabas" OR "avloclor" OR "cidanchin" OR "clopirim" OR "collagenan" OR "daraclor" OR "daramal" OR "dichinalex" OR "difosquin" OR "diroquine" OR "genocin" OR "heliopar" OR "klorokin" OR "malarex" OR "malaviron" OR "mirquin" OR "nivaquine" OR "novo chloroquine" OR "novochloroquine" OR "paluken" OR "palux" OR "pharmaquinine" OR "plasmoquine" OR "promal" OR "p roquine" OR "resoquin*" OR "savarine" OR "syncoquin" OR "weimerquin" OR "Azathioprine" OR "azathioprine" OR "Aseroprim" OR "Aseroprin" OR "Azaallen" OR "Azadus" OR "Azafalk" OR "Azafor" OR "Azafrine"

OR "Azaglax" OR "Azahexal" OR "Azamun*" OR "Azamedac" OR "Azap" OR "Azapin*" OR "Azapress" OR "Aza Q" OR "Azarek" OR "Azasan" OR "Azathiodura" OR "Azathiodura" OR "Azathioregio" OR "Azatrilem" OR "Azimune" OR "Azopin*" OR "Azoran" OR "Berkaprine" OR "Colinsan" OR "Glaxoprin" OR "Immunoprin" OR "Imuger" OR "Imunen" OR "Imuprin*" OR "Imuran" OR "Imureor Imuzat" OR "Oprisine" OR "Satedon" OR "Thioprine" OR "Tiosalprin" OR "Transimune" OR "Zaprine" OR "Zytrim" OR "Cyclosporine" OR "ciclosporin*" OR "cyclosporin*" OR "neoral" OR "gengraf" OR "restasis" OR "sandimmun*" OR "sangcya" OR "Penicillamine" OR "Penicillamine" OR "Adalkenor" OR "Artamin" OR "Atamir" OR "Byanodine" OR "Cilamin" OR "Cuprenil" OR "Cuprimine" OR "Cupripen" OR "Depen" OR "Distamin*" OR "D Penamine" OR "Gerodyl" OR "Kelatin*" OR "Mercaptyl" OR "Metalcaptase" OR "Pendramine" OR "Rhumantin" OR "Sufortan*" OR "Trisorcin" OR "Trolovol" OR "Cyclophosphamide" OR "cyclophosph*" OR "cytophosphan" OR "Cytoxan" OR "sendoxan" OR "endoxan" OR "neosar" OR "nsc 26271" OR "procytox" OR "b 518" OR "ifosfamide" OR "isophosphamide" OR "iphosphamide" OR "isofosfamide" OR "holoxan" OR "nsc 109*" OR "asta z 4942" OR "cfx" OR "phosphoramide mustard*" OR "Mycophenolic Acid" OR "mycophenolate" OR "Arzip" OR "Baxmune" OR "CellCept" OR "Cellmune" OR "Celprot" OR "Ceptolate" OR "Imulate" OR "Imuxgen" OR "Lanfetil" OR "Limfocept" OR "Metocris" OR "Micocept" OR "MMF" OR "Mofecept" OR "Mofetyl" OR "Mofilet" OR "Mofimutral" OR "Mometil" OR "Mophecen" OR "Munotras" OR "Myaccord" OR "Mycept" OR "Myclausenor" OR "Mycofenor" OR "Mycolat" OR "Mycoldosa" OR "Mycophen" OR "Myfenax Myfetil" OR "Mygref" OR "Myotec" OR "Mysept" OR "Presumin" OR "Refrat" OR "Renocell" OR "Supresta" OR "Tevacept" OR "Trixin" OR "Chlorambucil" OR "chlorambucil" OR "Amboclorin" OR "Clokeran" OR "Leukeran" OR "Linfolysin" OR "Lympholysin" OR "Minocycline" OR "minocyclin*" OR "Acneclin" OR "Akamin" OR "Aknemin" OR "Akne Puren" OR "Aknereduct" OR "Aknin Mino" OR "Aknin N" OR "Aknoral" OR "Aknosan" OR "Apominolin" OR "Arestinor" OR "Auramin" OR "Blemix" OR "Borymycin" OR "Cipancin" OR "Cyclimycin" OR "Dentomycin*" OR "durakne" OR "Dynacin" OR "Enca" OR "Icht Oralor" OR "Klinoc" OR "Klinomycin" OR "Klinotab" OR "Lederderm" OR "Logryx" OR "Meibi" OR "Mestacine" OR "Micromycin" OR "Minac 50" OR "Minakne" OR "Minaxen" OR "Mino 50" OR "Minocin" OR "Minoclin" OR "Minodene" OR "Minoderm" OR "Minogalen" OR "Minolis" OR "Minomax" OR "Minomycin" OR "Minoplus" OR "Minosil" OR "Minostad" OR "Minotab*" OR "Minotekor" OR "Minotrex" OR "Minotyrol" OR "Mino Wolff" OR "Minox" OR "Mynocine" OR "Myrac" OR "Oracyclin" OR "Parocline" OR "Periocline" OR "Peritrol" OR "Ranmino" OR "Romin" OR "Seboclear" OR "Sebomin" OR "Sebren" OR "Skid" OR "Skinocyclin" OR "Solodyn" OR "Spicline" OR "Triomin" OR "Udima" OR "Vectrin" OR "Yelnac" OR "Zacnan" OR "Pyrrole" OR "tofacitinib" OR "Xeljanz" OR "baricitinib" OR "peficitinib" OR "filgotinib" OR "upadacitinib" OR "fostamatinib" OR "Alefacept" OR "alefacept" OR "Amevive" OR "efalizumab" OR "efalizumab" OR "raptiva" OR "secukinumab" OR "secukinumab" OR "cosentyx" OR "recombinant interleukin 10" OR "human recombinant IL 10" OR "human recombinant Interleukin 10" OR "human rIL 10" OR "recombinant IL 10" OR "recombinant Interleukin 10" OR "rIL 10" OR "rIL10" OR "bimekizumab" OR "bimekizumab" OR "deucravacitinib" OR "deucravacitinib" OR "sonelokimab" OR "sonelokimab" OR "izokibep" OR "apremilast" OR "apremilast" OR "otezla" OR "Glucocorticoid" OR "glucocorticoids" OR "glucocorticoid" OR "glucocorticoid*" OR "alclometasone dipropionate" OR "amcinonide" OR "Beclomethasone" OR "Betamethasone" OR "betamethasone acetate" OR "betamethasone benzoate" OR "betamethasone dipropionate, betamethasone sodium phosphate drug combination" OR "betamethasone sodium phosphate" OR "Betamethasone Valerate" OR "Budesonide" OR "ciclesonide" OR "Clobetasol" OR "clobetasone butyrate" OR "clocortolone" OR "clocortolone pivalate" OR "Desoximetasone" OR "Dexamethasone" OR "dexamethasone 21 phosphate" OR "Dexamethasone Isonicotinate" OR "dichlorisone acetate" OR "diflorasone" OR "Diflucortolone" OR "difluprednate" OR "drocinonide phosphate potassium" OR "Flumethasone" OR "flumethasone pivalate" OR "Fluocinolone Acetonide" OR "Fluocinonide" OR "fluocortin butyl ester" OR "Fluocortolone" OR "Fluorometholone" OR "fluperolone acetate" OR "fluprednidene acetate" OR

"Fluprednisolone" OR "Flurandrenolone" OR "Fluticasone Salmeterol Drug Combination" OR "FX006" OR "halometasone" OR "medrysone" OR "Melengestrol Acetate" OR "Methylprednisolone" OR "Methylprednisolone Hemisuccinate" OR "Paramethasone" OR "prednicarbate" OR "Prednisolone" OR "prednisolone hemisuccinate" OR "prednisolone phosphate" OR "Prednisone" OR "rimexolone" OR "terofenamate" OR "Tobramycin, Dexamethasone Drug Combination" OR "Triamcinolone" OR "Triamcinolone Acetonide" OR "triamcinolone benetonide" OR "nonsteroid antiinflammatory agent" OR "Nonsteroidal Anti Inflammatory" OR "Nonsteroidal Antiinflammatory" OR "Non Steroidal Anti Inflammatory " OR "Non Steroidal Antiinflammatory " OR "NSAIDs" OR "NSAID" OR "((E) (5) (3,5 di tert butyl 4 hydroxybenzylidene) 2 ethyl 1,2 isothiazolidine 1,1 dioxide)" OR "1 ((4,5 bis(4 methoxyphenyl) 2 thiazoyl)carbonyl) 4 methylpiperazine" OR "1 ((4 methylsulfonyl)phenyl) 3 trifluoromethyl 5 (4 fluorophenyl)pyrazole" OR "1 (4 chlorobenzoyl) 3 (2 (1H imidazol 1 yl) 2 oxoethyl) 5 methoxy 2 methyl 1H indole" OR "2 (4 (quinolin 2 yl methoxy)phenyl) 2 cyclopentylacetic acid" OR "2 (4 acetoxyphenyl) 2 chloro N methylethylamine" OR "2 aminomethyl 4 t butyl 6 iodophenol" OR "2 diethylaminoethanol" OR "2 hydroxymethyl 4 (5 (4 methoxyphenyl) 3 trifluoromethyl 1H 1 pyrazolyl) 1 benzenesulfonamide" OR "4,5 Dihydro 1 (3 (trifluoromethyl)phenyl) 1H pyrazol 3 amine" OR "4 (5 (4 chlorophenyl) 3 (trifluoromethyl) 1H pyrazol 1 yl)benzenesulfonamide" OR "4 bromo 2,7 dimethoxy 3H phenothiazin 3 one" OR "6 (4 fluorophenyl) 2,3 dihydro 5 (4 pyridinyl)imidazo(2,1 b)thiazole" OR "6 acetylaminocaproic acid" OR "6 ethoxy 3 (4 methanesulfonylphenyl) 4 phenylpyran 2 one" OR "7 methoxy alpha methyl 2 naphthaleneacetic acid" OR "aceclofenac" OR "acemetacin" OR "acetaminophen, aspirin, caffeine drug combination" OR "acetaminophen, butalbital, caffeine drug combination" OR "acetaminophen, hydrocodone drug combination" OR "acetosyringone" OR "acetovanillone" OR "acetylsalicylic acid lysinate" OR "Adapalene" OR "Adapalene, Benzoyl Peroxide Drug Combination" OR "alclofenac" OR "alminoprofen" OR "alpha pentyl 3 (2 quinolinylmethoxy)benzenemethanol" OR "amiprilose" OR "Ampyrone" OR "amylase, phosphates, proteases drug combinations" OR "andrographolide" OR "anisodamine" OR "anisodine" OR "antiflammin P2" OR "Antipyrine" OR "Apazone" OR "apremilast" OR "Arteparon" OR "Arthrotec" OR "Aspirin" OR "aspirin, aluminum hydroxide, magnesium hydroxide drug combination" OR "aspirin, butalbital and caffeine drug combination" OR "aspirin, meprobamate drug combination" OR "atrinositol" OR "azulene" OR "baicalin" OR "balsalazide" OR "bendazac" OR "bendazac lysine" OR "benorilate" OR "benoxaprofen" OR "benzobarbital" OR "berbamine" OR "bevonium" OR "BI 607812 BS" OR "biphenylylacetic acid" OR "boldine" OR "boswellic acid" OR "bromfenac" OR "bucillamine" OR "Bufexamac" OR "bumadizone" OR "butibufen" OR "carbaspirin calcium" OR "carprofen" OR "caryophyllene" OR "castanospermine" OR "CDP 571" OR "Celecoxib" OR "cepharanthine" OR "chloroquine diphosphate" OR "choline magnesium trisalicylate" OR "chrysarobin" OR "Clonixin" OR "CP 96345" OR "Curcumin" OR "CX 659S" OR "dauricine" OR "dexketoprofen trometamol" OR "Diclofenac" OR "diclofenac hydroxyethylpyrrolidine" OR "difenpiramide" OR "Diflunisal" OR "dimephosphon" OR "Dipyrone" OR "diucifon" OR "droxicam" OR "dual inhibitor PTUPB" OR "DuP 697" OR "ebselen" OR "ecallantide" OR "eltenac" OR "enfenamic acid" OR "enkephalin Leu, Ala(2) Arg(6) " OR "Epirizole" OR "Etanercept" OR "ethenzamide" OR "Ethonium" OR "Etodolac" OR "etofenamate" OR "Etoricoxib" OR "evening primrose oil" OR "fenamic acid" OR "fenbufen" OR "fenclofenac" OR "fenflumizole" OR "Fenoprofen" OR "fentiazac" OR "fepradinol" OR "Feprazone" OR "ferulic acid" OR "floctafenine" OR "flosulide" OR "flunixin" OR "flunixin meglumine" OR "flunoxaprofen" OR "fluproquazone" OR "Flurbiprofen" OR "flurbiprofen axetil" OR "FR 167653" OR "FR 173657" OR "glucametacin" OR "guacetisal" OR "helenalin" OR "heliodermin" OR "hemodes" OR "higenamine" OR "Ibuprofen" OR "ibuproxam" OR "icatibant" OR "IH 764 3" OR "imidazole 2 hydroxybenzoate" OR "indobufen" OR "Indomethacin" OR "Indoprofen" OR "iodoantipyrine" OR "isoxicam" OR "kebuzone" OR "Ketoprofen" OR "ketoprofen lysine" OR "Ketorolac" OR "Ketorolac Tromethamine" OR "L 745337" OR "L 778736" OR "licofelone" OR "lipoxin A4" OR "lipoxin B4" OR "lisofylline" OR "lobenzarit" OR "lonazolac" OR "lornoxicam" OR "loxoprofen"

OR "LQFM 091" OR "lumiracoxib" OR "Magnesium Salicylate" OR "magnolol" OR "manoalide" OR "Masoprocol" OR "Meclofenamic Acid" OR "Mefenamic Acid" OR "Meloxicam" OR "Mesalamine" OR "mirikizumab" OR "mizoribine" OR "mofebutazone" OR "mofezolac" OR "muricarpone B" OR "N (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide" OR "N (9H (2,7 dimethylfluoren 9 ylmethoxy)carbonyl)leucine" OR "N succinimidyl 1 (4 chlorobenzoyl) 5 methoxy 2 methyl 1H indole 3 acetate" OR "NAAA inhibitor F215" OR "Nabumetone" OR "nafamostat" OR "Naproxen" OR "Nebacetin" OR "nepafenac" OR "nifenazone" OR "Niflumic Acid" OR "nimesulide" OR "nitroaspirin" OR "Olopatadine Hydrochloride" OR "olsalazine" OR "olvanil" OR "oren gedoku to" OR "orgotein" OR "Oxaprozin" OR "Oxyphenbutazone" OR "palmidrol" OR "parecoxib" OR "parthenolide" OR "peoniflorin" OR "phenidone" OR "Phenylbutazone" OR "pimecrolimus" OR "pirfenidone" OR "Piroxicam" OR "piroxicam beta cyclodextrin" OR "pirprofen" OR "proglumetacin" OR "propacetamol" OR "propionylcarnitine" OR "propyphenazone" OR "proquazone" OR "pyranoprofen" OR "pyrazolone" OR "pyrogenal" OR "RNS60" OR "rofecoxib" OR "rosmarinic acid" OR "Rumalon" OR "saiko keishi to" OR "saikosaponin D" OR "salicin" OR "salicylamide" OR "Salicylates" OR "salicylsalicylic acid" OR "SB 203580" OR "SC 299" OR "SC 41930" OR "SC 560" OR "semapimod" OR "seratrodast" OR "serratiopeptidase" OR "shikonin" OR "sinapaldehyde" OR "SK^ and F 105685" OR "Sodium Salicylate" OR "ST 679" OR "Sul 121" OR "Sulfasalazine" OR "Sulindac" OR "sulindac sulfide" OR "sulindac sulfone" OR "Suprofen" OR "suxibuzone" OR "tanshinone" OR "taxifolin" OR "tenidap" OR "tenoxicam" OR "tepoxalin" OR "teriflunomide" OR "tiaprofenic acid" OR "tiaramide" OR "tinoridine" OR "tolfenamic acid" OR "Tolmetin" OR "tramadol, dexketoprofen drug combination" OR "tranilast" OR "tribenoside" OR "ursolic acid" OR "valdecoxib" OR "zileuton" OR "zomepirac"):ti,ab,kw)

Text S1.4: Safety: MEDLINE Search strategy

(("Arthritis, Psoriatic"[Mesh] OR "Psoriatic Arthritis"[tw] OR "Arthritic Psoriasis"[tw] OR "Psoriatic Arthritis"[tw] OR "Psoriasis Arthropathica"[tw] OR "Psoriatic Arthropathy"[tw] OR "Psoriatic Arthropathies"[tw]) NOT (("Infant"[mesh] OR "infant"[ti] OR "infants"[ti] OR "Child"[mesh] OR "child"[ti] OR "children"[ti] OR "pediatric"[ti] OR "paediatric"[ti] OR "pediatrics"[ti] OR "paediatrics"[ti] OR "Adolescent"[mesh] OR "adolescent"[ti] OR "adolescents"[ti]) NOT ("Adult"[mesh] OR "adult"[ti] OR "adults"[ti] OR "middle aged"[ti] OR "elderly"[ti])) AND ("biological therapy"[mesh] OR "antibodies, monoclonal"[mesh] OR "monokines"[mesh] OR "receptors, interleukin-1"[mesh] OR "receptors, interleukin-6"[mesh] OR "immunoglobulin g"[mesh] OR "immunoconjugates"[mesh] OR "polyethylene glycols"[mesh] OR "immunoglobulin fab fragments"[mesh] OR "t-lymphocytes"[mesh] OR "biologic*"[tw] OR "bDMARD"[tw] OR "biosimilar"[tw] OR "abatacept"[tw] OR "actemra"[tw] OR "adalimumab"[tw] OR "anakinra"[tw] OR "Arzerra"[tw] OR "Brodalumab"[tw] OR "Certolizumab"[tw] OR "cimzia"[tw] OR "Clazakizumab"[tw] OR "enbrel"[tw] OR "Etanercept"[tw] OR "Golimumab"[tw] OR "Guselkumab"[tw] OR "humira"[tw] OR "infliximab"[tw] OR "Ixekizumab"[tw] OR "kineret"[tw] OR "mabthera"[tw] OR "mavrilimumab"[tw] OR "Ocrelizumab"[tw] OR "Ofatumumab"[tw] OR "Olokizumab"[tw] OR "orencia"[tw] OR "Pateclizumab"[tw] OR "remicade"[tw] OR "rituxan"[tw] OR "rituximab"[tw] OR "RoActemra"[tw] OR "Sarilumab"[tw] OR "Siliq"[tw] OR "simponi"[tw] OR "Sirukumab"[tw] OR "Stelara"[tw] OR "Tabalumab"[tw] OR "Taltz"[tw] OR "Tocilizumab"[tw] OR "trudexa"[tw] OR "Ustekinumab"[tw] OR "bDMARD*"[tw] OR "biosimilar*"[tw] OR "abatacept*"[tw] OR "actemra*"[tw] OR "adalimumab*"[tw] OR "anakinra*"[tw] OR "Arzerra*"[tw] OR "Brodalumab*"[tw] OR "Certolizumab*"[tw] OR "cimzia*"[tw] OR "Clazakizumab*"[tw] OR "enbrel*"[tw] OR "Etanercept*"[tw] OR "Golimumab*"[tw] OR "Guselkumab*"[tw] OR "humira*"[tw] OR "infliximab*"[tw] OR "Ixekizumab*"[tw] OR "kineret*"[tw] OR "mabthera*"[tw] OR "mavrilimumab*"[tw] OR "Ocrelizumab*"[tw] OR "Ofatumumab*"[tw] OR "Olokizumab*"[tw] OR "orencia*"[tw] OR "Pateclizumab*"[tw] OR "remicade*"[tw] OR "rituxan*"[tw] OR "rituximab*"[tw] OR "RoActemra*"[tw] OR "Sarilumab*"[tw] OR "Siliq*"[tw] OR "simponi*"[tw] OR "Sirukumab*"[tw] OR "Stelara*"[tw] OR "Tabalumab*"[tw] OR "Taltz*"[tw] OR "Tocilizumab*"[tw] OR "trudexa*"[tw] OR "Ustekinumab*"[tw] OR "Antirheumatic Agents"[mesh] OR "Antirheumatic Agents"[pharmacological action] OR "Antirheumatic*"[tw] OR "dmard*"[tw] OR "sdmard*"[tw] OR "Methotrexate"[mesh] OR "Methotrexate"[tw] OR "Abitrexate"[tw] OR "ametopterin*"[tw] OR "amethopterin*"[tw] OR "Abitrexate"[tw] OR "A Metopterin*"[tw] OR "A Methopterin*"[tw] OR "Antifolan"[tw] OR "Emtexate"[tw] OR "Emthexate"[tw] OR "Enthexate"[tw] OR "Farmitrexate"[tw] OR "Folex"[tw] OR "Ledertrexate"[tw] OR "Methoblastin"[tw] OR "Methohexate"[tw] OR "Methotrate"[tw] OR "Methylaminopterin"[tw] OR "Metotrexat*"[tw] OR "mtx"[tw] OR "Novatrex"[tw] OR "Rheumatrex"[tw] OR "Isoxazoles"[mesh] OR "isoxazole*"[tw] OR "leflunomide*"[tw] OR "Afiancen"[tw] OR "Arabloc"[tw] OR "Arava"[tw] OR "Artrilab"[tw] OR "Artrimod"[tw] OR "Filartros"[tw] OR "Inmunoartro"[tw] OR "Lefluar"[tw] OR "Leflucross"[tw] OR "Lefno"[tw] OR "Lefra"[tw] OR "Lefumide"[tw] OR "Lisifen"[tw] OR "Molagar"[tw] OR "Repso"[tw] OR "Rumalef"[tw] OR "Sulfasalazine"[mesh] OR "sulfasalazine"[tw] OR "Salazosulfapyridine"[tw] OR "sulfasalazine"[tw] OR "Sulfosalazine"[tw] OR "Sulfasalzine"[tw] OR "Salazopyridin*"[tw] OR "asulfidine"[tw] OR "azulfdine"[tw] OR "Hydroxychloroquine"[mesh] OR "Hydroxychloro*"[tw] OR "Axokineor"[tw] OR "Dolquine"[tw] OR "Ercoquin"[tw] OR "Evoquin"[tw] OR "HCQS"[tw] OR "HQT"[tw] OR "Hydrocad"[tw] OR "Hydroquin"[tw] OR "Ilinol"[tw] OR "Immard"[tw] OR "Metirel"[tw] OR "Narbon"[tw] OR "Oxcq"[tw] OR "Oxiklorin"[tw] OR "Oxy-Q"[tw] OR "Plaquen*"[tw] OR "Polirreuminor"[tw] OR "Quensyl"[tw] OR "Reuquinol"[tw] OR "Gold Compounds"[mesh] OR "Organogold Compounds"[mesh] OR "gold"[tw] OR "Chloroquine"[mesh] OR "chloroquine*"[tw] OR

"aralen"[tw] OR "arechine"[tw] OR "arequin"[tw] OR "chingamin"[tw] OR "chlorochin"[tw] OR "khingamin"[tw] OR "nivaquine"[tw] OR "oxychloroquine"[tw] OR "oxychlorochin"[tw] OR "plaquinol"[tw] OR "plaquinil"[tw] OR "quensy"[tw] OR "anoclor"[tw] OR "arthrabas"[tw] OR "avloclor"[tw] OR "cidanchin"[tw] OR "clopirim"[tw] OR "collagenan"[tw] OR "daraclor"[tw] OR "daramal"[tw] OR "dichinalex"[tw] OR "difosquin"[tw] OR "diroquine"[tw] OR "genocin"[tw] OR "heliopar"[tw] OR "klorokin"[tw] OR "malarex"[tw] OR "malaviron"[tw] OR "mirquin"[tw] OR "nivaquine"[tw] OR "novo-chloroquine"[tw] OR "novochloroquine"[tw] OR "paluken"[tw] OR "palux"[tw] OR "pharmaquinine"[tw] OR "plasmoquine"[tw] OR "promal"[tw] OR "p-roquine"[tw] OR "resoquin*"[tw] OR "savarine"[tw] OR "syncoquin"[tw] OR "weimerquin"[tw] OR "Azathioprine"[mesh] OR "azathioprine"[tw] OR "Aseroprim"[tw] OR "Aseroprin"[tw] OR "Azaallen"[tw] OR "Azadus"[tw] OR "Azafalk"[tw] OR "Azafor"[tw] OR "Azafrine"[tw] OR "Azaglax"[tw] OR "Azahexal"[tw] OR "Azamun*"[tw] OR "Azamedac"[tw] OR "Azap"[tw] OR "Azapin*"[tw] OR "Azapress"[tw] OR "Aza-Q"[tw] OR "Azarek"[tw] OR "Azasan"[tw] OR "Azathiodura"[tw] OR "Azathiodura"[tw] OR "Azathioregio"[tw] OR "Azatrilem"[tw] OR "Azimune"[tw] OR "Azopin*"[tw] OR "Azoran"[tw] OR "Berkaprine"[tw] OR "Colinsan"[tw] OR "Glaxoprin"[tw] OR "Immunoprin"[tw] OR "Imuger"[tw] OR "Imunen"[tw] OR "Imuprin*"[tw] OR "Imuran"[tw] OR "Imureor Imuzat"[tw] OR "Oprisine"[tw] OR "Satedon"[tw] OR "Thioprine"[tw] OR "Tiosalprin"[tw] OR "Transimune"[tw] OR "Zaprine"[tw] OR "Zytrim"[tw] OR "Cyclosporins"[mesh] OR "ciclosporin*"[tw] OR "cyclosporin*"[tw] OR "neoral"[tw] OR "gengraf"[tw] OR "restasis"[tw] OR "sandimmun*"[tw] OR "sangcya"[tw] OR "Penicillamine"[mesh] OR "Penicillamine"[tw] OR "Adalkenor"[tw] OR "Artamin"[tw] OR "Atamir"[tw] OR "Byanodine"[tw] OR "Cilamin"[tw] OR "Cuprenil"[tw] OR "Cuprimine"[tw] OR "Cupripen"[tw] OR "Depen"[tw] OR "Distamin*"[tw] OR "D-Penamine"[tw] OR "Gerodyl"[tw] OR "Kelatin*"[tw] OR "Mercaptyl"[tw] OR "Metalcaptase"[tw] OR "Pendramine"[tw] OR "Rhumantin"[tw] OR "Sufortan*"[tw] OR "Trisorcin"[tw] OR "Trolovol"[tw] OR "Cyclophosphamide"[mesh] OR "cyclophosph*"[tw] OR "cytophosphan"[tw] OR "Cytoxan"[tw] OR "sendoxan"[tw] OR "endoxan"[tw] OR "neosar"[tw] OR "nsc-26271"[tw] OR "procytox"[tw] OR "b-518"[tw] OR "ifosfamide"[tw] OR "isophosphamide"[tw] OR "iphosphamide"[tw] OR "isofosfamide"[tw] OR "holoxan"[tw] OR "nsc-109*"[tw] OR "asta z 4942"[tw] OR "cfx"[tw] OR "phosphoramide mustard*"[tw] OR "Mycophenolic Acid"[mesh] OR "mycophenolate"[tw] OR "Arzip"[tw] OR "Baxmune"[tw] OR "CellCept"[tw] OR "Cellmune"[tw] OR "Celprot"[tw] OR "Ceptolate"[tw] OR "Imulate"[tw] OR "Imuxgen"[tw] OR "Lanfetil"[tw] OR "Limfocept"[tw] OR "Metocris"[tw] OR "Micocept"[tw] OR "MMF"[tw] OR "Mofecept"[tw] OR "Mofetyl"[tw] OR "Mofilet"[tw] OR "Mofimutral"[tw] OR "Mometil"[tw] OR "Mophecen"[tw] OR "Munotras"[tw] OR "Myaccord"[tw] OR "Mycept"[tw] OR "Myclausenor"[tw] OR "Mycofenor"[tw] OR "Mycolat"[tw] OR "Mycoldosa"[tw] OR "Mycophen"[tw] OR "Myfenax Myfetil"[tw] OR "Mygref"[tw] OR "Myotec"[tw] OR "Mysept"[tw] OR "Presumin"[tw] OR "Refrat"[tw] OR "Renocell"[tw] OR "Supresta"[tw] OR "Tevacept"[tw] OR "Trixin"[tw] OR "Chlorambucil"[mesh] OR "chlorambucil"[tw] OR "Amboclorin"[tw] OR "Clokeran"[tw] OR "Leukeran"[tw] OR "Linfolysin"[tw] OR "Lympholysin"[tw] OR "Minocycline"[mesh] OR "minocyclin*"[tw] OR "Acneclin"[tw] OR "Akamin"[tw] OR "Aknemin"[tw] OR "Akne-Puren"[tw] OR "Aknereduct"[tw] OR "Aknin-Mino"[tw] OR "Aknin-N"[tw] OR "Aknoral"[tw] OR "Aknosan"[tw] OR "Apominolin"[tw] OR "Arestinor"[tw] OR "Auramin"[tw] OR "Blemix"[tw] OR "Borymycin"[tw] OR "Cipancin"[tw] OR "Cyclimycin"[tw] OR "Dentomycin*"[tw] OR "durakne"[tw] OR "Dynacin"[tw] OR "Enca"[tw] OR "Icht-Oralor"[tw] OR "Klinoc"[tw] OR "Klinomycin"[tw] OR "Klinotab"[tw] OR "Lederderm"[tw] OR "Logryx"[tw] OR "Meibi"[tw] OR "Mestacine"[tw] OR "Micromycin"[tw] OR "Minac 50"[tw] OR "Minakne"[tw] OR "Minaxen"[tw] OR "Mino-50"[tw] OR "Minocin"[tw] OR "Minoclin"[tw] OR "Minodene"[tw] OR "Minoderm"[tw] OR "Minogalen"[tw] OR "Minolis"[tw] OR "Minomax"[tw] OR "Minomycin"[tw] OR "Minoplus"[tw] OR "Minosil"[tw] OR "Minostad"[tw] OR "Minotab*"[tw] OR "Minotekor"[tw] OR "Minotrex"[tw] OR "Minotyrol"[tw] OR "Mino-Wolff"[tw] OR "Minox"[tw] OR "Mynocine"[tw] OR "Myrac"[tw] OR

"Oracyclin"[tw] OR "Parocline"[tw] OR "Periocline"[tw] OR "Peritrol"[tw] OR "Ranmino"[tw] OR "Romin"[tw] OR "Seboclear"[tw] OR "Sebomin"[tw] OR "Sebren"[tw] OR "Skid"[tw] OR "Skinocyclin"[tw] OR "Solodyn"[tw] OR "Spicline"[tw] OR "Triomin"[tw] OR "Udima"[tw] OR "Vectrin"[tw] OR "Yelnac"[tw] OR "Zacnan"[tw] OR "Pyrroles"[mesh] OR "tofacitinib"[tw] OR "Xeljanz"[tw] OR "baricitinib"[tw] OR "peficitinib"[tw] OR "filgotinib"[tw] OR "upadacitinib"[tw] OR "fostamatinib"[tw] OR "Alefacept"[Mesh] OR "alefacept"[tw] OR "Amevive"[tw] OR "efalizumab"[Supplementary Concept] OR "efalizumab"[tw] OR "raptiva"[tw] OR "secukinumab"[Supplementary Concept] OR "secukinumab"[tw] OR "cosentyx"[tw] OR "human recombinant IL 10"[tw] OR "human recombinant Interleukin 10"[tw] OR "human rIL 10"[tw] OR "recombinant IL 10"[tw] OR "recombinant Interleukin 10"[tw] OR "rIL 10"[tw] OR "rIL10"[tw] OR "bimekizumab"[Supplementary Concept] OR "bimekizumab"[tw] OR "deucravacitinib"[Supplementary Concept] OR "deucravacitinib"[tw] OR "sonelokimab"[Supplementary Concept] OR "sonelokimab"[tw] OR "izokibep"[tw] OR "apremilast"[Supplementary Concept] OR "apremilast"[tw] OR "otezla"[tw] OR "Glucocorticoids"[Mesh] OR "Glucocorticoids"[Pharmacological Action] OR "glucocorticoids"[tw] OR "glucocorticoid"[tw] OR "glucocorticoid*"[tw] OR "alclometasone dipropionate"[tw] OR "amcinonide"[tw] OR "Beclomethasone"[tw] OR "Betamethasone"[tw] OR "betamethasone acetate"[tw] OR "betamethasone benzoate"[tw] OR "betamethasone dipropionate, betamethasone sodium phosphate drug combination"[tw] OR "betamethasone sodium phosphate"[tw] OR "Betamethasone Valerate"[tw] OR "Budesonide"[tw] OR "ciclesonide"[tw] OR "Clobetasol"[tw] OR "clobetasone butyrate"[tw] OR "clocortolone"[tw] OR "clocortolone pivalate"[tw] OR "Desoximetasone"[tw] OR "Dexamethasone"[tw] OR "dexamethasone 21-phosphate"[tw] OR "Dexamethasone Isonicotinate"[tw] OR "dichlorisone acetate"[tw] OR "diflorasone"[tw] OR "Diflucortolone"[tw] OR "difluprednate"[tw] OR "drocinonide phosphate potassium"[tw] OR "Flumethasone"[tw] OR "flumethasone pivalate"[tw] OR "Fluocinolone Acetonide"[tw] OR "Fluocinonide"[tw] OR "fluocortin butyl ester"[tw] OR "Fluocortolone"[tw] OR "Fluorometholone"[tw] OR "fluperolone acetate"[tw] OR "fluprednidene acetate"[tw] OR "Fluprednisolone"[tw] OR "Flurandrenolone"[tw] OR "Fluticasone-Salmeterol Drug Combination"[tw] OR "FX006"[tw] OR "halometasone"[tw] OR "medrysone"[tw] OR "Melengestrol Acetate"[tw] OR "Methylprednisolone"[tw] OR "Methylprednisolone Hemisuccinate"[tw] OR "Paramethasone"[tw] OR "prednicarbate"[tw] OR "Prednisolone"[tw] OR "prednisolone hemisuccinate"[tw] OR "prednisolone phosphate"[tw] OR "Prednisone"[tw] OR "rimexolone"[tw] OR "terofenamate"[tw] OR "Tobramycin, Dexamethasone Drug Combination"[tw] OR "Triamcinolone"[tw] OR "Triamcinolone Acetonide"[tw] OR "triamcinolone benetonide"[tw] OR "Anti-Inflammatory Agents, Non-Steroidal"[Mesh] OR "Anti-Inflammatory Agents, Non-Steroidal"[Pharmacological Action] OR "Nonsteroidal Anti Inflammatory"[tw] OR "Nonsteroidal Antiinflammatory"[tw] OR "Non-Steroidal Anti-Inflammatory "[tw] OR "Non-Steroidal Antiinflammatory "[tw] OR "NSAIDs"[tw] OR "NSAID"[tw] OR "((E)-(5)-(3,5-di-tert-butyl-4-hydroxybenzylidene)- 2-ethyl-1,2-isothiazolidine-1,1-dioxide)"[tw] OR "1-((4,5-bis(4-methoxyphenyl)-2-thiazoyl)carbonyl)-4-methylpiperazine"[tw] OR "1-((4-methylsulfonyl)phenyl)-3-trifluoromethyl-5-(4-fluorophenyl)pyrazole"[tw] OR "1-(4-chlorobenzoyl)-3-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-methoxy-2-methyl-1H-indole"[tw] OR "2-(4-(quinolin-2-yl-methoxy)phenyl)-2-cyclopentylacetic acid"[tw] OR "2-(4-acetoxyphenyl)-2-chloro-N-methylethylamine"[tw] OR "2-aminomethyl-4-t-butyl-6-iodophenol"[tw] OR "2-diethylaminoethanol"[tw] OR "2-hydroxymethyl-4-(5-(4-methoxyphenyl)-3-trifluoromethyl-1H-1-pyrazolyl)-1-benzenesulfonamide"[tw] OR "4,5-Dihydro-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-3-amine"[tw] OR "4-(5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide"[tw] OR "4-bromo-2,7-dimethoxy-3H-phenothiazin-3-one"[tw] OR "6-(4-fluorophenyl)-2,3-dihydro-5-(4-pyridinyl)imidazo(2,1-b)thiazole"[tw] OR "6-acetylaminocaproic acid"[tw] OR "6-ethoxy-3-(4-methanesulfonylphenyl)-4-phenylpyran-2-one"[tw] OR "7-methoxy-alpha-methyl-2-naphthaleneacetic acid"[tw] OR

"aceclofenac"[tw] OR "acemetacin"[tw] OR "acetaminophen, aspirin, caffeine drug combination"[tw] OR "acetaminophen, butalbital, caffeine drug combination"[tw] OR "acetaminophen, hydrocodone drug combination"[tw] OR "acetosyringone"[tw] OR "acetovanillone"[tw] OR "acetylsalicylic acid lysinate"[tw] OR "Adapalene"[tw] OR "Adapalene, Benzoyl Peroxide Drug Combination"[tw] OR "alclofenac"[tw] OR "alminoprofen"[tw] OR "alpha-pentyl-3-(2-quinolinylmethoxy)benzenemethanol"[tw] OR "amiprilose"[tw] OR "Ampyrone"[tw] OR "amylase, phosphates, proteases drug combinations"[tw] OR "andrographolide"[tw] OR "anisodamine"[tw] OR "anisodine"[tw] OR "antiflammin P2"[tw] OR "Antipyrine"[tw] OR "Apazone"[tw] OR "apremilast"[tw] OR "Arteparon"[tw] OR "Arthrotec"[tw] OR "Aspirin"[tw] OR "aspirin, aluminum hydroxide, magnesium hydroxide drug combination"[tw] OR "aspirin, butalbital and caffeine drug combination"[tw] OR "aspirin, meprobamate drug combination"[tw] OR "atrinositol"[tw] OR "azulene"[tw] OR "baicalin"[tw] OR "balsalazide"[tw] OR "bendazac"[tw] OR "bendazac lysine"[tw] OR "benorilate"[tw] OR "benoxaprofen"[tw] OR "benzobarbital"[tw] OR "berbamine"[tw] OR "bevonium"[tw] OR "BI 607812 BS"[tw] OR "biphenylylacetic acid"[tw] OR "boldine"[tw] OR "boswellic acid"[tw] OR "bromfenac"[tw] OR "bucillamine"[tw] OR "Bufexamac"[tw] OR "bumadizone"[tw] OR "butibufen"[tw] OR "carbaspirin calcium"[tw] OR "carprofen"[tw] OR "caryophyllene"[tw] OR "castanospermine"[tw] OR "CDP 571"[tw] OR "Celecoxib"[tw] OR "cepharanthine"[tw] OR "chloroquine diphosphate"[tw] OR "choline magnesium trisalicylate"[tw] OR "chrysarobin"[tw] OR "Clonixin"[tw] OR "CP 96345"[tw] OR "Curcumin"[tw] OR "CX 659S"[tw] OR "dauricine"[tw] OR "dexketoprofen trometamol"[tw] OR "Diclofenac"[tw] OR "diclofenac hydroxyethylpyrrolidine"[tw] OR "difenpiramide"[tw] OR "Diflunisal"[tw] OR "dimephosphon"[tw] OR "Dipyrone"[tw] OR "diucifon"[tw] OR "droxicam"[tw] OR "dual inhibitor PTUPB"[tw] OR "DuP 697"[tw] OR "ebselen"[tw] OR "ecallantide"[tw] OR "eltenac"[tw] OR "enfenamic acid"[tw] OR "enkephalin-Leu, Ala(2)-Arg(6)-"[tw] OR "Epirizole"[tw] OR "Etanercept"[tw] OR "ethenzamide"[tw] OR "Ethonium"[tw] OR "Etodolac"[tw] OR "etofenamate"[tw] OR "Etoricoxib"[tw] OR "evening primrose oil"[tw] OR "fenamic acid"[tw] OR "fenbufen"[tw] OR "fenclofenac"[tw] OR "fenflumizole"[tw] OR "Fenoprofen"[tw] OR "fentiazac"[tw] OR "fepradinol"[tw] OR "Feprazone"[tw] OR "ferulic acid"[tw] OR "floctafenine"[tw] OR "flosulide"[tw] OR "flunixin"[tw] OR "flunixin meglumine"[tw] OR "flunoxaprofen"[tw] OR "fluproquazone"[tw] OR "Flurbiprofen"[tw] OR "flurbiprofen axetil"[tw] OR "FR 167653"[tw] OR "FR 173657"[tw] OR "glucametacin"[tw] OR "guacetisal"[tw] OR "helenalin"[tw] OR "heliodermin"[tw] OR "hemodes"[tw] OR "higenamine"[tw] OR "Ibuprofen"[tw] OR "ibuproxam"[tw] OR "icatibant"[tw] OR "IH 764-3"[tw] OR "imidazole-2-hydroxybenzoate"[tw] OR "indobufen"[tw] OR "Indomethacin"[tw] OR "Indoprofen"[tw] OR "iodoantipyrine"[tw] OR "isoxicam"[tw] OR "kebuzone"[tw] OR "Ketoprofen"[tw] OR "ketoprofen lysine"[tw] OR "Ketorolac"[tw] OR "Ketorolac Tromethamine"[tw] OR "L 745337"[tw] OR "L 778736"[tw] OR "licofelone"[tw] OR "lipoxin A4"[tw] OR "lipoxin B4"[tw] OR "lisofylline"[tw] OR "lobenzarit"[tw] OR "lonazolac"[tw] OR "lornoxicam"[tw] OR "loxoprofen"[tw] OR "LQFM-091"[tw] OR "lumiracoxib"[tw] OR "Magnesium Salicylate"[tw] OR "magnolol"[tw] OR "manoalide"[tw] OR "Masoprocol"[tw] OR "Meclofenamic Acid"[tw] OR "Mefenamic Acid"[tw] OR "Meloxicam"[tw] OR "Mesalamine"[tw] OR "mirikizumab"[tw] OR "mizoribine"[tw] OR "mofebutazone"[tw] OR "mofezolac"[tw] OR "muricarpone B"[tw] OR "N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide"[tw] OR "N-(9H-(2,7-dimethylfluoren-9-ylmethoxy)carbonyl)leucine"[tw] OR "N-succinimidyl-1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetate"[tw] OR "NAAA inhibitor F215"[tw] OR "Nabumetone"[tw] OR "nafamostat"[tw] OR "Naproxen"[tw] OR "Nebacetin"[tw] OR "nepafenac"[tw] OR "nifenazone"[tw] OR "Niflumic Acid"[tw] OR "nimesulide"[tw] OR "nitroaspirin"[tw] OR "Olopatadine Hydrochloride"[tw] OR "olsalazine"[tw] OR "olvanil"[tw] OR "oren gedoku to"[tw] OR "orgotein"[tw] OR "Oxaprozin"[tw] OR "Oxyphenbutazone"[tw] OR "palmidrol"[tw] OR "parecoxib"[tw] OR "parthenolide"[tw] OR "peoniflorin"[tw] OR "phenidone"[tw] OR "Phenylbutazone"[tw] OR "pimecrolimus"[tw] OR

"pirfenidone"[tw] OR "Piroxicam"[tw] OR "piroxicam-beta-cyclodextrin"[tw] OR "pirprofen"[tw] OR "proglumetacin"[tw] OR "propacetamol"[tw] OR "propionylcarnitine"[tw] OR "propyphenazone"[tw] OR "proquazone"[tw] OR "pyranoprofen"[tw] OR "pyrazolone"[tw] OR "pyrogenal"[tw] OR "RNS60"[tw] OR "rofecoxib"[tw] OR "rosmarinic acid"[tw] OR "Rumalon"[tw] OR "saiko-keishi-to"[tw] OR "saikosaponin D"[tw] OR "salicin"[tw] OR "salicylamide"[tw] OR "Salicylates"[tw] OR "salicylsalicylic acid"[tw] OR "SB 203580"[tw] OR "SC 299"[tw] OR "SC 41930"[tw] OR "SC 560"[tw] OR "semapimod"[tw] OR "seratrodast"[tw] OR "serratiopeptidase"[tw] OR "shikonin"[tw] OR "sinapaldehyde"[tw] OR "SK^ and F 105685"[tw] OR "Sodium Salicylate"[tw] OR "ST 679"[tw] OR "Sul-121"[tw] OR "Sulfasalazine"[tw] OR "Sulindac"[tw] OR "sulindac sulfide"[tw] OR "sulindac sulfone"[tw] OR "Suprofen"[tw] OR "suxibuzone"[tw] OR "tanshinone"[tw] OR "taxifolin"[tw] OR "tenidap"[tw] OR "tenoxicam"[tw] OR "tepoxalin"[tw] OR "teriflunomide"[tw] OR "tiaprofenic acid"[tw] OR "tiaramide"[tw] OR "tinoridine"[tw] OR "tolfenamic acid"[tw] OR "Tolmetin"[tw] OR "tramadol, dexketoprofen drug combination"[tw] OR "tranilast"[tw] OR "tribenoside"[tw] OR "ursolic acid"[tw] OR "valdecoxib"[tw] OR "zileuton"[tw] OR "zomepirac"[tw]) AND ("safe"[tw] OR "safety"[tw] OR "side effect*"[tw] OR (("adverse"[tw] OR "undesirable"[tw] OR "harms"[tw] OR "harm"[tw] OR "serious"[tw] OR "toxic"[tw] OR "risk"[tw] OR "risks"[tw]) AND ("effect"[tw] OR "effects"[tw] OR "reaction"[tw] OR "reactions"[tw] OR "events"[tw] OR "event"[tw] OR "outcome*"[tw])) OR "Product surveillance, postmarketing"[mesh] OR "adverse drug reaction reporting systems"[mesh] OR "clinical trial, phase iv"[pt] OR "Clinical Trial, Phase III"[pt] OR "poisoning"[mesh] OR "substance-related disorders"[mesh] OR "Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "abnormalities, drug induced"[mesh] OR "drug monitoring"[mesh] OR "drug hypersensitivity"[mesh] OR "toxicity"[tw] OR "complication*"[tw] OR "noxious"[tw] OR "tolerability"[tw] OR "Thromboembolism"[Mesh] OR "thromboembolism"[tw] OR "thrombo embolism"[tw] OR "thromboembol*"[tw] OR "thrombo embol*"[tw] OR "thromboembolism"[tw] OR "Pulmonary embolism"[mesh] OR "pulmonary embolism"[tw] OR "Infections"[mesh] OR "infection"[tw] OR "infections"[tw] OR "Neoplasms"[mesh] OR "cancer"[tw] OR "lymphoma"[tw] OR "lymphomas"[tw] OR "leukemia"[tw] OR "leukaemia"[tw] OR "malignancies"[tw] OR "malignancy"[tw] OR "melanoma"[tw] OR "melanomas"[tw] OR "solid tumour"[tw] OR "solid tumours"[tw] OR "solid tumor"[tw] OR "solid tumors"[tw] OR "Death"[Mesh] OR "Death"[tw] OR "Deaths"[tw] OR "Mortality"[mesh] OR "Mortality"[subheading] OR "Mortality"[tw] OR "Tuberculosis"[tw] OR "Herpes Zoster"[Mesh] OR "Herpes Zoster"[tw] OR "COVID-19"[tw] OR "COVID19"[tw] OR "COVID"[tw] OR "COVID-19"[mesh] OR "SARS-CoV-2"[tw] OR "SARSCoV2"[tw] OR "sars-cov-2"[mesh] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[tw] OR "NCOV"[tw] OR "2019 NCOV"[tw] OR "SARS-CoV2"[tw] OR "SARSCoV2"[tw] OR "SARSCoV 2"[tw] OR "SARSCoV"[tw] OR "SARSCoV*"[tw] OR "SARS CoV"[tw] OR "SARS CoV*"[tw] OR "covid"[tw] OR "longCOVID"[tw] OR "Congestive heart failure"[tw] OR "heart failure"[mesh] OR "heart failure"[tw] OR "Coronary Disease"[Mesh] OR "Coronary Disease"[tw] OR "Coronary Diseases"[tw] OR "Coronary Heart Disease"[tw] OR "Coronary Heart Diseases"[tw] OR "Myocardial Ischemia"[Mesh] OR "Myocardial Ischemia"[tw] OR "Myocardial Ischaemia"[tw] OR "Myocardial Infarction"[tw] OR "Angina"[tw] OR "Stroke"[mesh] OR "stroke"[tw] OR "Cerebrovascular Accident"[tw] OR "Cerebrovascular Accidents"[tw] OR "Injection Site Reaction"[Mesh] OR "Injection Site Adverse Event"[tw] OR "Injection Site Adverse Events"[tw] OR "Injection Site Adverse Reaction"[tw] OR "Injection Site Adverse Reactions"[tw] OR "Injection Site Event"[tw] OR "Injection Site Events"[tw] OR "Injection Site Reaction"[tw] OR "Injection Site Reactions"[tw] OR "Infusion Site Adverse Event"[tw] OR "Infusion Site Adverse Events"[tw] OR "Infusion Site Adverse Reaction"[tw] OR "Infusion Site Adverse Reactions"[tw] OR "Infusion Site Event"[tw] OR "Infusion Site Events"[tw] OR "Infusion Site Reaction"[tw] OR "Infusion Site Reactions"[tw] OR "Lipid levels"[tw] OR "lipid level"[tw] OR "Renal function"[tw] OR "Kidney function"[tw] OR "creatinine levels"[tw] OR "creatinine level"[tw] OR "Hepatic effects"[tw] OR "Hepatic effect"[tw] OR "Liver Diseases/chemically induced"[Mesh] OR

"transaminases"[mesh] OR "Bilirubin"[Mesh] OR "transaminases elevation"[tw] OR "transaminase elevation"[tw] OR "transaminases level"[tw] OR "transaminase level"[tw] OR "transaminases levels"[tw] OR "transaminase levels"[tw] OR "bilirubin elevation"[tw] OR "bilirubin level"[tw] OR "bilirubin levels"[tw] OR "Haematological abnormalities"[tw] OR "Haematological abnormality"[tw] OR "Haematologic abnormalities"[tw] OR "Haematologic abnormality"[tw] OR "Hematological abnormalities"[tw] OR "Hematological abnormality"[tw] OR "Hematologic abnormalities"[tw] OR "Hematologic abnormality"[tw] OR "Neutropenia"[mesh] OR "neutropenia"[tw] OR "Hematologic Diseases/chemically induced"[Mesh] OR "Gastrointestinal Diseases/chemically induced"[mesh] OR "Gastro-intestinal effects"[tw] OR "Gastro-intestinal effect"[tw] OR "Gastrointestinal effects"[tw] OR "Gastrointestinal effect"[tw] OR "Demyelinating Diseases"[Mesh] OR "Demyelinating Diseases"[tw] OR "Demyelinating disease"[tw] OR "Autoimmune Diseases"[Mesh] OR "Autoimmune Diseases"[tw] OR "Autoimmune Disease"[tw] OR "Auto immune Diseases"[tw] OR "Auto immune Disease"[tw] OR "Antibodies, Antinuclear"[Mesh] OR "anti-nuclear antibodies"[tw] OR "anti-nuclear antibody"[tw] OR "antinuclear antibodies"[tw] OR "antinuclear antibody"[tw] OR "anti-dsDNA autoantibody"[Supplementary Concept] OR "anti-dsDNA"[tw] OR "anti-drug antibodies"[tw] OR "anti-drug antibody"[tw] OR "antidrug antibodies"[tw] OR "antidrug antibody"[tw] OR "anti-chimeric antibodies"[tw] OR "anti-chimeric antibody"[tw] OR "antichimeric antibodies"[tw] OR "antichimeric antibody"[tw] OR "Fertility"[mesh] OR "Infertility"[mesh] OR "Pregnancy"[mesh] OR "Pregnancy Complications"[mesh] OR "Fertility"[tw] OR "Infertility"[tw] OR "Pregnancy"[tw] OR "Abortion, Induced"[Mesh] OR "induced abortion"[tw] OR "elective abortion"[tw] OR "Abortion, Spontaneous"[Mesh] OR "Spontaneous Abortion"[tw] OR "miscarriage"[tw] OR "abortion"[tw] OR "abortions"[tw] OR "medical termination"[tw] OR "Premature Birth"[Mesh] OR "premature birth"[tw] OR "preterm birth"[tw] OR "premature births"[tw] OR "preterm births"[tw] OR "premature childbirth"[tw] OR "preterm childbirth"[tw] OR "premature childbirths"[tw] OR "preterm childbirths"[tw] OR "premature child birth"[tw] OR "preterm child birth"[tw] OR "premature child births"[tw] OR "preterm child births"[tw] OR "Infant, Small for Gestational Age"[Mesh] OR "small for gestational age"[tw] OR "Pre-Eclampsia"[Mesh] OR "Pre-Eclampsia"[tw] OR "preeclampsia"[tw] OR "Eclampsia"[mesh] OR "eclampsia"[tw] OR "Cesarean Section"[Mesh] OR "Cesarean Section"[tw] OR "Caesarean Section"[tw] OR "c-section"[tw] OR "Teratogenesis"[Mesh] OR "Teratogenesis"[tw] OR "Teratogenicity"[tw] OR "Teratogen*"[tw]) AND ("Cohort Studies"[Mesh] OR "Cohort Study"[tw] OR "Cohort"[tw] OR "Cohorts"[tw] OR "Follow-Up Studies"[tw] OR "Longitudinal Studies"[tw] OR "Prospective Studies"[tw] OR "Retrospective Studies"[tw] OR "Follow-Up Study"[tw] OR "Longitudinal Study"[tw] OR "Prospective Study"[tw] OR "Retrospective Study"[tw] OR "Follow-Up"[tw] OR "Longitudinal"[tw] OR "Prospective"[tw] OR "Retrospective"[tw] OR "FollowUp"[tw] OR "Longitudinal*"[tw] OR "Prospective*"[tw] OR "Retrospective*"[tw] OR "Case-Control Studies"[Mesh] OR "Case-Control"[tw] OR "Case-Controlled"[tw] OR "Case-Controls"[tw] OR "Case-Control*"[tw] OR "Registries"[Mesh] OR "Registry"[tw] OR "Registries"[tw] OR "Register"[tw] OR "Registers"[tw] OR "systematic"[sb] OR "Long term extensions"[tw] OR "Long term extensions"[tw] OR "LTE"[tw] OR "LTEs"[tw]) NOT ("animals"[mesh] NOT "humans"[mesh]) AND ("2018/01/01"[PDAT] : "3000/12/31"[PDAT]))

Text S1.5: Safety: EMBASE Search strategy

((exp *"Psoriatic Arthritis"/ OR "Psoriatic Arthritis".ti,ab OR "Arthritic Psoriasis".ti,ab OR "Psoriatic Arthritis".ti,ab OR "Psoriasis Arthropathica".ti,ab OR "Psoriatic Arthropathy".ti,ab OR "Psoriatic Arthropathies".ti,ab) NOT ((exp "Infant"/ OR "infant".ti OR "infants".ti OR exp "Child"/ OR "child".ti OR "children".ti OR "pediatric".ti OR "paediatric".ti OR "pediatrics".ti OR "paediatrics".ti OR exp "Adolescent"/ OR "adolescent".ti OR "adolescents".ti) NOT (exp "Adult"/ OR "adult".ti OR "adults".ti OR "middle aged".ti OR "elderly".ti)) AND (exp *"biological therapy"/ OR exp *"monoclonal antibody"/ OR exp *"monokine"/ OR exp *"interleukin 1 receptor"/ OR exp *"interleukin 1 receptor accessory protein"/ OR exp *"interleukin 1 receptor like 1 protein"/ OR exp *"interleukin 1 receptor type I"/ OR exp *"interleukin 1 receptor type II"/ OR exp *"interleukin 6 receptor"/ OR exp *"interleukin 6 receptor alpha"/ OR exp *"immunoglobulin g"/ OR exp *"antibody conjugate"/ OR exp *"macrogol derivative"/ OR exp *"immunoglobulin F(ab) fragment"/ OR exp *"T lymphocyte"/ OR "biologic*".ti,ab OR "bDMARD".ti,ab OR "biosimilar".ti,ab OR "abatacept".ti,ab OR "actemra".ti,ab OR "adalimumab".ti,ab OR "anakinra".ti,ab OR "Arzerra".ti,ab OR "Brodalumab".ti,ab OR "Certolizumab".ti,ab OR "cimzia".ti,ab OR "Clazakizumab".ti,ab OR "enbrel".ti,ab OR "Etanercept".ti,ab OR "Golimumab".ti,ab OR "Guselkumab".ti,ab OR "humira".ti,ab OR "infliximab".ti,ab OR "Ixekizumab".ti,ab OR "kineret".ti,ab OR "mabthera".ti,ab OR "mavrilimumab".ti,ab OR "Ocrelizumab".ti,ab OR "Ofatumumab".ti,ab OR "Olokizumab".ti,ab OR "orencia".ti,ab OR "Pateclizumab".ti,ab OR "remicade".ti,ab OR "rituxan".ti,ab OR "rituximab".ti,ab OR "RoActemra".ti,ab OR "Sarilumab".ti,ab OR "Siliq".ti,ab OR "simponi".ti,ab OR "Sirukumab".ti,ab OR "Stelara".ti,ab OR "Tabalumab".ti,ab OR "Taltz".ti,ab OR "Tocilizumab".ti,ab OR "trudexa".ti,ab OR "Ustekinumab".ti,ab OR "bDMARD*".ti,ab OR "biosimilar*".ti,ab OR "abatacept*".ti,ab OR "actemra*".ti,ab OR "adalimumab*".ti,ab OR "anakinra*".ti,ab OR "Arzerra*".ti,ab OR "Brodalumab*".ti,ab OR "Certolizumab*".ti,ab OR "cimzia*".ti,ab OR "Clazakizumab*".ti,ab OR "enbrel*".ti,ab OR "Etanercept*".ti,ab OR "Golimumab*".ti,ab OR "Guselkumab*".ti,ab OR "humira*".ti,ab OR "infliximab*".ti,ab OR "Ixekizumab*".ti,ab OR "kineret*".ti,ab OR "mabthera*".ti,ab OR "mavrilimumab*".ti,ab OR "Ocrelizumab*".ti,ab OR "Ofatumumab*".ti,ab OR "Olokizumab*".ti,ab OR "orencia*".ti,ab OR "Pateclizumab*".ti,ab OR "remicade*".ti,ab OR "rituxan*".ti,ab OR "rituximab*".ti,ab OR "RoActemra*".ti,ab OR "Sarilumab*".ti,ab OR "Siliq*".ti,ab OR "simponi*".ti,ab OR "Sirukumab*".ti,ab OR "Stelara*".ti,ab OR "Tabalumab*".ti,ab OR "Taltz*".ti,ab OR "Tocilizumab*".ti,ab OR "trudexa*".ti,ab OR "Ustekinumab*".ti,ab OR exp *"Antirheumatic Agent"/ OR "Antirheumatic*".ti,ab OR "dmard*".ti,ab OR "sdmard*".ti,ab OR exp *"Methotrexate"/ OR "Methotrexate".ti,ab OR "Abitrexate".ti,ab OR "ametopterin*".ti,ab OR "amethopterin*".ti,ab OR "Abitrexate".ti,ab OR "A Metopterin*".ti,ab OR "A Methopterin*".ti,ab OR "Antifolan".ti,ab OR "Emtexate".ti,ab OR "Emthexate".ti,ab OR "Enthexate".ti,ab OR "Farmitrexate".ti,ab OR "Folex".ti,ab OR "Ledertrexate".ti,ab OR "Methoblastin".ti,ab OR "Methohexate".ti,ab OR "Methotrate".ti,ab OR "Methylaminopterin".ti,ab OR "Metotrexat*".ti,ab OR "mtx".ti,ab OR "Novatrex".ti,ab OR "Rheumatrex".ti,ab OR exp *"Isoxazole"/ OR "isoxazole*".ti,ab OR "leflunomide*".ti,ab OR "Afiancen".ti,ab OR "Arabloc".ti,ab OR "Arava".ti,ab OR "Artrilab".ti,ab OR "Artrimod".ti,ab OR "Filartros".ti,ab OR "Inmunoartro".ti,ab OR "Lefluar".ti,ab OR "Leflucross".ti,ab OR "Lefno".ti,ab OR "Lefra".ti,ab OR "Lefumide".ti,ab OR "Lisifen".ti,ab OR "Molagar".ti,ab OR "Repso".ti,ab OR "Rumalef".ti,ab OR exp *"salazosulfapyridine"/ OR "sulfasalazine".ti,ab OR "Salazosulfapyridine".ti,ab OR "sulfasalazine".ti,ab OR "Sulfosalazine".ti,ab OR "Sulfasalzine".ti,ab OR "Salazopyridin*".ti,ab OR "asulfidine".ti,ab OR "azulfdine".ti,ab OR exp *"Hydroxychloroquine"/ OR "Hydroxychloro*".ti,ab OR "Axokineor".ti,ab OR "Dolquine".ti,ab OR "Ercoquin".ti,ab OR "Evoquin".ti,ab OR "HCQS".ti,ab OR "HQT".ti,ab OR "Hydrocad".ti,ab OR "Hydroquin".ti,ab OR "Ilinol".ti,ab OR "Immard".ti,ab OR "Metirel".ti,ab OR "Narbon".ti,ab OR "Oxcq".ti,ab OR

"Oxiklorin".ti,ab OR "Oxy-Q".ti,ab OR "Plaquen*".ti,ab OR "Polirreuminor".ti,ab OR "Quensyl".ti,ab OR "Reuquinol".ti,ab OR exp *"Gold Derivative"/ OR exp *"Organogold Compound"/ OR exp *"Gold"/ OR "gold".ti,ab OR exp *"Chloroquine"/ OR "chloroquine*".ti,ab OR "aralen".ti,ab OR "arechine".ti,ab OR "arequin".ti,ab OR "chingamin".ti,ab OR "chlorochin".ti,ab OR "khingamin".ti,ab OR "nivaquine".ti,ab OR "oxychloroquine".ti,ab OR "oxychlorochin".ti,ab OR "plaquinol".ti,ab OR "plaquinil".ti,ab OR "quensy".ti,ab OR "anoclor".ti,ab OR "arthrabas".ti,ab OR "avloclor".ti,ab OR "cidanchin".ti,ab OR "clopirim".ti,ab OR "collagenan".ti,ab OR "daraclor".ti,ab OR "daramal".ti,ab OR "dichinalex".ti,ab OR "difosquin".ti,ab OR "diroquine".ti,ab OR "genocin".ti,ab OR "heliopar".ti,ab OR "klorokin".ti,ab OR "malarex".ti,ab OR "malaviron".ti,ab OR "mirquin".ti,ab OR "nivaquine".ti,ab OR "novo-chloroquine".ti,ab OR "novochloroquine".ti,ab OR "paluken".ti,ab OR "palux".ti,ab OR "pharmaquinine".ti,ab OR "plasmoquine".ti,ab OR "promal".ti,ab OR "p-roquine".ti,ab OR "resoquin*".ti,ab OR "savarine".ti,ab OR "syncoquin".ti,ab OR "weimerquin".ti,ab OR exp *"Azathioprine"/ OR "azathioprine".ti,ab OR "Aseroprim".ti,ab OR "Aseroprin".ti,ab OR "Azaallen".ti,ab OR "Azadus".ti,ab OR "Azafalk".ti,ab OR "Azafor".ti,ab OR "Azafrine".ti,ab OR "Azaglax".ti,ab OR "Azahexal".ti,ab OR "Azamun*".ti,ab OR "Azamedac".ti,ab OR "Azap".ti,ab OR "Azapin*".ti,ab OR "Azapress".ti,ab OR "Aza-Q".ti,ab OR "Azarek".ti,ab OR "Azasan".ti,ab OR "Azathiodura".ti,ab OR "Azathiodura".ti,ab OR "Azathioregio".ti,ab OR "Azatrilem".ti,ab OR "Azimune".ti,ab OR "Azopin*".ti,ab OR "Azoran".ti,ab OR "Berkaprine".ti,ab OR "Colinsan".ti,ab OR "Glaxoprin".ti,ab OR "Immunoprin".ti,ab OR "Imuger".ti,ab OR "Imunen".ti,ab OR "Imuprin*".ti,ab OR "Imuran".ti,ab OR "Imureor Imuzat".ti,ab OR "Oprisine".ti,ab OR "Satedon".ti,ab OR "Thioprine".ti,ab OR "Tiosalprin".ti,ab OR "Transimune".ti,ab OR "Zaprine".ti,ab OR "Zytrim".ti,ab OR exp *"Cyclosporine"/ OR "ciclosporin*".ti,ab OR "cyclosporin*".ti,ab OR "neoral".ti,ab OR "gengraf".ti,ab OR "restasis".ti,ab OR "sandimmun*".ti,ab OR "sangcya".ti,ab OR exp *"Penicillamine"/ OR "Penicillamine".ti,ab OR "Adalkenor".ti,ab OR "Artamin".ti,ab OR "Atamir".ti,ab OR "Byanodine".ti,ab OR "Cilamin".ti,ab OR "Cuprenil".ti,ab OR "Cuprimine".ti,ab OR "Cupripen".ti,ab OR "Depen".ti,ab OR "Distamin*".ti,ab OR "D-Penamine".ti,ab OR "Gerodyl".ti,ab OR "Kelatin*".ti,ab OR "Mercaptyl".ti,ab OR "Metalcaptase".ti,ab OR "Pendramine".ti,ab OR "Rhumantin".ti,ab OR "Sufortan*".ti,ab OR "Trisorcin".ti,ab OR "Trolovol".ti,ab OR exp *"Cyclophosphamide"/ OR "cyclophosph*".ti,ab OR "cytophosphan".ti,ab OR "Cytoxan".ti,ab OR "sendoxan".ti,ab OR "endoxan".ti,ab OR "neosar".ti,ab OR "nsc-26271".ti,ab OR "procytox".ti,ab OR "b-518".ti,ab OR "ifosfamide".ti,ab OR "isophosphamide".ti,ab OR "iphosphamide".ti,ab OR "isofosfamide".ti,ab OR "holoxan".ti,ab OR "nsc-109*".ti,ab OR "asta z 4942".ti,ab OR "cfx".ti,ab OR "phosphoramide mustard*".ti,ab OR exp *"Mycophenolic Acid"/ OR "mycophenolate".ti,ab OR "Arzip".ti,ab OR "Baxmune".ti,ab OR "CellCept".ti,ab OR "Cellmune".ti,ab OR "Celprot".ti,ab OR "Ceptolate".ti,ab OR "Imulate".ti,ab OR "Imuxgen".ti,ab OR "Lanfetil".ti,ab OR "Limfocept".ti,ab OR "Metocris".ti,ab OR "Micocept".ti,ab OR "MMF".ti,ab OR "Mofecept".ti,ab OR "Mofetyl".ti,ab OR "Mofilet".ti,ab OR "Mofimutral".ti,ab OR "Mometil".ti,ab OR "Mophecen".ti,ab OR "Munotras".ti,ab OR "Myaccord".ti,ab OR "Mycept".ti,ab OR "Myclausenor".ti,ab OR "Mycofenor".ti,ab OR "Mycolat".ti,ab OR "Mycoldosa".ti,ab OR "Mycophen".ti,ab OR "Myfenax Myfetil".ti,ab OR "Mygref".ti,ab OR "Myotec".ti,ab OR "Mysept".ti,ab OR "Presumin".ti,ab OR "Refrat".ti,ab OR "Renocell".ti,ab OR "Supresta".ti,ab OR "Tevacept".ti,ab OR "Trixin".ti,ab OR exp *"Chlorambucil"/ OR "chlorambucil".ti,ab OR "Amboclorin".ti,ab OR "Clokeran".ti,ab OR "Leukeran".ti,ab OR "Linfolysin".ti,ab OR "Lympholysin".ti,ab OR exp *"Minocycline"/ OR "minocyclin*".ti,ab OR "Acneclin".ti,ab OR "Akamin".ti,ab OR "Aknemin".ti,ab OR "Akne-Puren".ti,ab OR "Aknereduct".ti,ab OR "Aknin-Mino".ti,ab OR "Aknin-N".ti,ab OR "Aknoral".ti,ab OR "Aknosan".ti,ab OR "Apominolin".ti,ab OR "Arestinor".ti,ab OR "Auramin".ti,ab OR "Blemix".ti,ab OR "Borymycin".ti,ab OR "Cipancin".ti,ab OR "Cyclimycin".ti,ab OR "Dentomycin*".ti,ab OR "durakne".ti,ab OR "Dynacin".ti,ab OR "Enca".ti,ab OR "Icht-Oralor".ti,ab OR "Klinoc".ti,ab OR "Klinomycin".ti,ab OR "Klinotab".ti,ab OR "Lederderm".ti,ab OR "Logryx".ti,ab OR "Meibi".ti,ab OR "Mestacine".ti,ab OR "Micromycin".ti,ab OR "Minac 50".ti,ab OR "Minakne".ti,ab OR "Minaxen".ti,ab

OR "Mino-50".ti,ab OR "Minocin".ti,ab OR "Minoclin".ti,ab OR "Minodene".ti,ab OR "Minoderm".ti,ab OR "Minogalen".ti,ab OR "Minolis".ti,ab OR "Minomax".ti,ab OR "Minomycin".ti,ab OR "Minoplus".ti,ab OR "Minosil".ti,ab OR "Minostad".ti,ab OR "Minotab*".ti,ab OR "Minotekor".ti,ab OR "Minotrex".ti,ab OR "Minotyrol".ti,ab OR "Mino-Wolff".ti,ab OR "Minox".ti,ab OR "Mynocine".ti,ab OR "Myrac".ti,ab OR "Oracyclin".ti,ab OR "Parocline".ti,ab OR "Periocline".ti,ab OR "Peritrol".ti,ab OR "Ranmino".ti,ab OR "Romin".ti,ab OR "Seboclear".ti,ab OR "Sebomin".ti,ab OR "Sebren".ti,ab OR "Skid".ti,ab OR "Skinocyclin".ti,ab OR "Solodyn".ti,ab OR "Spicline".ti,ab OR "Triomin".ti,ab OR "Udima".ti,ab OR "Vectrin".ti,ab OR "Yelnac".ti,ab OR "Zacnan".ti,ab OR exp *"Pyrrole"/ OR "tofacitinib".ti,ab OR "Xeljanz".ti,ab OR "baricitinib".ti,ab OR "peficitinib".ti,ab OR "filgotinib".ti,ab OR "upadacitinib".ti,ab OR "fostamatinib".ti,ab OR exp *"Alefacept"/ OR "alefacept".ti,ab OR "Amevive".ti,ab OR exp *"efalizumab"/ OR "efalizumab".ti,ab OR "raptiva".ti,ab OR exp *"secukinumab"/ OR "secukinumab".ti,ab OR "cosentyx".ti,ab OR exp *"recombinant interleukin 10"/ OR "human recombinant IL 10".ti,ab OR "human recombinant Interleukin 10".ti,ab OR "human rIL 10".ti,ab OR "recombinant IL 10".ti,ab OR "recombinant Interleukin 10".ti,ab OR "rIL 10".ti,ab OR "rIL10".ti,ab OR exp *"bimekizumab"/ OR "bimekizumab".ti,ab OR exp *"deucravacitinib"/ OR "deucravacitinib".ti,ab OR exp *"sonelokimab"/ OR "sonelokimab".ti,ab OR "izokibep".ti,ab OR exp *"apremilast"/ OR "apremilast".ti,ab OR "otezla".ti,ab OR exp *"Glucocorticoid"/ OR "glucocorticoids".ti,ab OR "glucocorticoid".ti,ab OR "glucocorticoid*".ti,ab OR "alclometasone dipropionate".ti,ab OR "amcinonide".ti,ab OR "Beclomethasone".ti,ab OR "Betamethasone".ti,ab OR "betamethasone acetate".ti,ab OR "betamethasone benzoate".ti,ab OR "betamethasone dipropionate, betamethasone sodium phosphate drug combination".ti,ab OR "betamethasone sodium phosphate".ti,ab OR "Betamethasone Valerate".ti,ab OR "Budesonide".ti,ab OR "ciclesonide".ti,ab OR "Clobetasol".ti,ab OR "clobetasone butyrate".ti,ab OR "clocortolone".ti,ab OR "clocortolone pivalate".ti,ab OR "Desoximetasone".ti,ab OR "Dexamethasone".ti,ab OR "dexamethasone 21-phosphate".ti,ab OR "Dexamethasone Isonicotinate".ti,ab OR "dichlorisone acetate".ti,ab OR "diflorasone".ti,ab OR "Diflucortolone".ti,ab OR "difluprednate".ti,ab OR "drocinonide phosphate potassium".ti,ab OR "Flumethasone".ti,ab OR "flumethasone pivalate".ti,ab OR "Fluocinolone Acetonide".ti,ab OR "Fluocinonide".ti,ab OR "fluocortin butyl ester".ti,ab OR "Fluocortolone".ti,ab OR "Fluorometholone".ti,ab OR "fluperolone acetate".ti,ab OR "fluprednidene acetate".ti,ab OR "Fluprednisolone".ti,ab OR "Flurandrenolone".ti,ab OR "Fluticasone-Salmeterol Drug Combination".ti,ab OR "FX006".ti,ab OR "halometasone".ti,ab OR "medrysone".ti,ab OR "Melengestrol Acetate".ti,ab OR "Methylprednisolone".ti,ab OR "Methylprednisolone Hemisuccinate".ti,ab OR "Paramethasone".ti,ab OR "prednicarbate".ti,ab OR "Prednisolone".ti,ab OR "prednisolone hemisuccinate".ti,ab OR "prednisolone phosphate".ti,ab OR "Prednisone".ti,ab OR "rimexolone".ti,ab OR "terofenamate".ti,ab OR "Tobramycin, Dexamethasone Drug Combination".ti,ab OR "Triamcinolone".ti,ab OR "Triamcinolone Acetonide".ti,ab OR "triamcinolone benetonide".ti,ab OR exp *"nonsteroid antiinflammatory agent"/ OR "Nonsteroidal Anti Inflammatory".ti,ab OR "Nonsteroidal Antiinflammatory".ti,ab OR "Non-Steroidal Anti-Inflammatory ".ti,ab OR "Non-Steroidal Antiinflammatory ".ti,ab OR "NSAIDs".ti,ab OR "NSAID".ti,ab OR "((E)-(5)-(3,5-di-tert-butyl-4-hydroxybenzylidene)- 2-ethyl-1,2-isothiazolidine-1,1-dioxide)".ti,ab OR "1-((4,5-bis(4-methoxyphenyl)-2-thiazoyl)carbonyl)-4-methylpiperazine".ti,ab OR "1-((4-methylsulfonyl)phenyl)-3-trifluoromethyl-5-(4-fluorophenyl)pyrazole".ti,ab OR "1-(4-chlorobenzoyl)-3-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-methoxy-2-methyl-1H-indole".ti,ab OR "2-(4-(quinolin-2-yl-methoxy)phenyl)-2-cyclopentylacetic acid".ti,ab OR "2-(4-acetoxyphenyl)-2-chloro-N-methylethylamine".ti,ab OR "2-aminomethyl-4-t-butyl-6-iodophenol".ti,ab OR "2-diethylaminoethanol".ti,ab OR "2-hydroxymethyl-4-(5-(4-methoxyphenyl)-3-trifluoromethyl-1H-1-pyrazolyl)-1-benzenesulfonamide".ti,ab OR "4,5-Dihydro-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-3-amine".ti,ab OR "4-(5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide".ti,ab OR "4-bromo-2,7-dimethoxy-3H-phenothiazin-3-one".ti,ab OR "6-(4-

fluorophenyl)-2,3-dihydro-5-(4-pyridinyl)imidazo(2,1-b)thiazole".ti,ab OR "6-acetylaminocaproic acid".ti,ab OR "6-ethoxy-3-(4-methanesulfonylphenyl)-4-phenylpyran-2-one".ti,ab OR "7-methoxy-alpha-methyl-2-naphthaleneacetic acid".ti,ab OR "aceclofenac".ti,ab OR "acemetacin".ti,ab OR "acetaminophen, aspirin, caffeine drug combination".ti,ab OR "acetaminophen, butalbital, caffeine drug combination".ti,ab OR "acetaminophen, hydrocodone drug combination".ti,ab OR "acetosyringone".ti,ab OR "acetovanillone".ti,ab OR "acetylsalicylic acid lysinate".ti,ab OR "Adapalene".ti,ab OR "Adapalene, Benzoyl Peroxide Drug Combination".ti,ab OR "alclofenac".ti,ab OR "alminoprofen".ti,ab OR "alpha-pentyl-3-(2-quinolinylmethoxy)benzenemethanol".ti,ab OR "amiprilose".ti,ab OR "Ampyrone".ti,ab OR "amylase, phosphates, proteases drug combinations".ti,ab OR "andrographolide".ti,ab OR "anisodamine".ti,ab OR "anisodine".ti,ab OR "antiflammin P2".ti,ab OR "Antipyrine".ti,ab OR "Apazone".ti,ab OR "apremilast".ti,ab OR "Arteparon".ti,ab OR "Arthrotec".ti,ab OR "Aspirin".ti,ab OR "aspirin, aluminum hydroxide, magnesium hydroxide drug combination".ti,ab OR "aspirin, butalbital and caffeine drug combination".ti,ab OR "aspirin, meprobamate drug combination".ti,ab OR "atrinositol".ti,ab OR "azulene".ti,ab OR "baicalin".ti,ab OR "balsalazide".ti,ab OR "bendazac".ti,ab OR "bendazac lysine".ti,ab OR "benorilate".ti,ab OR "benoxaprofen".ti,ab OR "benzobarbital".ti,ab OR "berbamine".ti,ab OR "bevonium".ti,ab OR "BI 607812 BS".ti,ab OR "biphenylylacetic acid".ti,ab OR "boldine".ti,ab OR "boswellic acid".ti,ab OR "bromfenac".ti,ab OR "bucillamine".ti,ab OR "Bufexamac".ti,ab OR "bumadizone".ti,ab OR "butibufen".ti,ab OR "carbaspirin calcium".ti,ab OR "carprofen".ti,ab OR "caryophyllene".ti,ab OR "castanospermine".ti,ab OR "CDP 571".ti,ab OR "Celecoxib".ti,ab OR "cepharanthine".ti,ab OR "chloroquine diphosphate".ti,ab OR "choline magnesium trisalicylate".ti,ab OR "chrysarobin".ti,ab OR "Clonixin".ti,ab OR "CP 96345".ti,ab OR "Curcumin".ti,ab OR "CX 659S".ti,ab OR "dauricine".ti,ab OR "dexketoprofen trometamol".ti,ab OR "Diclofenac".ti,ab OR "diclofenac hydroxyethylpyrrolidine".ti,ab OR "difenpiramide".ti,ab OR "Diflunisal".ti,ab OR "dimephosphon".ti,ab OR "Dipyrone".ti,ab OR "diucifon".ti,ab OR "droxicam".ti,ab OR "dual inhibitor PTUPB".ti,ab OR "DuP 697".ti,ab OR "ebselen".ti,ab OR "ecallantide".ti,ab OR "eltenac".ti,ab OR "enfenamic acid".ti,ab OR "enkephalin-Leu, Ala(2)-Arg(6)-".ti,ab OR "Epirizole".ti,ab OR "Etanercept".ti,ab OR "ethenzamide".ti,ab OR "Ethonium".ti,ab OR "Etodolac".ti,ab OR "etofenamate".ti,ab OR "Etoricoxib".ti,ab OR "evening primrose oil".ti,ab OR "fenamic acid".ti,ab OR "fenbufen".ti,ab OR "fenclofenac".ti,ab OR "fenflumizole".ti,ab OR "Fenoprofen".ti,ab OR "fentiazac".ti,ab OR "fepradinol".ti,ab OR "Feprazone".ti,ab OR "ferulic acid".ti,ab OR "floctafenine".ti,ab OR "flosulide".ti,ab OR "flunixin".ti,ab OR "flunixin meglumine".ti,ab OR "flunoxaprofen".ti,ab OR "fluproquazone".ti,ab OR "Flurbiprofen".ti,ab OR "flurbiprofen axetil".ti,ab OR "FR 167653".ti,ab OR "FR 173657".ti,ab OR "glucametacin".ti,ab OR "guacetisal".ti,ab OR "helenalin".ti,ab OR "heliodermin".ti,ab OR "hemodes".ti,ab OR "higenamine".ti,ab OR "Ibuprofen".ti,ab OR "ibuproxam".ti,ab OR "icatibant".ti,ab OR "IH 764-3".ti,ab OR "imidazole-2-hydroxybenzoate".ti,ab OR "indobufen".ti,ab OR "Indomethacin".ti,ab OR "Indoprofen".ti,ab OR "iodoantipyrine".ti,ab OR "isoxicam".ti,ab OR "kebuzone".ti,ab OR "Ketoprofen".ti,ab OR "ketoprofen lysine".ti,ab OR "Ketorolac".ti,ab OR "Ketorolac Tromethamine".ti,ab OR "L 745337".ti,ab OR "L 778736".ti,ab OR "licofelone".ti,ab OR "lipoxin A4".ti,ab OR "lipoxin B4".ti,ab OR "lisofylline".ti,ab OR "lobenzarit".ti,ab OR "lonazolac".ti,ab OR "lornoxicam".ti,ab OR "loxoprofen".ti,ab OR "LQFM-091".ti,ab OR "lumiracoxib".ti,ab OR "Magnesium Salicylate".ti,ab OR "magnolol".ti,ab OR "manoalide".ti,ab OR "Masoprocol".ti,ab OR "Meclofenamic Acid".ti,ab OR "Mefenamic Acid".ti,ab OR "Meloxicam".ti,ab OR "Mesalamine".ti,ab OR "mirikizumab".ti,ab OR "mizoribine".ti,ab OR "mofebutazone".ti,ab OR "mofezolac".ti,ab OR "muricarpone B".ti,ab OR "N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide".ti,ab OR "N-(9H-(2,7-dimethylfluoren-9-ylmethoxy)carbonyl)leucine".ti,ab OR "N-succinimidyl-1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetate".ti,ab OR "NAAA inhibitor F215".ti,ab OR "Nabumetone".ti,ab OR "nafamostat".ti,ab OR "Naproxen".ti,ab OR "Nebacetin".ti,ab OR "nepafenac".ti,ab OR

"nifenazone".ti,ab OR "Niflumic Acid".ti,ab OR "nimesulide".ti,ab OR "nitroaspirin".ti,ab OR "Olopatadine Hydrochloride".ti,ab OR "olsalazine".ti,ab OR "olvanil".ti,ab OR "oren gedoku to".ti,ab OR "orgotein".ti,ab OR "Oxaprozin".ti,ab OR "Oxyphenbutazone".ti,ab OR "palmidrol".ti,ab OR "parecoxib".ti,ab OR "parthenolide".ti,ab OR "peoniflorin".ti,ab OR "phenidone".ti,ab OR "Phenylbutazone".ti,ab OR "pimecrolimus".ti,ab OR "pirfenidone".ti,ab OR "Piroxicam".ti,ab OR "piroxicam-beta-cyclodextrin".ti,ab OR "pirprofen".ti,ab OR "proglumetacin".ti,ab OR "propacetamol".ti,ab OR "propionylcarnitine".ti,ab OR "propyphenazone".ti,ab OR "proquazone".ti,ab OR "pyranoprofen".ti,ab OR "pyrazolone".ti,ab OR "pyrogenal".ti,ab OR "RNS60".ti,ab OR "rofecoxib".ti,ab OR "rosmarinic acid".ti,ab OR "Rumalon".ti,ab OR "saiko-keishi-to".ti,ab OR "saikosaponin D".ti,ab OR "salicin".ti,ab OR "salicylamide".ti,ab OR "Salicylates".ti,ab OR "salicylsalicylic acid".ti,ab OR "SB 203580".ti,ab OR "SC 299".ti,ab OR "SC 41930".ti,ab OR "SC 560".ti,ab OR "semapimod".ti,ab OR "seratrodast".ti,ab OR "serratiopeptidase".ti,ab OR "shikonin".ti,ab OR "sinapaldehyde".ti,ab OR "SK^ and F 105685".ti,ab OR "Sodium Salicylate".ti,ab OR "ST 679".ti,ab OR "Sul-121".ti,ab OR "Sulfasalazine".ti,ab OR "Sulindac".ti,ab OR "sulindac sulfide".ti,ab OR "sulindac sulfone".ti,ab OR "Suprofen".ti,ab OR "suxibuzone".ti,ab OR "tanshinone".ti,ab OR "taxifolin".ti,ab OR "tenidap".ti,ab OR "tenoxicam".ti,ab OR "tepoxalin".ti,ab OR "teriflunomide".ti,ab OR "tiaprofenic acid".ti,ab OR "tiaramide".ti,ab OR "tinoridine".ti,ab OR "tolfenamic acid".ti,ab OR "Tolmetin".ti,ab OR "tramadol, dexketoprofen drug combination".ti,ab OR "tranilast".ti,ab OR "tribenoside".ti,ab OR "ursolic acid".ti,ab OR "valdecoxib".ti,ab OR "zileuton".ti,ab OR "zomepirac".ti,ab) AND (exp *"drug safety"/ OR "safe".ti,ab OR "safety".ti,ab OR exp *"side effect"/ OR "side effect".ti,ab OR "side effects".ti,ab OR exp *"Adverse Drug Reaction"/ OR (("adverse".ti,ab OR "undesirable".ti,ab OR "harms".ti,ab OR "harm".ti,ab OR "serious".ti,ab OR "toxic".ti,ab OR "risk".ti,ab OR "risks".ti,ab) ADJ4 ("effect".ti,ab OR "effects".ti,ab OR "reaction".ti,ab OR "reactions".ti,ab OR "events".ti,ab OR "event".ti,ab OR "outcome*".ti,ab)) OR exp *"postmarketing surveillance"/ OR exp *"pharmacovigilance"/ OR "phase 4 clinical trial"/ OR "phase 3 clinical trial"/ OR exp *"intoxication"/ OR exp *"drug dependence"/ OR exp *"drug induced disease"/ OR exp *"drug monitoring"/ OR eexp *"drug hypersensitivity"/ OR "toxicity".ti,ab OR "complication*".ti,ab OR "noxious".ti,ab OR "tolerability".ti,ab OR exp *"Thromboembolism"/ OR "thromboembolism".ti,ab OR "thrombo embolism".ti,ab OR "thromboembol*".ti,ab OR "thrombo embol*".ti,ab OR "thromboembolism".ti,ab OR exp *"Lung embolism"/ OR "pulmonary embolism".ti,ab OR exp *"Infection"/ OR "infection".ti,ab OR "infections".ti,ab OR exp *"Neoplasm"/ OR "cancer".ti,ab OR "lymphoma".ti,ab OR "lymphomas".ti,ab OR "leukemia".ti,ab OR "leukaemia".ti,ab OR "malignancies".ti,ab OR "malignancy".ti,ab OR "melanoma".ti,ab OR "melanomas".ti,ab OR "solid tumour".ti,ab OR "solid tumours".ti,ab OR "solid tumor".ti,ab OR "solid tumors".ti,ab OR exp *"Death"/ OR "Death".ti,ab OR "Deaths".ti,ab OR exp *"Mortality"/ OR "Mortality".ti,ab OR "Tuberculosis".ti,ab OR "Herpes Zoster"/ OR "Herpes Zoster".ti,ab OR "COVID-19".ti,ab OR "COVID19".ti,ab OR "COVID".ti,ab OR "COVID-19"/ OR "SARS-CoV-2".ti,ab OR "SARSCoV2".ti,ab OR "sars-cov-2"/ OR "Severe Acute Respiratory Syndrome Coronavirus 2".ti,ab OR "NCOV".ti,ab OR "2019 NCOV".ti,ab OR "SARS-CoV2".ti,ab OR "SARSCoV2".ti,ab OR "SARSCoV 2".ti,ab OR "SARSCoV".ti,ab OR "SARSCoV*".ti,ab OR "SARS CoV".ti,ab OR "SARS CoV*".ti,ab OR "covid".ti,ab OR "longCOVID".ti,ab OR "Congestive heart failure".ti,ab OR exp *"heart failure"/ OR "heart failure".ti,ab OR exp *"Coronary Artery Disease"/ OR "Coronary Disease".ti,ab OR "Coronary Diseases".ti,ab OR "Coronary Heart Disease".ti,ab OR "Coronary Heart Diseases".ti,ab OR exp *"Ischemic Heart Disease"/ OR "Myocardial Ischemia".ti,ab OR "Myocardial Ischaemia".ti,ab OR "Myocardial Infarction".ti,ab OR "Angina".ti,ab OR exp *"Cerebrovascular Accident"/ OR "stroke".ti,ab OR "Cerebrovascular Accident".ti,ab OR "Cerebrovascular Accidents".ti,ab OR exp *"Injection Site Reaction"/ OR "Injection Site Adverse Event".ti,ab OR "Injection Site Adverse Events".ti,ab OR "Injection Site Adverse Reaction".ti,ab OR "Injection Site Adverse Reactions".ti,ab OR "Injection Site Event".ti,ab OR "Injection Site Events".ti,ab OR "Injection Site Reaction".ti,ab OR

"Injection Site Reactions".ti,ab OR "Infusion Site Adverse Event".ti,ab OR "Infusion Site Adverse Events".ti,ab OR "Infusion Site Adverse Reaction".ti,ab OR "Infusion Site Adverse Reactions".ti,ab OR "Infusion Site Event".ti,ab OR "Infusion Site Events".ti,ab OR "Infusion Site Reaction".ti,ab OR "Infusion Site Reactions".ti,ab OR exp *"Lipid Level"/ OR "Lipid levels".ti,ab OR "lipid level".ti,ab OR exp *"Kidney Function"/ OR "Renal function".ti,ab OR "Kidney function".ti,ab OR exp *"creatinine blood level"/ OR "creatinine levels".ti,ab OR "creatinine level".ti,ab OR "Hepatic effects".ti,ab OR "Hepatic effect".ti,ab OR exp *"Liver toxicity"/ OR "Liver Disease"/si OR exp *"aminotransferase"/ OR exp *"Bilirubin"/ OR "transaminases elevation".ti,ab OR "transaminase elevation".ti,ab OR "transaminases level".ti,ab OR "transaminase level".ti,ab OR "transaminases levels".ti,ab OR "transaminase levels".ti,ab OR exp *"bilirubin blood level"/ OR "bilirubin elevation".ti,ab OR "bilirubin level".ti,ab OR "bilirubin levels".ti,ab OR "Haematological abnormalities".ti,ab OR "Haematological abnormality".ti,ab OR "Haematologic abnormalities".ti,ab OR "Haematologic abnormality".ti,ab OR "Hematological abnormalities".ti,ab OR "Hematological abnormality".ti,ab OR "Hematologic abnormalities".ti,ab OR "Hematologic abnormality".ti,ab OR "Neutropenia"/ OR "neutropenia".ti,ab OR exp *"Hematologic Disease"/si OR exp *"Gastrointestinal Disease"/si OR "Gastro-intestinal effects".ti,ab OR "Gastro-intestinal effect".ti,ab OR "Gastrointestinal effects".ti,ab OR "Gastrointestinal effect".ti,ab OR exp *"Demyelinating Disease"/ OR "Demyelinating Diseases".ti,ab OR "Demyelinating disease".ti,ab OR exp *"Autoimmune Disease"/ OR "Autoimmune Diseases".ti,ab OR "Autoimmune Disease".ti,ab OR "Auto immune Diseases".ti,ab OR "Auto immune Disease".ti,ab OR exp *"Antinuclear Antibody"/ OR "anti-nuclear antibodies".ti,ab OR "anti-nuclear antibody".ti,ab OR "antinuclear antibodies".ti,ab OR "antinuclear antibody".ti,ab OR exp *"double stranded DNA antibody"/ OR "anti-dsDNA".ti,ab OR exp *"Drug Antibody"/ OR "anti-drug antibodies".ti,ab OR "anti-drug antibody".ti,ab OR "antidrug antibodies".ti,ab OR "antidrug antibody".ti,ab OR exp *"chimeric antibody"/ OR "anti-chimeric antibodies".ti,ab OR "anti-chimeric antibody".ti,ab OR "antichimeric antibodies".ti,ab OR "antichimeric antibody".ti,ab OR exp *"Fertility"/ OR exp *"Infertility"/ OR exp *"Pregnancy"/ OR exp *"Pregnancy Complication"/ OR "Fertility".ti,ab OR "Infertility".ti,ab OR "Pregnancy".ti,ab OR exp *"Induced Abortion"/ OR "induced abortion".ti,ab OR "elective abortion".ti,ab OR exp *"Spontaneous Abortion"/ OR "Spontaneous Abortion".ti,ab OR "miscarriage".ti,ab OR "abortion".ti,ab OR "abortions".ti,ab OR "medical termination".ti,ab OR exp *"Prematurity"/ OR "premature birth".ti,ab OR "preterm birth".ti,ab OR "premature births".ti,ab OR "preterm births".ti,ab OR "premature childbirth".ti,ab OR "preterm childbirth".ti,ab OR "premature childbirths".ti,ab OR "preterm childbirths".ti,ab OR "premature child birth".ti,ab OR "preterm child birth".ti,ab OR "premature child births".ti,ab OR "preterm child births".ti,ab OR exp *"Small for Date Infant"/ OR "small for gestational age".ti,ab OR exp *"Preeclampsia"/ OR "Pre-Eclampsia".ti,ab OR "preeclampsia".ti,ab OR exp *"Eclampsia"/ OR "eclampsia".ti,ab OR exp *"Cesarean Section"/ OR "Cesarean Section".ti,ab OR "Caesarean Section".ti,ab OR "c-section".ti,ab OR exp *"teratogenicity"/ OR exp * "Teratogenesis"/ OR "Teratogenesis".ti,ab OR "Teratogenicity".ti,ab OR "Teratogen*".ti,ab) AND (exp "Cohort Analysis"/ OR "Cohort Study".mp OR "Cohort".mp OR "Cohorts".mp OR "Follow Up"/ OR "Follow-Up Studies".mp OR exp "Longitudinal Study"/ OR "Longitudinal Studies".mp OR exp "Prospective Study"/ OR "Prospective Studies".mp OR exp "Retrospective Study"/ OR "Retrospective Studies".mp OR "Follow-Up Study".mp OR "Longitudinal Study".mp OR "Prospective Study".mp OR "Retrospective Study".mp OR "Follow-Up".mp OR "Longitudinal".mp OR "Prospective".mp OR "Retrospective".mp OR "FollowUp".mp OR "Longitudinal*".mp OR "Prospective*".mp OR "Retrospective*".mp OR exp "Case Control Study"/ OR "Case-Control".mp OR "Case-Controlled".mp OR "Case-Controls".mp OR "Case-Control*".mp OR exp "Register"/ OR "Registry".mp OR "Registries".mp OR "Register".mp OR "Registers".mp OR exp "systematic review"/ OR "Long term extensions".mp OR "Long term extensions".mp OR "LTE".mp OR "LTEs".mp) NOT (exp "animals"/ NOT exp "humans"/) AND 2018:2023.(sa_year))

Text S1.6: Safety: Cochrane CENTRAL search strategy

(("Psoriatic Arthritis" OR "Psoriatic Arthritis" OR "Arthritic Psoriasis" OR "Psoriatic Arthritis" OR "Psoriasis Arthropathica" OR "Psoriatic Arthropathy" OR "Psoriatic Arthropathies"):ti,ab,kw NOT ((exp "Infant" OR "infant" OR "infants" OR exp "Child" OR "child" OR "children" OR "pediatric" OR "paediatric" OR "pediatrics" OR "paediatrics" OR exp "Adolescent" OR "adolescent" OR "adolescents") NOT (exp "Adult" OR "adult" OR "adults" OR "middle aged" OR "elderly")):ti AND ("biological therapy" OR "monoclonal antibody" OR "monokine" OR "interleukin 1 receptor" OR "interleukin 1 receptor accessory protein" OR "interleukin 1 receptor like 1 protein" OR "interleukin 1 receptor type I" OR "interleukin 1 receptor type II" OR "interleukin 6 receptor" OR "interleukin 6 receptor alpha" OR "immunoglobulin g" OR "antibody conjugate" OR "macrogol derivative" OR "immunoglobulin F(ab) fragment" OR "T lymphocyte" OR "biologic*" OR "bDMARD" OR "biosimilar" OR "abatacept" OR "actemra" OR "adalimumab" OR "anakinra" OR "Arzerra" OR "Brodalumab" OR "Certolizumab" OR "cimzia" OR "Clazakizumab" OR "enbrel" OR "Etanercept" OR "Golimumab" OR "Guselkumab" OR "humira" OR "infliximab" OR "Ixekizumab" OR "kineret" OR "mabthera" OR "mavrilimumab" OR "Ocrelizumab" OR "Ofatumumab" OR "Olokizumab" OR "orencia" OR "Pateclizumab" OR "remicade" OR "rituxan" OR "rituximab" OR "RoActemra" OR "Sarilumab" OR "Siliq" OR "simponi" OR "Sirukumab" OR "Stelara" OR "Tabalumab" OR "Taltz" OR "Tocilizumab" OR "trudexa" OR "Ustekinumab" OR "bDMARD*" OR "biosimilar*" OR "abatacept*" OR "actemra*" OR "adalimumab*" OR "anakinra*" OR "Arzerra*" OR "Brodalumab*" OR "Certolizumab*" OR "cimzia*" OR "Clazakizumab*" OR "enbrel*" OR "Etanercept*" OR "Golimumab*" OR "Guselkumab*" OR "humira*" OR "infliximab*" OR "Ixekizumab*" OR "kineret*" OR "mabthera*" OR "mavrilimumab*" OR "Ocrelizumab*" OR "Ofatumumab*" OR "Olokizumab*" OR "orencia*" OR "Pateclizumab*" OR "remicade*" OR "rituxan*" OR "rituximab*" OR "RoActemra*" OR "Sarilumab*" OR "Siliq*" OR "simponi*" OR "Sirukumab*" OR "Stelara*" OR "Tabalumab*" OR "Taltz*" OR "Tocilizumab*" OR "trudexa*" OR "Ustekinumab*" OR "Antirheumatic Agent" OR "Antirheumatic*" OR "dmard*" OR "sdmard*" OR "Methotrexate" OR "Methotrexate" OR "Abitrexate" OR "ametopterin*" OR "amethopterin*" OR "Abitrexate" OR "A Metopterin*" OR "A Methopterin*" OR "Antifolan" OR "Emtexate" OR "Emthexate" OR "Enthexate" OR "Farmitrexate" OR "Folex" OR "Ledertrexate" OR "Methoblastin" OR "Methohexate" OR "Methotrate" OR "Methylaminopterin" OR "Metotrexat*" OR "mtx" OR "Novatrex" OR "Rheumatrex" OR "Isoxazole" OR "isoxazole*" OR "leflunomide*" OR "Afiancen" OR "Arabloc" OR "Arava" OR "Artrilab" OR "Artrimod" OR "Filartros" OR "Inmunoartro" OR "Lefluar" OR "Leflucross" OR "Lefno" OR "Lefra" OR "Lefumide" OR "Lisifen" OR "Molagar" OR "Repso" OR "Rumalef" OR "salazosulfapyridine" OR "sulfasalazine" OR "Salazosulfapyridine" OR "sulfasalazine" OR "Sulfosalazine" OR "Sulfasalzine" OR "Salazopyridin*" OR "asulfidine" OR "azulfdine" OR "Hydroxychloroquine" OR "Hydroxychloro*" OR "Axokineor" OR "Dolquine" OR "Ercoquin" OR "Evoquin" OR "HCQS" OR "HQT" OR "Hydrocad" OR "Hydroquin" OR "Ilinol" OR "Immard" OR "Metirel" OR "Narbon" OR "Oxcq" OR "Oxiklorin" OR "Oxy Q" OR "Plaquen*" OR "Polirreuminor" OR "Quensyl" OR "Reuquinol" OR "Gold Derivative" OR "Organogold Compound" OR "Gold" OR "gold" OR "Chloroquine" OR "chloroquine*" OR "aralen" OR "arechine" OR "arequin" OR "chingamin" OR "chlorochin" OR "khingamin" OR "nivaquine" OR "oxychloroquine" OR "oxychlorochin" OR "plaquinol" OR "plaquinil" OR "quensy" OR "anoclor" OR "arthrabas" OR "avloclor" OR "cidanchin" OR "clopirim" OR "collagenan" OR "daraclor" OR "daramal" OR "dichinalex" OR "difosquin" OR "diroquine" OR "genocin" OR "heliopar" OR "klorokin" OR "malarex" OR "malaviron" OR "mirquin" OR "nivaquine" OR "novo chloroquine" OR "novochloroquine" OR "paluken" OR "palux" OR "pharmaquinine" OR "plasmoquine" OR "promal" OR "p roquine" OR "resoquin*" OR "savarine" OR "syncoquin" OR "weimerquin" OR "Azathioprine" OR "azathioprine" OR "Aseroprim" OR "Aseroprin" OR "Azaallen" OR "Azadus" OR "Azafalk" OR "Azafor" OR "Azafrine"

OR "Azaglax" OR "Azahexal" OR "Azamun*" OR "Azamedac" OR "Azap" OR "Azapin*" OR "Azapress" OR "Aza Q" OR "Azarek" OR "Azasan" OR "Azathiodura" OR "Azathiodura" OR "Azathioregio" OR "Azatrilem" OR "Azimune" OR "Azopin*" OR "Azoran" OR "Berkaprine" OR "Colinsan" OR "Glaxoprin" OR "Immunoprin" OR "Imuger" OR "Imunen" OR "Imuprin*" OR "Imuran" OR "Imureor Imuzat" OR "Oprisine" OR "Satedon" OR "Thioprine" OR "Tiosalprin" OR "Transimune" OR "Zaprine" OR "Zytrim" OR "Cyclosporine" OR "ciclosporin*" OR "cyclosporin*" OR "neoral" OR "gengraf" OR "restasis" OR "sandimmun*" OR "sangcya" OR "Penicillamine" OR "Penicillamine" OR "Adalkenor" OR "Artamin" OR "Atamir" OR "Byanodine" OR "Cilamin" OR "Cuprenil" OR "Cuprimine" OR "Cupripen" OR "Depen" OR "Distamin*" OR "D Penamine" OR "Gerodyl" OR "Kelatin*" OR "Mercaptyl" OR "Metalcaptase" OR "Pendramine" OR "Rhumantin" OR "Sufortan*" OR "Trisorcin" OR "Trolovol" OR "Cyclophosphamide" OR "cyclophosph*" OR "cytophosphan" OR "Cytoxan" OR "sendoxan" OR "endoxan" OR "neosar" OR "nsc 26271" OR "procytox" OR "b 518" OR "ifosfamide" OR "isophosphamide" OR "iphosphamide" OR "isofosfamide" OR "holoxan" OR "nsc 109*" OR "asta z 4942" OR "cfx" OR "phosphoramide mustard*" OR "Mycophenolic Acid" OR "mycophenolate" OR "Arzip" OR "Baxmune" OR "CellCept" OR "Cellmune" OR "Celprot" OR "Ceptolate" OR "Imulate" OR "Imuxgen" OR "Lanfetil" OR "Limfocept" OR "Metocris" OR "Micocept" OR "MMF" OR "Mofecept" OR "Mofetyl" OR "Mofilet" OR "Mofimutral" OR "Mometil" OR "Mophecen" OR "Munotras" OR "Myaccord" OR "Mycept" OR "Myclausenor" OR "Mycofenor" OR "Mycolat" OR "Mycoldosa" OR "Mycophen" OR "Myfenax Myfetil" OR "Mygref" OR "Myotec" OR "Mysept" OR "Presumin" OR "Refrat" OR "Renocell" OR "Supresta" OR "Tevacept" OR "Trixin" OR "Chlorambucil" OR "chlorambucil" OR "Amboclorin" OR "Clokeran" OR "Leukeran" OR "Linfolysin" OR "Lympholysin" OR "Minocycline" OR "minocyclin*" OR "Acneclin" OR "Akamin" OR "Aknemin" OR "Akne Puren" OR "Aknereduct" OR "Aknin Mino" OR "Aknin N" OR "Aknoral" OR "Aknosan" OR "Apominolin" OR "Arestinor" OR "Auramin" OR "Blemix" OR "Borymycin" OR "Cipancin" OR "Cyclimycin" OR "Dentomycin*" OR "durakne" OR "Dynacin" OR "Enca" OR "Icht Oralor" OR "Klinoc" OR "Klinomycin" OR "Klinotab" OR "Lederderm" OR "Logryx" OR "Meibi" OR "Mestacine" OR "Micromycin" OR "Minac 50" OR "Minakne" OR "Minaxen" OR "Mino 50" OR "Minocin" OR "Minoclin" OR "Minodene" OR "Minoderm" OR "Minogalen" OR "Minolis" OR "Minomax" OR "Minomycin" OR "Minoplus" OR "Minosil" OR "Minostad" OR "Minotab*" OR "Minotekor" OR "Minotrex" OR "Minotyrol" OR "Mino Wolff" OR "Minox" OR "Mynocine" OR "Myrac" OR "Oracyclin" OR "Parocline" OR "Periocline" OR "Peritrol" OR "Ranmino" OR "Romin" OR "Seboclear" OR "Sebomin" OR "Sebren" OR "Skid" OR "Skinocyclin" OR "Solodyn" OR "Spicline" OR "Triomin" OR "Udima" OR "Vectrin" OR "Yelnac" OR "Zacnan" OR "Pyrrole" OR "tofacitinib" OR "Xeljanz" OR "baricitinib" OR "peficitinib" OR "filgotinib" OR "upadacitinib" OR "fostamatinib" OR "Alefacept" OR "alefacept" OR "Amevive" OR "efalizumab" OR "efalizumab" OR "raptiva" OR "secukinumab" OR "secukinumab" OR "cosentyx" OR "recombinant interleukin 10" OR "human recombinant IL 10" OR "human recombinant Interleukin 10" OR "human rIL 10" OR "recombinant IL 10" OR "recombinant Interleukin 10" OR "rIL 10" OR "rIL10" OR "bimekizumab" OR "bimekizumab" OR "deucravacitinib" OR "deucravacitinib" OR "sonelokimab" OR "sonelokimab" OR "izokibep" OR "apremilast" OR "apremilast" OR "otezla" OR "Glucocorticoid" OR "glucocorticoids" OR "glucocorticoid" OR "glucocorticoid*" OR "alclometasone dipropionate" OR "amcinonide" OR "Beclomethasone" OR "Betamethasone" OR "betamethasone acetate" OR "betamethasone benzoate" OR "betamethasone dipropionate, betamethasone sodium phosphate drug combination" OR "betamethasone sodium phosphate" OR "Betamethasone Valerate" OR "Budesonide" OR "ciclesonide" OR "Clobetasol" OR "clobetasone butyrate" OR "clocortolone" OR "clocortolone pivalate" OR "Desoximetasone" OR "Dexamethasone" OR "dexamethasone 21 phosphate" OR "Dexamethasone Isonicotinate" OR "dichlorisone acetate" OR "diflorasone" OR "Diflucortolone" OR "difluprednate" OR "drocinonide phosphate potassium" OR "Flumethasone" OR "flumethasone pivalate" OR "Fluocinolone Acetonide" OR "Fluocinonide" OR "fluocortin butyl ester" OR "Fluocortolone" OR "Fluorometholone" OR "fluperolone acetate" OR "fluprednidene acetate" OR

"Fluprednisolone" OR "Flurandrenolone" OR "Fluticasone Salmeterol Drug Combination" OR "FX006" OR "halometasone" OR "medrysone" OR "Melengestrol Acetate" OR "Methylprednisolone" OR "Methylprednisolone Hemisuccinate" OR "Paramethasone" OR "prednicarbate" OR "Prednisolone" OR "prednisolone hemisuccinate" OR "prednisolone phosphate" OR "Prednisone" OR "rimexolone" OR "terofenamate" OR "Tobramycin, Dexamethasone Drug Combination" OR "Triamcinolone" OR "Triamcinolone Acetonide" OR "triamcinolone benetonide" OR "nonsteroid antiinflammatory agent" OR "Nonsteroidal Anti Inflammatory" OR "Nonsteroidal Antiinflammatory" OR "Non Steroidal Anti Inflammatory " OR "Non Steroidal Antiinflammatory " OR "NSAIDs" OR "NSAID" OR "((E) (5) (3,5 di tert butyl 4 hydroxybenzylidene) 2 ethyl 1,2 isothiazolidine 1,1 dioxide)" OR "1 ((4,5 bis(4 methoxyphenyl) 2 thiazoyl)carbonyl) 4 methylpiperazine" OR "1 ((4 methylsulfonyl)phenyl) 3 trifluoromethyl 5 (4 fluorophenyl)pyrazole" OR "1 (4 chlorobenzoyl) 3 (2 (1H imidazol 1 yl) 2 oxoethyl) 5 methoxy 2 methyl 1H indole" OR "2 (4 (quinolin 2 yl methoxy)phenyl) 2 cyclopentylacetic acid" OR "2 (4 acetoxyphenyl) 2 chloro N methylethylamine" OR "2 aminomethyl 4 t butyl 6 iodophenol" OR "2 diethylaminoethanol" OR "2 hydroxymethyl 4 (5 (4 methoxyphenyl) 3 trifluoromethyl 1H 1 pyrazolyl) 1 benzenesulfonamide" OR "4,5 Dihydro 1 (3 (trifluoromethyl)phenyl) 1H pyrazol 3 amine" OR "4 (5 (4 chlorophenyl) 3 (trifluoromethyl) 1H pyrazol 1 yl)benzenesulfonamide" OR "4 bromo 2,7 dimethoxy 3H phenothiazin 3 one" OR "6 (4 fluorophenyl) 2,3 dihydro 5 (4 pyridinyl)imidazo(2,1 b)thiazole" OR "6 acetylaminocaproic acid" OR "6 ethoxy 3 (4 methanesulfonylphenyl) 4 phenylpyran 2 one" OR "7 methoxy alpha methyl 2 naphthaleneacetic acid" OR "aceclofenac" OR "acemetacin" OR "acetaminophen, aspirin, caffeine drug combination" OR "acetaminophen, butalbital, caffeine drug combination" OR "acetaminophen, hydrocodone drug combination" OR "acetosyringone" OR "acetovanillone" OR "acetylsalicylic acid lysinate" OR "Adapalene" OR "Adapalene, Benzoyl Peroxide Drug Combination" OR "alclofenac" OR "alminoprofen" OR "alpha pentyl 3 (2 quinolinylmethoxy)benzenemethanol" OR "amiprilose" OR "Ampyrone" OR "amylase, phosphates, proteases drug combinations" OR "andrographolide" OR "anisodamine" OR "anisodine" OR "antiflammin P2" OR "Antipyrine" OR "Apazone" OR "apremilast" OR "Arteparon" OR "Arthrotec" OR "Aspirin" OR "aspirin, aluminum hydroxide, magnesium hydroxide drug combination" OR "aspirin, butalbital and caffeine drug combination" OR "aspirin, meprobamate drug combination" OR "atrinositol" OR "azulene" OR "baicalin" OR "balsalazide" OR "bendazac" OR "bendazac lysine" OR "benorilate" OR "benoxaprofen" OR "benzobarbital" OR "berbamine" OR "bevonium" OR "BI 607812 BS" OR "biphenylylacetic acid" OR "boldine" OR "boswellic acid" OR "bromfenac" OR "bucillamine" OR "Bufexamac" OR "bumadizone" OR "butibufen" OR "carbaspirin calcium" OR "carprofen" OR "caryophyllene" OR "castanospermine" OR "CDP 571" OR "Celecoxib" OR "cepharanthine" OR "chloroquine diphosphate" OR "choline magnesium trisalicylate" OR "chrysarobin" OR "Clonixin" OR "CP 96345" OR "Curcumin" OR "CX 659S" OR "dauricine" OR "dexketoprofen trometamol" OR "Diclofenac" OR "diclofenac hydroxyethylpyrrolidine" OR "difenpiramide" OR "Diflunisal" OR "dimephosphon" OR "Dipyrone" OR "diucifon" OR "droxicam" OR "dual inhibitor PTUPB" OR "DuP 697" OR "ebselen" OR "ecallantide" OR "eltenac" OR "enfenamic acid" OR "enkephalin Leu, Ala(2) Arg(6) " OR "Epirizole" OR "Etanercept" OR "ethenzamide" OR "Ethonium" OR "Etodolac" OR "etofenamate" OR "Etoricoxib" OR "evening primrose oil" OR "fenamic acid" OR "fenbufen" OR "fenclofenac" OR "fenflumizole" OR "Fenoprofen" OR "fentiazac" OR "fepradinol" OR "Feprazone" OR "ferulic acid" OR "floctafenine" OR "flosulide" OR "flunixin" OR "flunixin meglumine" OR "flunoxaprofen" OR "fluproquazone" OR "Flurbiprofen" OR "flurbiprofen axetil" OR "FR 167653" OR "FR 173657" OR "glucametacin" OR "guacetisal" OR "helenalin" OR "heliodermin" OR "hemodes" OR "higenamine" OR "Ibuprofen" OR "ibuproxam" OR "icatibant" OR "IH 764 3" OR "imidazole 2 hydroxybenzoate" OR "indobufen" OR "Indomethacin" OR "Indoprofen" OR "iodoantipyrine" OR "isoxicam" OR "kebuzone" OR "Ketoprofen" OR "ketoprofen lysine" OR "Ketorolac" OR "Ketorolac Tromethamine" OR "L 745337" OR "L 778736" OR "licofelone" OR "lipoxin A4" OR "lipoxin B4" OR "lisofylline" OR "lobenzarit" OR "lonazolac" OR "lornoxicam" OR "loxoprofen"

OR "LQFM 091" OR "lumiracoxib" OR "Magnesium Salicylate" OR "magnolol" OR "manoalide" OR "Masoprocol" OR "Meclofenamic Acid" OR "Mefenamic Acid" OR "Meloxicam" OR "Mesalamine" OR "mirikizumab" OR "mizoribine" OR "mofebutazone" OR "mofezolac" OR "muricarpone B" OR "N (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide" OR "N (9H (2,7 dimethylfluoren 9 ylmethoxy)carbonyl)leucine" OR "N succinimidyl 1 (4 chlorobenzoyl) 5 methoxy 2 methyl 1H indole 3 acetate" OR "NAAA inhibitor F215" OR "Nabumetone" OR "nafamostat" OR "Naproxen" OR "Nebacetin" OR "nepafenac" OR "nifenazone" OR "Niflumic Acid" OR "nimesulide" OR "nitroaspirin" OR "Olopatadine Hydrochloride" OR "olsalazine" OR "olvanil" OR "oren gedoku to" OR "orgotein" OR "Oxaprozin" OR "Oxyphenbutazone" OR "palmidrol" OR "parecoxib" OR "parthenolide" OR "peoniflorin" OR "phenidone" OR "Phenylbutazone" OR "pimecrolimus" OR "pirfenidone" OR "Piroxicam" OR "piroxicam beta cyclodextrin" OR "pirprofen" OR "proglumetacin" OR "propacetamol" OR "propionylcarnitine" OR "propyphenazone" OR "proquazone" OR "pyranoprofen" OR "pyrazolone" OR "pyrogenal" OR "RNS60" OR "rofecoxib" OR "rosmarinic acid" OR "Rumalon" OR "saiko keishi to" OR "saikosaponin D" OR "salicin" OR "salicylamide" OR "Salicylates" OR "salicylsalicylic acid" OR "SB 203580" OR "SC 299" OR "SC 41930" OR "SC 560" OR "semapimod" OR "seratrodast" OR "serratiopeptidase" OR "shikonin" OR "sinapaldehyde" OR "SK^ and F 105685" OR "Sodium Salicylate" OR "ST 679" OR "Sul 121" OR "Sulfasalazine" OR "Sulindac" OR "sulindac sulfide" OR "sulindac sulfone" OR "Suprofen" OR "suxibuzone" OR "tanshinone" OR "taxifolin" OR "tenidap" OR "tenoxicam" OR "tepoxalin" OR "teriflunomide" OR "tiaprofenic acid" OR "tiaramide" OR "tinoridine" OR "tolfenamic acid" OR "Tolmetin" OR "tramadol, dexketoprofen drug combination" OR "tranilast" OR "tribenoside" OR "ursolic acid" OR "valdecoxib" OR "zileuton" OR "zomepirac"):ti,ab,kw AND ("drug safety" OR "safe" OR "safety" OR "side effect" OR "side effect" OR "side effects" OR "Adverse Drug Reaction" OR (("adverse" OR "undesirable" OR "harms" OR "harm" OR "serious" OR "toxic" OR "risk" OR "risks") NEAR/4 ("effect" OR "effects" OR "reaction" OR "reactions" OR "events" OR "event" OR "outcome*")) OR "postmarketing surveillance" OR "pharmacovigilance" OR "phase 4 clinical trial" OR "phase 3 clinical trial" OR "intoxication" OR "drug dependence" OR "drug induced disease" OR "drug monitoring" OR e"drug hypersensitivity" OR "toxicity" OR "complication*" OR "noxious" OR "tolerability" OR "Thromboembolism" OR "thromboembolism" OR "thrombo embolism" OR "thromboembol*" OR "thrombo embol*" OR "thromboembolism" OR "Lung embolism" OR "pulmonary embolism" OR "Infection" OR "infection" OR "infections" OR "Neoplasm" OR "cancer" OR "lymphoma" OR "lymphomas" OR "leukemia" OR "leukaemia" OR "malignancies" OR "malignancy" OR "melanoma" OR "melanomas" OR "solid tumour" OR "solid tumours" OR "solid tumor" OR "solid tumors" OR "Death" OR "Death" OR "Deaths" OR "Mortality" OR "Mortality" OR "Tuberculosis" OR "Herpes Zoster" OR "Herpes Zoster" OR "COVID 19" OR "COVID19" OR "COVID" OR "COVID 19" OR "SARS CoV 2" OR "SARSCoV2" OR "sars cov 2" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "NCOV" OR "2019 NCOV" OR "SARS CoV2" OR "SARSCoV2" OR "SARSCoV 2" OR "SARSCoV" OR "SARSCoV*" OR "SARS CoV" OR "SARS CoV*" OR "covid" OR "longCOVID" OR "Congestive heart failure" OR "heart failure" OR "heart failure" OR "Coronary Artery Disease" OR "Coronary Disease" OR "Coronary Diseases" OR "Coronary Heart Disease" OR "Coronary Heart Diseases" OR "Ischemic Heart Disease" OR "Myocardial Ischemia" OR "Myocardial Ischaemia" OR "Myocardial Infarction" OR "Angina" OR "Cerebrovascular Accident" OR "stroke" OR "Cerebrovascular Accident" OR "Cerebrovascular Accidents" OR "Injection Site Reaction" OR "Injection Site Adverse Event" OR "Injection Site Adverse Events" OR "Injection Site Adverse Reaction" OR "Injection Site Adverse Reactions" OR "Injection Site Event" OR "Injection Site Events" OR "Injection Site Reaction" OR "Injection Site Reactions" OR "Infusion Site Adverse Event" OR "Infusion Site Adverse Events" OR "Infusion Site Adverse Reaction" OR "Infusion Site Adverse Reactions" OR "Infusion Site Event" OR "Infusion Site Events" OR "Infusion Site Reaction" OR "Infusion Site Reactions" OR "Lipid Level" OR "Lipid levels" OR "lipid level" OR "Kidney Function" OR "Renal function" OR "Kidney function" OR "creatinine blood level" OR "creatinine levels" OR

"creatinine level" OR "Hepatic effects" OR "Hepatic effect" OR "Liver toxicity" OR "Liver Disease"si OR "aminotransferase" OR "Bilirubin" OR "transaminases elevation" OR "transaminase elevation" OR "transaminases level" OR "transaminase level" OR "transaminases levels" OR "transaminase levels" OR "bilirubin blood level" OR "bilirubin elevation" OR "bilirubin level" OR "bilirubin levels" OR "Haematological abnormalities" OR "Haematological abnormality" OR "Haematologic abnormalities" OR "Haematologic abnormality" OR "Hematological abnormalities" OR "Hematological abnormality" OR "Hematologic abnormalities" OR "Hematologic abnormality" OR "Neutropenia" OR "neutropenia" OR "Hematologic Disease"si OR "Gastrointestinal Disease"si OR "Gastro intestinal effects" OR "Gastro intestinal effect" OR "Gastrointestinal effects" OR "Gastrointestinal effect" OR "Demyelinating Disease" OR "Demyelinating Diseases" OR "Demyelinating disease" OR "Autoimmune Disease" OR "Autoimmune Diseases" OR "Autoimmune Disease" OR "Auto immune Diseases" OR "Auto immune Disease" OR "Antinuclear Antibody" OR "anti nuclear antibodies" OR "anti nuclear antibody" OR "antinuclear antibodies" OR "antinuclear antibody" OR "double stranded DNA antibody" OR "anti dsDNA" OR "Drug Antibody" OR "anti drug antibodies" OR "anti drug antibody" OR "antidrug antibodies" OR "antidrug antibody" OR "chimeric antibody" OR "anti chimeric antibodies" OR "anti chimeric antibody" OR "antichimeric antibodies" OR "antichimeric antibody" OR "Fertility" OR "Infertility" OR "Pregnancy" OR "Pregnancy Complication" OR "Fertility" OR "Infertility" OR "Pregnancy" OR "Induced Abortion" OR "induced abortion" OR "elective abortion" OR "Spontaneous Abortion" OR "Spontaneous Abortion" OR "miscarriage" OR "abortion" OR "abortions" OR "medical termination" OR "Prematurity" OR "premature birth" OR "preterm birth" OR "premature births" OR "preterm births" OR "premature childbirth" OR "preterm childbirth" OR "premature childbirths" OR "preterm childbirths" OR "premature child birth" OR "preterm child birth" OR "premature child births" OR "preterm child births" OR "Small for Date Infant" OR "small for gestational age" OR "Preeclampsia" OR "Pre Eclampsia" OR "preeclampsia" OR "Eclampsia" OR "eclampsia" OR "Cesarean Section" OR "Cesarean Section" OR "Caesarean Section" OR "c section" OR "teratogenicity" OR "Teratogenesis" OR "Teratogenesis" OR "Teratogenicity" OR "Teratogen*"):ti,ab,kw AND ("Cohort Analysis" OR "Cohort Study" OR "Cohort" OR "Cohorts" OR "Follow Up" OR "Follow Up Studies" OR "Longitudinal Study" OR "Longitudinal Studies" OR "Prospective Study" OR "Prospective Studies" OR "Retrospective Study" OR "Retrospective Studies" OR "Follow Up Study" OR "Longitudinal Study" OR "Prospective Study" OR "Retrospective Study" OR "Follow Up" OR "Longitudinal" OR "Prospective" OR "Retrospective" OR "FollowUp" OR "Longitudinal*" OR "Prospective*" OR "Retrospective*" OR "Case Control Study" OR "Case Control" OR "Case Controlled" OR "Case Controls" OR "Case Control*" OR "Register" OR "Registry" OR "Registries" OR "Register" OR "Registers" OR "systematic review" OR "Long term extensions" OR "Long term extensions" OR "LTE" OR "LTEs"):ti,ab,kw)

Table S1.7: Pharmacologic interventions of interest

Biological DMARDs (bDMARDs)	all formulations and duration (biosimilars included): anakinra (ANA), infliximab (INF), etanercept (ETN), adalimumab (ADA), golimumab (GLM), certolizumab pegol (CZP), rituximab (RTX), abatacept (ABA), tocilizumab (TCZ), efalizumab (EFA), secukinumab (SEC), ixekizumab (IXE), brodalumab (BLM), guselkumab (GKM), clazakizumab (CZK), bimekizumab (BMK), ustekinumab (UKM), sonelokimab (SLM), izokibep (IZO)
Targeted synthetic DMARDs (tsDMARDs)	tofacitinib (TOFA), baricitinib (BARI), filgotinib (FILGO), upadacitinib (UPA), apremilast (APR), deucravacitinib (DEUC),
Conventional synthetic DMARDs (csDMARDs)	Methotrexate (MTX), leflunomide (LEF), sulfasalazine (SZP), hydroxychloroquine (HCQ), injectable gold (GOLD), chloroquine (CQ), azathioprine, cyclosporine, penicillamin, cyclophosphamide, mycophenolate, chlorambucil, minocyclin
Non-steroidal anti-inflammatory drugs (NSAIDs)	Aceclofenac, Acemetacin, Aspirin, Diclofenac, Diflunisal, Etodolac, Etoricoxib, Fenoprofen, Flunixin, Flunoxaprofen, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Ketorolac, Meloxicam, Naproxen, Niflumic Acid, Nimesulide, Oxaprozin, Piroxicam, Sulindac, Tolfenamic Acid, Tolmetin
Any combination of the previous	

Table S1.8: Efficacy outcomes of interest

Core set measures of signs and symptoms	**Composite measures**	**Questionnaires / additional measurements**
▪ SJC ▪ TJC ▪ Pain ▪ Patient global assessment ▪ Physician global ▪ Axial involvement ▪ Enthesitis ▪ Dactylitis ▪ Fatigue ▪ NAPSI (Nail Psoriasis Severity Index) ▪ Erythrocyte sedimentation rate (ESR) ▪ C-reactive protein	▪ ACR 20/50/70 responses ▪ DAPSA score ▪ DAPSA remission and low disease activity ▪ cDAPSA score ▪ cDAPSA remission and low disease activity ▪ Minimal disease activity/ very low disease activity ▪ EULAR responses (EULAR good or moderate response; EULAR moderate response) ▪ Psoriatic Arthritis Response Criteria (PsARC) ▪ PASI 75, PASI 90, PASI 100	▪ Dermatology Quality of Life Index (DLQI) ▪ Psoriasis Arthritis Impact of Disease Questionnaire (PSAID) ▪ FACIT-F ▪ Work productivity (if reported) ▪ Health Assessment Questionnaire Disability Index (HAQ-DI) ▪ Short-Form 36 Physical/Mental component score (SF-36 PCS/MCS) ▪ Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

List S1.9: Safety outcomes of special interest

- Serious adverse events (number and rate)
- Withdrawals due to AEs
- Serious infections
- Tuberculosis
- Malignancies (lymphoma, non-melanoma skin-cancer, melanoma, solid tumors, other hematological malignancies, unspecified)
- Skin exacerbation
- Major Adverse Cardiac Events (MACE)
- Demyelinating disease
- Herpes zoster
- Venous thromboembolic events
- Gastrointestinal adverse events / toxicities, including IBD
- Depression
- Suicide attempt / suicide
- Candidiasis / fungal infection
- Hepatosteatosis / liver disease
- Drug-drug interactions
- Opportunistic infections

Kerschbaumer A, *et al. Ann Rheum Dis* 2024;0:1–15. doi: 10.1136/ard-2024-225534

Table S1.10: Table of patient population, Intervention, Control (PICO) definition.

See table S1.7 for specific definitions of interventions, table S1.8 for specific efficacy outcomes of interest and list S1.9 for safety outcomes of interest.

#	Research question	Population	Intervention	Control	Outcome
1	What is the efficacy of pharmacological treatments in PsA since the last update?	Adult Patients with PsA	As described in Table S1.7	• Placebo • (Another) cs/b/tsDMARD • Systemic • glucocorticoids • NSAIDs • Combination of any of the previous	See Table S1.8
2	What is the safety of pharmacological treatments in PsA since the last update?	As in #1	As described in Table S1.7	Appropriate comparator receiving another DMARD or Placebo	As described in Table S1.8
3	Are there important safety signals in JAKi PsA trials?	As in #1	Any JAKi therapy with or without concomitant csDMARD	Appropriate comparator receiving another DMARD or placebo	MACE, VTE, malignancies, opportunistic infections, Herpes zoster
4	What is the evidence on new/emerging molecules (efficacy and safety): JAKi (Filgotinib, Upadacitinib), TYK2	As in #1	Filgotinib, upadacitinib, deucravacitinib	Appropriate comparator receiving another DMARD or Placebo	As in #1 / #2
5	What are the efficacy and safety differences between different DMARDs? Which safety differences could be observed in head-to-head trials?	As in #1	b/tsDMARD + MTX ± other csDMARDs	Other b/tsDMARD + MTX ± other csDMARDs	As in #1 / #2
6	What is known about Drug-drug interactions and potential safety issues in PsA?	As in #1	As described in Table S1.7+	Alternative bDMARD / tsDMARD + respective drug suspected to cause any interaction	As in #1 / #2
7	What is the efficacy of different drugs on different disease entities of PsA?	As in #1	As in #1	As in #1	Outcomes assessing: axial disease, enthesitis, dactylitis, psoriasis,
8	Is there data regarding a window of opportunity?	As in #1	Any DMARD T2T strategy	No T2T strategy	As in #1
9	What is the efficacy of drugs as first versus second or third line?	As in #1	Any DMARD initiation first line	Any DMARD second/third line	As in #1
10	What is the evidence for DMARD dose reduction or stopping?	As In #1	DMARD dose reduction / stopping	DMARD continuation	As in #1

Section 2: Efficacy

Table S2.1: Details of articles and abstracts selected for inclusion.

PICO	Study identifier	Trial name (if available)	Treatment	Target	Background therapy	Population	Treatment arms
1, 4	Behrens EULAR/ACR 2022; de Vlam ACR 2022		Izokibep (ABY-035)	IL17A	NSAIDs / csDMARDs	mixed (NSAID / csDMARD / TNFi) iR	Placebo
							Izokibep 40mg Q2W
							Izokibep 80mg Q2W
1, 3, 4	Mease ACR 2021 / Mease 2023		Brepocitinib	TYK2 / JAK1	NSAIDs / csDMARDs	mixed (NSAID / csDMARD / TNFi) iR	Placebo
							Brepocitinib 10mg QD
							Brepocitinib 30mg QD
							Brepocitinib 60mg QD
1, 4	Mease 2021a		Tildrakizumab	IL23-p19	NSAIDs / csDMARDs	mixed (NSAID / csDMARD / TNFi) iR	Placebo Q4W
							Tildrakizumab 200mg Q4W
							Tildrakizumab 200mg Q12W
							Tildrakizumab 100mg Q12W
							Tildrakizumab 20mg Q12W
1, 3, 4	Mease 2022a		Deucravacitinib	TYK2 (allosteric inhibition)	NSAIDs / csDMARDs	mixed (NSAID / csDMARD / TNFi) iR	Placebo
							Deucravacitinib 6mg QD
							Deucravacitinib 12mg QD
1, 4, 7	Deodhar 2020	DISCOVER-1	Guselkumab	IL23-p19	NSAIDs / csDMARDs	mixed (NSAID / csDMARD / TNFi) iR; up to 30% TNFi-IR	Placebo
							Guselkumab 100 mg Q4W
							Guselkumab 100 mg Q8W
1, 4, 7	Mease 2020a	DISCOVER-2	Guselkumab	IL23-p19	NSAIDs / csDMARDs	NSAID / csDMARD IR, biologic naive	Placebo
							Guselkumab 100 mg Q4W

							Guselkumab 100 mg Q8W
1, 4, 7	Mease 2021b	DISCOVER 1/2	Guselkumab	IL23-p19	NSAIDs / csDMARDs	mixed (NSAID / csDMARD / TNFi) iR	Placebo
							Guselkumab 100 mg Q4W
							Guselkumab 100 mg Q8W
1, 4	Coates 2021a	COSMOS	Guselkumab	IL23-p19	NSAIDs / csDMARDs	TNFi IR	Placebo
							Guselkumab 100 mg Q8W
1, 4	Merola 2023	BE COMPLETE	Bimekizumab	IL17A/F	NSAIDs / csDMARDs	TNFi IR	Placebo
							Bimekizumab 160mg Q4W
1, 4, 5	McInnes 2023	BE OPTIMAL	Bimekizumab	IL17A/F vs. TNF	NSAIDs / csDMARDs	NSAID / csDMARD IR, biologic naive	Placebo
							Bimekizumab 160mg Q4W
							Adalimumab 40mg Q2W
1, 4	Kristensen 2022	KEEPsAKE 1	Risankizumab	IL23-p19	csDMARDs / none	csDMARD iR	Placebo
							Risankizumab 150 mg (wk0, wk4, wk16)
1, 4	Östör 2022a	KEEPsAKE 2	Risankizumab	IL23-p19	csDMARDs / none	mixed (csDMARD / bDMARD) iR	Placebo
							Risankizumab 150 mg (wk0, wk4, wk16)
1, 3, 5	McInnes 2021	SELECT-PsA 1	Upadacitinib	JAK1/2 vs. TNF	NSAIDs / csDMARDs	csDMARD iR	Placebo
							Upadacitinib 15 mg QD
							Upadacitinib 30 mg QD
							Adalimumab 40mg Q2W
1	Mease 2021c	SELECT-PsA 2	Upadacitinib	JAK1/2	csDMARDs / none	bDMARD iR	Placebo
							Upadacitinib 15 mg QD
							Upadacitinib 30 mg QD
1, 4	Mease 2021d	AMVISION-1/2	Brodalumab	IL17A	NSAIDs / csDMARDs	csDMARD iR	Placebo
							Brodalumab 140mg Q2W
							Brodalumab 210mg Q2W
1	Koem 2023	MUST	Ustekinumab + MTX vs. Ustekinumab + Placebo	IL12/23	MTX / Placebo	mixed (csDMARD / bDMARD) iR	Ustekinumab + Placebo
							Ustekinumab + MTX 15mg QW

1, 5	McInnes 2020	EXCEED	Secukinumab vs. Adalimumab	IL17A vs. TNF	none	csDMARD iR	Adalimumab 40mg Q2W
							Secukinumab 300mg
1	Nguyen 2022	CHOICE	Secukinumab vs. Placebo	IL17A	MTX / none	csDMARD iR, biologic naive	Placebo
							Secukinumab 300mg
							Secukinumab 150mg
1	D'Agostino 2022	ULTIMATE	Secukinumab vs. Placebo	IL17A	MTX / none	csDMARD iR, biologic naive	Placebo
							Secukinumab (150mg/300mg)
1, 7	Baraliakos 2021	MAXIMISE	Secukinumab vs. Placebo	IL17A	MTX / none	axial symptoms, NSAID iR	Placebo
							Secukinumab 300mg
							Secukinumab 150mg
1	Kivitz 2019	FUTURE-4	Secukinumab with loading vs. Secukinumab without loading vs. Placebo	IL17A	MTX / none	mixed (NSAID / csDMARD / TNFi) iR	Placebo
							Secukinumab 150mg load
							Secukinumab 150mg no load
1,5	Mease 2020b	SPIRIT-H2H	Ixekizumab vs. Adalimumab	IL17A vs. TNF	csDMARDs / none	csDMARD iR, biologic naive	Adalimumab 40mg Q2W
							Ixekizumab 80mg Q4W
1,5	Smolen 2020	SPIRIT-H2H	Ixekizumab vs. Adalimumab	IL17A vs. TNF	csDMARDs / none	csDMARD iR, biologic naive	Adalimumab 40mg Q2W
							Ixekizumab 80mg Q4W
1,7	Vieira-Sousa 2020	GO-DACT	Golimumab + MTX vs. Placebo + MTX	TNF	MTX	MTX naive, bDMARD naive, active dactylitis	Placebo + MTX
							Golimumab 50mg Q4W + MTX
1	Syversen 2021a	NOR DRUM	Infliximab TDM vs. Infliximab 3mg/kg	TNF	csDMARD	mixed cs/bDMARD-iR	Infliximab 5mg/kg + csDMARD
							Infliximab TDM + csDMARD
1	Syversen 2021a	NOR DRUM	Infliximab TDM vs. Infliximab 3mg/kg	TNF	csDMARD	mixed cs/bDMARD-iR	Infliximab 5mg/kg + csDMARD
							Infliximab TDM + csDMARD
10	Michielsens 2022		T2T with TNFi tapering vs. T2T without TNFi tapering	TNF	csDMARD / none	stable PASDAS≤3.2 (LDA) + BSA≤3% for 6 months	T2T with tapering
							T2T without tapering

10	Coates 2021b	SPIRIT-P3	Ixekizumab continuation vs. Placebo (withdrawal)	IL17A	csDMARD / none	sustained MDA>3 months after 36 weeks of open-label IXE treatment; bDMARD naive; csDMARD-IR	Ixekizumab withdrawal
							Ixekizumab 80mg Q2W
10	Nash 2021	OPAL Balance	Tofacitinib + MTX vs. Tofacitinib + Placebo	JAK1-3	MTX / none	TOFA 5mg BID + stable MTX treatment	Tofacitinib 5 mg BID + placebo
							Tofacitinib 5 mg BID + MTX
10	Ruwaard 2023		Etanercept interval prolongation vs. Continuation	TNFR	csDMARD / NSAID / none	ETA treatment + sustained MDA for 6 months	Etanercept interval prolongation (Q2W)
							Etanercept interval continuation (QW)
1, 5, 10	Coates 2022	CONTROL	Adalimumab 40mg Q2W + MTX vs. MTX dose-escalation	TNF	MTX	MTX-IR, bDMARD naive	Adalimumab 40mg Q2W + MTX
							MTX escalation to 25mg QW
1, 5	Mulder 2022	COMPLETE-PsA	MTX + LEF vs. MTX + Placebo		NSAIDs	early PsA, no DMARD since 6 months	Placebo + Methotrexate 25mg QW
							Methotrexate 25mg QW + Leflunomide 10mg QD

Table S2.2: Risk of bias analysis (Cochrane Collaborations RoB tool for RCTs v2)

Study identifier	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Summary	Comment
Behrens EULAR/ACR 2022; de Vlam ACR 2022	not assessed	not assessed	not assessed	not assessed	not assessed	not assessed	not assessed	not assessed	conference abstract
Mease ACR 2021	low	low	low	low	low	low	low	low	
Mease 2021a	low	low	low	low	low	low	low	low	
Mease 2022a	low	low	low	low	low	low	low	low	
Deodhar 2020	low	low	low	low	low	low	low	low	
Mease 2020a	low	low	low	low	low	low	low	low	
Mease 2021b	not assessed	not assessed	not assessed	not assessed	not assessed	not assessed	not assessed	not assessed	pooled analysis
Coates 2021a	unclear	unclear	low	low	low	low	low	unclear	random sequence generation + allocation concealment not reported
Merola 2023	low	low	low	low	low	low	low	low	
McInnes 2023	low	low	low	low	low	low	low	low	no reporting of mSvDH Score at baseline
Kristensen 2022	low	low	low	low	low	low	low	low	
Östör 2022a	low	low	low	low	low	low	low	low	
McInnes 2021	low	low	low	low	low	low	low	low	
Mease 2021c	low	low	low	low	low	low	low	low	
Mease 2021d	low	low	low	low	low	low	low	low	
Koem 2023	low	low	high	low	low	low	low	high	open-label
McInnes 2020	low	low	low	low	low	low	low	low	

Nguyen 2022	unclear	unclear	low	low	low	low	low	unclear	random sequence generation + allocation concealment not reported
D'Agostino 2022	low	low	low	low	low	low	low	low	
Baraliakos 2021	low	low	low	low	low	low	low	low	
Kivitz 2019	low	low	low	low	low	high	low	high	safety data for placebo controlled period not reported
Mease 2020b	low	low	high	low	low	low	low	high	single/investigator blinded
Smolen 2020	low	low	high	low	low	low	low	high	single/investigator blinded
Vieira-Sousa 2020	low	low	low	low	low	low	low	low	
Syversen 2021a	low	low	high	high	low	low	low	high	open-label
Syversen 2021a	low	low	high	high	low	low	low	high	open-label
Michielsens 2022	low	low	high	high	low	low	low	high	open-label
Coates 2021b	low	low	low	low	low	low	low	low	
Nash 2021	low	low	low	low	low	low	low	low	
Ruwaard 2023	low	low	high	high	low	low	high	high	open-label, background therapy adjustments allowed
Coates 2022	low	low	high	high	low	low	low	high	open-label
Mulder 2022	low	low	low	low	low	low	low	low	

Table S2.3: Baseline demographics and treatments.

Study identifier	Treatment arm	n	Age	Female (%)	BMI (kg/m²)	Prev. TNFi (%)	Concom. csDMARD (%)	Concom. MTX (%)	MTX dose (mg)	Concom. steroids (%)	Disease duration (years)
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	48.5 ± 12		29.0 ± 4.8	13	80				7.1 ± 7.8
	Izokibep 40mg Q2W	44									
	Izokibep 80mg Q2W	47									
Mease ACR 2021 / Mease 2023	Placebo	67	48.2 ± 12.1	36 (53.7)	28.8 ± 5.2	7 (10.4)	49 (73.1)	48 (71.6)	16.8	11 (16.4)	6.9 ± 7.5
	Brepocitinib 10mg QD	31	47.8 ± 13.4	14 (45.2)	28.7 ± 6.0	3 (9.7)	23 (74.2)	21 (67.7)	16.4	5 (16.1)	6.4 ± 6.6
	Brepocitinib 30mg QD	60	45.9 ± 10.2	32 (53.3)	30.2 ± 6.5	4 (6.7)	40 (66.7)	38 (63.3)	15.5	6 (10.0)	6.1 ± 7.2
	Brepocitinib 60mg QD	59	48.7 ± 11.5	33 (55.6)	28.7 ± 5.6	4 (6.7)	50 (83.3)	46 (76.7)	16.7	9 (15.0)	5.7 ± 4.9
Mease 2021a	Placebo Q4W	79	48.1 ± 13.3	44 (55.7)	29.5 ± 6.0	18 (23.7)		47 (59.5)	16.9 ± 5.0		6.3 ± 6.1
	Tildrakizumab 200mg Q4W	78	50.1 ± 13.3	46 (59.0)	30.1 ± 6.5	18 (22.8)		44 (56.4)	16.5 ± 5.3		7.5 ± 8.5
	Tildrakizumab 200mg Q12W	79	49.3 ± 11.2	37 (46.8)	30.2 ± 6.5	17 (21.8)		47 (59.5)	15.0 ± 3.8		6.2 ± 7.2
	Tildrakizumab 100mg Q12W	77	49.2 ± 11.9	47 (61.0)	29.5 ± 6.8	19 (23.8)		49 (63.6)	14.3 ± 4.8		7.0 ± 6.6
	Tildrakizumab 20mg Q12W	78	47.2 ± 13.4	41 (52.6)	29.4 ± 5.2	19 (24.4)		42 (53.8)	16.7 ± 5.5		6.6 ± 6.7
Mease 2022a	Placebo	66	48.5 (13.2)	40 (60.6)	31.2 ± 7.2	11 (16.7)	44 (66.7)	39 (59.1)	16.7 ± 4.8	12 (18.2)	4.5 (0.6–22.9)
	Deucravacitinib 6mg QD	70	50.5 (13.7)	30 (42.9)	29.6 ± 5.4	12 (17.1)	45 (64.3)	35 (50.0)	16.4 ± 4.9	7 (10.0)	5.3 (0.1–42.8)
	Deucravacitinib 12mg QD	67	50.5 (13.8)	34 (50.7)	30.3 ± 5.4	9 (13.4)	43 (64.2)	37 (55.2)	16.5 ± 4.6	6 (9.0)	3.8 (0.6–27.7)
Deodhar 2020	Placebo	126	49.0 ± 11.1	65 (52)		39 (31)	82 (65)	71 (56)	15.9 ± 4.5	20 (16)	7.2 ± 7.6
	Guselkumab 100 mg Q4W	128	47.4 ± 11.6	62 (48)		38 (30)	82 (64)	72 (56)	15.6 ± 4.1	16 (13)	6.6 ± 6.3

	Guselkumab 100 mg Q8W	127	48.9 ± 11.5	59 (46)		41 (32)	83 (65)	68 (54)	16.7 ± 5.4	18 (14)	6.4 ± 5.9
Mease 2020a	Placebo	246	46.3 ± 11.7	129 (52)			172 (70)	156 (63)	15.2 ± 4.6	49 (20)	5.8 ± 5.6
	Guselkumab 100 mg Q4W	245	45.9 ± 11.5	103 (42)			170 (69)	146 (60)	15.6 ± 5.0	46 (19)	5.5 ± 5.9
	Guselkumab 100 mg Q8W	248	44.9 ± 11.9	119 (48)			170 (69)	141 (57)	15.3 ± 5.2	50 (20)	5.1 ± 5.5
Mease 2021b	Placebo	118	45.3 ± 11.0	49 (42)	28.5 ± 6.2			84 (71)	15.6 ± 4.6	29 (25)	6.7 ± 6.4
	Guselkumab 100 mg Q4W	103	44.9 ± 11.8	35 (34)	28.0 ± 6.1			70 (68)	15.2 ± 4.2	17 (17)	5.5 ± 5.5
	Guselkumab 100 mg Q8W	91	45.0 ± 10.7	37 (41)	27.6 ± 6.5			60 (66)	14.8 ± 4.5	23 (25)	4.8 ± 5.0
Coates 2021a	Placebo	96	49 ± 12	44 (46)	31 ± 7			51 (53)			8.7 ± 7.2
	Guselkumab 100 mg Q8W	189	49 ± 12	103 (54)	29 ± 6			105 (56)			8.3 ± 7.8
Merola 2023	Placebo	133	51.3 ± 12.9	73 (55)	29.0 ± 5.4		63 (47)	51 (38)			9.2 ± 8.1
	Bimekizumab 160mg Q4W	267	50.1 ± 12.4	137 (51)	30.1 ± 6.5		139 (52)	119 (45)			9.6 ± 9.9
McInnes 2023	Placebo	281	48.7 ± 11.7	154 (55)	29.6 ± 6.1		192 (68)	162 (58)			5.6 ± 6.5
	Bimekizumab 160mg Q4W	431	48.5 ± 12.6	230 (53)	29.2 ± 6.8		301 (70)	252 (58)			6.0 ± 7.3
	Adalimumab 40mg Q2W	140	49.0 ± 12.8	69 (49)	28.4 ± 5.9		99 (71)	82 (59)			6.1 ± 6.8
Kristensen 2022	Placebo	481	52 (22–79)	247 (51.4)	30.3 ± 6.2		49 (10.2)	315 (65.5)		87 (18.1)	7.1 ± 7.7
	Risankizumab 150 mg (wk0, wk4, wk16)	483	52 (20–85)	231 (47.8)	30.7 ± 6.4		52 (10.8)	314 (65.0)		101 (20.9)	7.1 ± 7.0
Östör 2022a	Placebo	219	52 (24–83)		31.2 ± 6.8	100 (45.7)	30 (13.7)	99 (45.2)		22 (10.0)	8.2 ± 8.3
	Risankizumab 150 mg (wk0, wk4, wk16)	224	53 (23–84)		31.5 ± 8.0	103 (46.0)	31 (13.8)	110 (49.1)		28 (12.5)	8.2 ± 8.2
McInnes 2021	Placebo	423	50.4 ± 12.2	211 (49.9)			347 (82.0)	267 (63.1)		70 (16.5)	6.2 ± 7.0
	Upadacitinib 15 mg QD	429	51.6 ± 12.2	238 (55.5)			353 (82.3)	279 (65.0)		73 (17.0)	6.2 ± 7.4
	Upadacitinib 30 mg QD	423	49.9 ± 12.4	236 (55.8)			346 (81.8)	268 (63.4)		71 (16.8)	5.9 ± 6.4

	Adalimumab 40mg Q2W	429	51.4 ± 12.0	222 (51.7)			347 (80.9)	270 (62.9)		72 (16.8)	5.9 ± 7.1
Mease 2021c	Placebo	212	54.1 ± 11.5	120 (56.6)				75 (35.4)	16.26		11.0 ± 10.3
	Upadacitinib 15 mg QD	211	53.0 ± 12.0	113 (53.6)				74 (35.1)	15.06		9.6 ± 8.4
	Upadacitinib 30 mg QD	218	53.0 ± 11.9	115 (52.8)				73 (33.5)	16.76		9.7 ± 8.7
Mease 2021d	Placebo	322	48.2 ± 12.4	165 (51.2)		102 (31.7)					7.9 ± 8.6
	Brodalumab 140mg Q2W	318	48.6 ± 12.8	160 (50.3)		96 (30.2)					7.3 ± 7.8
	Brodalumab 210mg Q2W	322	48.1 ± 12.4	154 (47.8)		102 (31.7)					7.7 ± 7.9
Koem 2023	Ustekinumab + Placebo	79	48 (35–58)	32 (41%)	28.1 (25.6–31.0)	11 (14%)					1.3 (0.3–4.9)
	Ustekinumab + MTX 15mg QW	87	51 (38–61)	37 (43%)	28.8 (25.6–32.2)	14 (16%)					1.4 (0.2–5.8)
McInnes 2020	Adalimumab 40mg Q2W	427	49.5 ± 12.44	198 (46%)	28.9 ± 5.55					58 (14%)	5.7 ± 7.29
	Secukinumab 300mg	426	48.5 ± 12.38	218 (51%)	28.8 ± 6.03					61 (14%)	5.1 ± 7.60
Nguyen 2022	Placebo	52	53.1 ± 12.7		34.1 ± 7.8			18 (34.6)		3 (5.8)	3.9 ± 5.0
	Secukinumab 300mg	103	51.9 ± 12.6		32.8 ± 8.2			34 (33.0)		12 (11.7)	3.0 ± 4.4
	Secukinumab 150mg	103	51.3 ± 14.6		30.7 ± 7.6			23 (22.3)		11 (10.7)	3.8 ± 5.6
D'Agostino 2022	Placebo	83	47 ± 12	46 (55)				34 (41)		19 (23)	7 ± 7
	Secukinumab (150mg/300mg)	83	47 ± 12	45 (54)				35 (42)		13 (16)	6 ± 7
Baraliakos 2021	Placebo	166	46.6 ± 11.5		28.3 ± 5.5						
	Secukinumab 300mg	167	46.2 ± 12.3		27.3 ± 4.8						
	Secukinumab 150mg	165	46.9 ± 11.5		29.0 ± 6.4						
Kivitz 2019	Placebo	114	48.5 ± 12.2	69 (60.5)				60 (52.6)		20 (17.5)	6.9 ± 7.6
	Secukinumab 150mg load	114	48.3 ± 12.2	67 (58.8)				57 (50.0)		19 (16.7)	5.6 ± 7.3

	Secukinumab 150mg no load	113	50.4 ± 11.8	62 (54.9)				53 (46.9)		26 (23)	5.7 ± 7.7
Mease 2020b	Adalimumab 40mg Q2W	283	48.3 ± 12.3	133 (47)	29.7 ± 8.3		199 (70)	169 (60)			5.9 ± 6.4
	Ixekizumab 80mg Q4W	283	47.5 ± 12.0	121 (43)	30.0 ± 6.9		193 (68)	167 (59)			6.6 ± 7.4
Smolen 2020	Adalimumab 40mg Q2W	283									
	Ixekizumab 80mg Q4W	283									
Vieira-Sousa 2020	Placebo + MTX	23	44.1 (24.6)		25.9 (5.4)						4.2 (6.1)
	Golimumab 50mg Q4W + MTX	21	46.2 (15.5)		29.0 (4.5)						3.8 (6.7)
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	46.1 (12.9)	10 (45%)			17 (77%)			4 (18%)	2.3 (0.7-9.5)
	Infliximab TDM + csDMARD	20	53.5 (13.7)	16 (80%)			16 (80%)			1 (5%)	10.9 (3.1-20.5)
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	44.9 (10.7)	11 (44.0)		8 (32.0)	23 (92.0)			1 (4.0)	7.6 (2.4-10.5)
	Infliximab TDM + csDMARD	28	45.3 (13.0)	14 (50.0)		12 (42.9)	23 (82.1)			2 (7.1)	7.1 (2.6-11.9)
Michielsens 2022	T2T with tapering	42	52 ± 14	14 (33)	28 ± 5			8 (19)			
	T2T without tapering	22	57 ± 13	13 (59)	26 ± 3			6 (27)			
Coates 2021b	Ixekizumab withdrawal	79	43 ± 10.5	40 (51)	29 ± 7.2		60 (76)				7.5 ± 7.5
	Ixekizumab 80mg Q2W	79	44 ± 10.8	47 (60)	28 ± 5.0		59 (75)				7.1 ± 6.3
Nash 2021	Tofacitinib 5 mg BID + placebo	90	53.1 ± 11.0	47 (52%)	30.5 ± 5.4				15.3 ± 4.0		
	Tofacitinib 5 mg BID + MTX	89	51.8 ± 11.4	49 (55%)	30.0 ± 5.4				14.6 ± 4.4		11.3 ± 8.2
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	50 ± 12		26 ± 4			10 (48)	13 (10–21)	0 (0)	9 (7–15)
	Etanercept interval continuation (QW)	20	52 ± 13		28 ± 4			9 (45)	13 (8–15)	0 (0)	10 (8–20)
Coates 2022	Adalimumab 40mg Q2W + MTX	123	51.4 ± 12.2	64 (52%)	31.1 ± 7.0						
	MTX escalation to 25mg QW	122	48.8 ± 12.7	59 (48%)	30.0 ± 6.2						

Mulder 2022	Placebo + Methotrexate 25mg QW	39	51.0 (40.0–59.0)	12 (31%)	27.6 ± 4.0						
	Methotrexate 25mg QW + Leflunomide 10mg QD	39	58.0 (51.0–65.0)	16 (41%)	27.0 ± 4.3						

Table S2.4: Baseline characteristics (signs and symptoms)

Study identifier	Treatment arm	n	SJC66 (0-66)	TJC68 (0-68)	PGA (mm)	EGA (mm)	Pain (mm)	HAQ (0-3)	CRP (mg/L)	DAPSA	PASDAS	Dactylitis (%)	Enthesitis (%)	LEI (0-6)	BSA, (%)	BSA ≥3%, n (%)	PASI
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	9.9 ± 6.6	16.7 ± 10.4													
	Izokibep 40mg Q2W	44															
	Izokibep 80mg Q2W	47															
Mease ACR 2021 / Mease 2023	Placebo	67	9.8 ± 6.2	16.0 ± 9.6			58.5 ± 21.1	1.1 ± 0.6	7.3 ± 10.2	37.9 ± 16.4	5.7 ± 1.1	21 ± 31.3	35 ± 52.2	2.0 ± 1.4		42 ± 62.7	11.2 ± 9.5
	Brepocitinib 10mg QD	31	11.1 ± 7.8	16.5 ± 10.8			57.3 ± 23.3	1.1 ± 0.7	6.3 ± 17.0	39.9 ± 20.4	5.7 ± 1.0	9 ± 29.0	18 ± 58.1	2.2 ± 1.0		21 ± 67.7	11.9 ± 10.5
	Brepocitinib 30mg QD	60	9.6 ± 6.1	16.6 ± 10.5			57.1 ± 22.5	1.1 ± 0.6	8.1 ± 14.4	38.6 ± 17.2	5.7 ± 1.0	19 ± 31.7	28 ± 46.7	2.2 ± 1.3		39 ± 65.0	10.5 ± 9.4
	Brepocitinib 60mg QD	59	9.3 ± 5.6	17.3 ± 10.4			50.1 ± 18.8	1.0 ± 0.6	6.7 ± 11.0	37.2 ± 15.0	5.4 ± 0.9	14 ± 23.3	29 ± 48.3	2.1 ± 1.3		40 ± 66.7	10.8 ± 7.3
Mease 2021a	Placebo Q4W	79	11.8 ± 9.8	19.7 ± 14.7	65.2 ± 18.1	59.5 ± 15.6	64.2 ± 20.4	1.2 ± 0.6	13.0 ± 20.8	45.7 ± 23.5	5.4 ± 0.89			2.8 ± 1.8	8.2 ± 12.2	42 (53.2)	5.0 ± 6.5
	Tildrakizumab 200mg Q4W	78	10.4 ± 7.4	16.6 ± 11.9	57.8 ± 18.3	54.0 ± 16.1	55.4 ± 19.1	1.0 ± 0.6	7.8 ± 18.6	39.2 ± 20.2	5.2 ± 0.86			3.1 ± 1.7	11.9 ± 16.0	53 (67.9)	7.6 ± 9.8
	Tildrakizumab 200mg Q12W	79	10.0 ± 8.0	19.5 ± 13.9	61.1 ± 20.7	55.4 ± 16.2	59.6 ± 23.5	1.0 ± 0.6	10.5 ± 14.4	42.6 ± 22.1	5.2 ± 0.78			2.8 ± 1.7	9.0 ± 12.4	44 (55.7)	6.2 ± 7.4
	Tildrakizumab 100mg Q12W	77	11.0 ± 8.2	21.3 ± 14.8	60.3 ± 20.2	57.3 ± 17.3	59.2 ± 22.1	1.0 ± 0.7	10.6 ± 20.0	45.3 ± 22.4	5.3 ± 0.89			3.2 ± 1.8	13.1 ± 16.0	55 (71.4)	8.8 ± 9.5
	Tildrakizumab 20mg Q12W	78	9.4 ± 6.4	19.0 ± 13.0	61.9 ± 17.4	59.4 ± 14.4	60.9 ± 19.7	1.1 ± 0.6	10.7 ± 14.0	41.8 ± 17.8	5.3 ± 0.85			3.1 ± 1.7	10.4 ± 14.1	41 (52.6)	6.6 ± 7.0

Mease 2022a	Placebo	66	10.5 ± 7.7	16.9 ± 9.8			64.9 ± 18.2	1.3 ± 0.6	20.4 ± 39.1			25 (37.9)	31 (47.0)	2.8 ± 1.7		54 (81.8)	9.1 ± 7.4
	Deucravacitinib 6mg QD	70	11.9 ± 7.0	18.1 ± 10.3			63.6 ± 21.7	1.3 ± 0.6	17.6 ± 23.6			30 (42.6)	39 (55.7)	2.5 ± 1.6		59 (84.3)	8.5 ± 6.8
	Deucravacitinib 12mg QD	67	11.3 ± 9.0	19.4 ± 11.8			63.8 ± 15.9	1.3 ± 0.6	16.5 ± 21.7			24 (35.8)	26 (38.8)	2.9 ± 1.4		52 (77.6)	7.9 ± 5.9
Deodhar 2020	Placebo	126	10.1 ± 7.1	19.8 ± 14.4	6.1 ± 2.2	6.3 ± 1.7	5.8 ± 2.2	1.1 ± 0.6	8.0 (3.0–15.0)			55 (44)	77 (61)	2.8 ± 1.6	12.0 ± 16.0		7.7 ± 8.8
	Guselkumab 100 mg Q4W	128	8.6 ± 5.8	17.7 ± 13.1	6.1 ± 2.0	6.2 ± 1.6	5.9 ± 2.0	1.1 ± 0.6	6.0 (3.0–13.0)			38 (30)	73 (57)	3.0 ± 1.5	15.0 ± 18.0		9.5 ± 10.1
	Guselkumab 100 mg Q8W	127	10.9 ± 9.3	20.2 ± 14.5	6.5 ± 2.0	6.2 ± 1.7	6.0 ± 2.1	1.2 ± 0.6	7.0 (4.0–19.0)			49 (39)	72 (57)	2.7 ± 1.6	13.1 ± 18.0		8.4 ± 9.8
Mease 2020a	Placebo	246	12.3 ± 6.9	21.6 ± 13.1	6.5 ± 1.8	6.6 ± 1.5	6.3 ± 1.8	1.3 ± 0.6	12 (5–26)			99 (40)	178 (72)	2.8 ± 1.6	17.1 ± 20.0		9.3 ± 9.8
	Guselkumab 100 mg Q4W	245	12.9 ± 7.8	22.4 ± 13.5	6.4 ± 1.9	6.6 ± 1.5	6.2 ± 2.0	1.2 ± 0.6	12 (6–23)			121 (49)	170 (69)	3.0 ± 1.7	18.2 ± 20.0		10.8 ± 11.7
	Guselkumab 100 mg Q8W	248	11.7 ± 6.8	19.8 ± 11.9	6.5 ± 1.9	6.6 ± 1.6	6.3 ± 2.0	1.3 ± 0.6	13 (7–25)			111 (45)	158 (64)	2.6 ± 1.5	17.0 ± 21.0		9.7 ± 11.7
Mease 2021b	Placebo	118	10.9 ± 6.9	21.8 ± 13.7	6.7 ± 1.7				24 ± 29	48.2 ± 18.8		50 (42)	82 (70)	2.8 ± 1.7			11.0 ± 11.0
	Guselkumab 100 mg Q4W	103	12.3 ± 8.8	23.5 ± 15.5	6.5 ± 1.8				23 ± 29	50.7 ± 23.3		57 (55)	78 (76)	2.8 ± 1.7			12.0 ± 13.0
	Guselkumab 100 mg Q8W	91	10.7 ± 5.6	20.7 ± 12.5	6.6 ± 2.0				27 ± 34	47.0 ± 20.7		50 (55)	66 (73)	2.7 ± 1.6			9.3 ± 9.5
Coates 2021a	Placebo	96	9 ± 6	18 ± 11	6.2 ± 1.7	6.4 ± 1.7	6.0 ± 1.8	1.2 ± 0.6	12 ± 25	40.6 ± 15.8		36 (38)	64 (67)	2.7 ± 1.5	13.4 ± 17.7	96	9.2 ± 9.4
	Guselkumab 100 mg Q8W	189	10 ± 7	21 ± 13	6.5 ± 1.7	6.9 ± 1.5	6.5 ± 1.9	1.3 ± 0.6‡	12 ± 20	45.5 ± 19.9		67 (36)	126 (67)	2.9 ± 1.5	17.9 ± 21.5	188	11.7 ± 11.9
Merola 2023	Placebo	133	10.3 ± 8.2	19.3 ± 14.2	63.0 ± 22.0	57.7 ± 18.8	61.7 ± 24.6	1.04 ± 0.69				14 (11)	36 (27)	2.9 ± 1.6		88 (66)	8.5 ± 6.6

	Bimekizumab 160mg Q4W	267	9.7 ± 7.5	18.4 ± 13.5	60.5 ± 22.5	59.3 ± 17.2	58.3 ± 24.2	0.97 ± 0.59				34 (13)	106 (40)	2.6 ± 1.5		176 (66)	10.1 ± 9.1
McInnes 2023	Placebo	281	9.5 ± 7.3	17.1 ± 12.5	58.6 ± 23.5	57.2 ± 15.1	56.8 ± 23.2	0.89 ± 0.61				33 (12)	70 (25)	2.9 ± 1.5		140 (50)	7.9 ± 5.6
	Bimekizumab 160mg Q4W	431	9.0 ± 6.2	16.8 ± 11.8	54.4 ± 23.4	57.2 ± 16.3	53.6 ± 24.3	0.82 ± 0.59				56 (13)	143 (33)	2.5 ± 1.5		217 (50)	8.2 ± 6.8
	Adalimumab 40mg Q2W	140	9.6 ± 7.1	17.5 ± 13.1	57.1 ± 21.8	57.3 ± 17.5	56.7 ± 23.9	0.86 ± 0.54				11 (8)	36 (26)	2.3 ± 1.6		68 (49)	8.5 ± 7.6
Kristensen 2022	Placebo	481	12.2 ± 8.0	20.5 ± 12.8	57.4 ± 22.1	62.4 ± 17.0	57.1 ± 22.6	1.17 ± 0.65	11.3 ± 14.1			147 (30.6)	290 (60.3)	2.6 ± 1.5	16.5 ± 20.8	272 (56.5)	10.0 ± 10.4
	Risankizumab 150 mg (wk0, wk4, wk16)	483	12.1 ± 7.8	20.8 ± 14.1	57.9 ± 21.8	61.3 ± 17.6	57.1 ± 22.6	1.15 ± 0.66	11.9 ± 15.9			148 (30.6)	297 (61.5)	2.7 ± 1.5	16.8 ± 19.7	273 (56.5)	10.9 ± 10.1
Östör 2022a	Placebo	219	13.6 ± 9.0	22.3 ± 13.8	56.2 ± 23.0	60.7 ± 16.4	57.0 ± 23.1	1.13 ± 0.63	8.2 ± 17.1			57 (26.3)	158 (72.1)	3.0 ± 1.6	11.7 ± 14.9	119 (54.3)	8.4 ± 9.9
	Risankizumab 150 mg (wk0, wk4, wk16)	224	13.0 ± 8.7	22.8 ± 14.9	56.2 ± 21.8	63.0 ± 17.0	55.0 ± 23.5	1.10 ± 0.62	7.5 ± 10.9			40 (17.9)	147 (65.6)	3.0 ± 1.5	12.5 ± 15.4	123 (54.9)	7.7 ± 6.7
McInnes 2021	Placebo	423	11.0 ± 8.2	20.0 ± 14.3			6.1 ± 2.1	1.1 ± 0.6				126 (29.8)	241 (57.0)			211 (49.9)	11.2 ± 11.4
	Upadacitinib 15 mg QD	429	11.6 ± 9.3	20.4 ± 14.7			6.2 ± 2.1	1.2 ± 0.7				136 (31.7)	270 (62.9)			214 (49.9)	9.8 ± 10.0
	Upadacitinib 30 mg QD	423	10.6 ± 7.1	19.4 ± 13.3			5.9 ± 2.1	1.1 ± 0.6				127 (30.0)	267 (63.1)			210 (49.6)	9.5 ± 8.8
	Adalimumab 40mg Q2W	429	11.6 ± 8.8	20.1 ± 13.8			6.0 ± 2.1	1.1 ± 0.6				127 (29.6)	265 (61.8)			211 (49.2)	9.4 ± 8.5
Mease 2021c	Placebo	212	12.0 ± 8.9	25.3 ± 17.6			6.6 ± 2.1	1.23 ± 0.7	10.4 ± 18.5			64 (30.2)			12.8 ± 18.4	131 (61.8)	11.7 ± 11.4
	Upadacitinib 15 mg QD	211	11.3 ± 8.2	24.9 ± 17.3			6.4 ± 2.1	1.10 ± 0.6	11.2 ± 18.5			55 (26.1)			10.0 ± 15.7	130 (61.6)	10.1 ± 9.2
	Upadacitinib 30 mg QD	218	12.9 ± 9.4	24.2 ± 15.9			6.2 ± 2.2	1.19 ± 0.7	10.5 ± 17.2			50 (22.9)			10.0 ± 15.8	131 (60.1)	8.9 ± 9.1

Mease 2021d	Placebo	322	11.7 ± 8.5	21.1 ± 14.5				1.1 ± 0.6	12 ± 19			161 (50.0)	208 (64.6)	1.8 ± 1.9		221 (68.6)	7.7 ± 9.0
	Brodalumab 140mg Q2W	318	12.4 ± 9.7	21.9 ± 15.6				1.2 ± 0.7	15 ± 25			139 (43.7)	185 (58.2)	1.8 ± 2.0		220 (69.2)	8.6 ± 10.0
	Brodalumab 210mg Q2W	322	11.7 ± 9.4	18.9 ± 13.6				1.1 ± 0.6	13 ± 21			149 (46.3)	193 (59.9)	1.6 ± 1.8		219 (68.0)	7.8 ± 9.3
Koem 2023	Ustekinumab + Placebo	79	8 (5–10)	12 (8–17)	60 (46–75)	59 (42–72)	61 (47–74)	0.9 (0.4–1.4)	3.9 (1.8–11.7)	33.2 (26.8–37.5)		15 (19%)	40 (51%)		1.0 (0.6–4.7)		2.4 (0.4–6.4)
	Ustekinumab + MTX 15mg QW	87	8 (6–11)	12 (8–18)	60 (43–72)	61 (45–74)	59 (42–70)	0.9 (0.4–1.5)	6.0 (2.1–14.0)	32.8 (25.4–45.3)		21 (24%)	44 (51%)		2.9 (1.0–7.1)		2.8 (0.8–6.4)
McInnes 2020	Adalimumab 40mg Q2W	427	10.2 ± 7.86	20.6 ± 14.81	61.9 ± 20.75	61.4 ± 15.92	57.9 ± 22.42	1.2 ± 0.64				137 (32%)	264 (62%)			202 (47%)	10.0 ± 8.15
	Secukinumab 300mg	426	9.7 ± 7.30	19.4 ± 13.86	64.0 ± 19.67	60.0 ± 17.12	58.6 ± 23.49	1.3 ± 0.64				130 (31%)	234 (55%)			215 (50%)	10.6 ± 9.00
Nguyen 2022	Placebo	52	13.8 ± 11.9	25.2 ± 15.0				1.3 ± 0.7			6.2 ± 1.3	23 (44.2)		39 (75.0)			5.9 ± 5.4
	Secukinumab 300mg	103	17.7 ± 16.4	27.1 ± 19.6				1.1 ± 0.6			6.2 ± 1.3	49 (47.6)		74 (71.8)			8.3 ± 8.0
	Secukinumab 150mg	103	14.4 ± 13.9	25.6 ± 18.6				1.0 ± 0.6			6.0 ± 1.3	52 (50.5)		76 (73.8)			9.0 ± 10.0
D'Agostino 2022	Placebo	83	9 ± 9	15 ± 12	60 ± 23	52 ± 22	59 ± 24	1.2 ± 0.7	5 (0–102)							33 (40)	11 ± 9
	Secukinumab (150mg/300mg)	83	10 ± 8	13 ± 8	60 ± 23	56 ± 18	59 ± 21	1.3 ± 0.6	7 (1–77)							36 (43)	9 ± 6
Baraliakos 2021	Placebo	166	6.2 ± 9.0	15.6 ± 15.0	72.4 ± 15.6	64.0 ± 17.6		1.5 ± 0.5	8.7 ± 15.4								
	Secukinumab 300mg	167	6.1 ± 8.7	15.3 ± 15.3	71.7 ± 14.4	62.6 ± 15.7		1.4 ± 0.5	11.7 ± 23.3								
	Secukinumab 150mg	165	5.9 ± 7.7	14.9 ± 14.5	74.5 ± 14.2	62.2 ± 19.5		1.4 ± 0.6	11.5 ± 21.2								
Kivitz 2019	Placebo	114	9.4 ± 7.2	21.2 ± 15.7								44 (38.6)	76 (66.7)			62 (54.4)	

	Secukinumab 150mg load	114	9.6 ± 8.5	20.1 ± 15.5								40 (35.1)	74 (64.9)			55 (48.2)	
	Secukinumab 150mg no load	113	10.2 ± 9.1	19.0 ± 16.3								38 (33.6)	66 (58.4)			54 (47.8)	
Mease 2020b	Adalimumab 40mg Q2W	283	10.7 ± 8.1	21.3 ± 15.4	65.2 ± 20.7	59.4 ± 18.2	62.4 ± 21.1	1.3 ± 0.7	10.5 ± 19.3	45.8 ± 23.5	5.8 ± 1.0	58 (21)	147 (52)	2.7 ± 1.5	12.9 ± 15.6	283 (100)	7.7 ± 7.3
	Ixekizumab 80mg Q4W	283	10.1 ± 7.5	19.1 ± 12.7	62.4 ± 20.3	58.9 ± 17.5	59.7 ± 21.9	1.2 ± 0.6	9.8 ± 13.7	42.7 ± 20.6	5.8 ± 0.9	42 (15)	159 (56)	2.5 ± 1.4	14.8 ± 18.4	283 (100)	7.9 ± 8.7
Smolen 2020	Adalimumab 40mg Q2W	283															
	Ixekizumab 80mg Q4W	283															
Vieira-Sousa 2020	Placebo + MTX	23	6 (5)	6 (8)				0.875 (1.25)		24.5 (20.20)	6.2 (2.58)		12/23 (52.2%)	0 (1)	8.2 (15.3)		2.4 (2.65)
	Golimumab 50mg Q4W + MTX	21	7 (10)	8 (9)				0.875 (0.625)		24.3 (20.84)	6.1 (1.83)		11/21 (52.4%)	0 (1)	13 (29.5)		4 (4)
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22			60.4 (20.7)	42.9 (19.7)			6.5 (1.0-24.0)	36.6 (25.1)							
	Infliximab TDM + csDMARD	20			52.5 (19.3)	42.3 (23.1)			3.5 (2.0-11.5)	31.4 (12.6)							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25			22.7 (18.4)	7.4 (8.7)			1.0 (1.0-2.0)	6.2 (5.1)							
	Infliximab TDM + csDMARD	28			24.5 (18.2)	7.8 (8.0)			1.0 (1.0-2.5)	10.2 (9.0)							
Michielsens 2022	T2T with tapering	42						0.32 ± 0.5			1.6 ± 1.26						
	T2T without tapering	22						0.48 ± 0.61			1.63 ± 0.98						
Coates 2021b	Ixekizumab withdrawal	79	9.0 ± 5.6	16 ± 12.3	61 ± 19.5		59 ± 18.9	1.0 ± 0.5					47 (59.5)	2.5 ± 1.3	14 ± 17.8		7.6 ± 10.2

	Ixekizumab 80mg Q2W	79	9.4 ± 7.4	17 ± 11.5	59 ± 18.3		60 ± 19.4	1.1 ± 0.6					48 (60.8)	2.4 ± 1.3	17 ± 18.2		8.4 ± 8.2
Nash 2021	Tofacitinib 5 mg BID + placebo	90	0.5 ± 1.2	2.8 ± 4.3	9.2 ± 10.7	22.7 ± 20.6	20.6 ± 20.3	0.52 ± 0.58	5.0 ± 12.2		2.53 ± 1.24	1 (1%)	16 (18%)	2.0 ± 1.3; n1=16	4 ± 5; n1=42		
	Tofacitinib 5 mg BID + MTX	89	0.8 ± 1.5	2.9 ± 3.6	11.8 ± 12.0	26.1 ± 22.0	25.4 ± 21.6	0.64 ± 0.67	3.3 ± 4.2		2.74 ± 1.23	7 (8%)	15 (17)	1.4 ± 0.7; n1=15	4 ± 5; n1=47		
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	0 (0–0)	0 (0–0)	12 (2–18)	4 (2–5)	8 (3–17)	0.0 (0.0–0.5)	1 (1–3)	3 (1–4)				0 (0–0)			0.0 (0.0–0.8)
	Etanercept interval continuation (QW)	20	0 (0–0)	0 (0–0)	5 (1–19)	4 (2–8)	5 (0–12)	0.0 (0.0–0.3)	1 (1–3)	2 (0–3)				0 (0–0)			0.0 (0.0–0.3)
Coates 2022	Adalimumab 40mg Q2W + MTX	123	10.1 ± 6.4	22.0 ± 13.1	65.0 ± 19.9		63.7 ± 19.5	1.2 ± 0.6				65 (53%)	97 (79%)	2.9 (1.5)	14.2% ± 20.0	74 (60%)	9.6 (8.8)
	MTX escalation to 25mg QW	122	11.5 ± 7.7	22.2 ± 15.0	62.9 ± 21.0		62.3 ± 20.9	1.2 ± 0.7				74 (61%)	101 (83%)	2.9 (1.6)	12.3% ± 16.2	78 (64%)	7.9 (6.7)
Mulder 2022	Placebo + Methotrexate 25mg QW	39	4.0 (2.0–6.0)	4.0 (2.0–10.0)	54.4 ± 20.2	34.3 ± 13.4	50.1 ± 24.9	0.7 ± 0.5	5.0 (1.0–13.0)	31.3 ± 16.0–38.5	4.9 ± 1.0	12 (31%)		0.0 (0.0–1.0)	0.8 (0.0–1.0)	26 (67%)	1.0 (0.0–2.2)
	Methotrexate 25mg QW + Leflunomide 10mg QD	39	4.0 (3.0–5.0)	4.0 (1.0–11.0)	53.9 ± 22.4	36.3 ± 17.1	50.3 ± 23.8	0.7 ± 0.6	3.0 (1.0–13.0)	26.5 ± 17.5–44.5	4.9 ± 1.0	6 (15%)		0.0 (0.0–2.0)	1.0 (0.0–2.5)	29 (74%)	0.6 (0.0–3.3)

Table S2.5: Efficacy outcomes (composite outcomes, PASI)

Study identifier	Treatment arm	No. of patients (n)	Timepoint (weeks)	ACR20 (%)	ACR50 (%)	ACR70 (%)	ΔDAPSA	DAPSA LDA	DAPSA rem	MDA	VLDA	ΔPASDAS	PASI 75 (%)	PASI 90 (%)	PASI 100 (%)
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16	26	13	5				5					
	Izokibep 40mg Q2W	44		60	48	37				42					
	Izokibep 80mg Q2W	47		75	52	18				39					
Mease ACR 2021 / Mease 2023	Placebo	67	16	43	10	1				3		-0.9 (-1.18 to -0.63)	24	12	
	Brepocitinib 10mg QD	31		65	32	10				19		-1.86 (-2.27 to -1.45)	57	33	
	Brepocitinib 30mg QD	60		67	48	27				35		-2.2 (-2.49 to -1.91)	59	33	
	Brepocitinib 60mg QD	59		75	44	24				36		-2.35 (-2.64 to -2.06)	69	54	
Mease 2021a	Placebo Q4W	79	24	50.6	24.1	10.1	–19.3 ± 1.8		3.8	6.3	1.3	–1.0 ± 0.1	16.7	7.1	4.8
	Tildrakizumab 200mg Q4W	78		79.5	52.6	28.2	–25.1 ± 1.8		21.8	33.3	15.4	–1.5 ± 0.1	64.2	47.2	30.2
	Tildrakizumab 200mg Q12W	79		77.2	50.6	29.1	–25.5 ± 1.8		19	34.2	16.5	–1.5 ± 0.1	79.6	50.0	25.0
	Tildrakizumab 100mg Q12W	77		71.4	45.5	22.1	–27.0 ± 1.8		11.7	28.6	6.5	–1.5 ± 0.1	56.4	40.0	27.3
	Tildrakizumab 20mg Q12W	78		73.1	39.7	16.7	–23.1 ± 1.8		9	19.2	6.4	–1.4 ± 0.1	46.3	36.6	22.0

Mease 2022a	Placebo	66	16	31.8 (20.6 to 43.1)	10.6 (3.2 to 18.0)	1.5 (0.0 to 4.5)	−13.3 (−17.7 to −9.0)			7.6 (1.2 to 14.0)		−1.1 (−1.5 to −0.7)	20.4 (9.6 to 31.1)		
	Deucravacitinib 6mg QD	70		52.9 (41.2 to 64.6)	24.3 (14.2 to 34.3)	14.3 (6.1 to 22.5)	−23.2 (−27.5 to −19.0)			22.9 (13.0 to 32.7)		−2.0 (−2.4 to −1.6)	42.4 (29.8 to 55.0)		
	Deucravacitinib 12mg QD	67		62.7 (51.1 to 74.3)	32.8 (21.6 to 44.1)	19.4 (9.9 to 28.9)	−25.6 (−30.0 to −21.2)			23.9 (13.7 to 34.1)		−2.1 (−2.5 to −1.8)	59.6 (46.3 to 73.0)		
Deodhar 2020	Placebo	126	24	28 (22)	11 (9)	7 (6)				14 (11)			11/78 (14)	9/78 (12)	5/78 (6)
	Guselkumab 100 mg Q4W	128		76 (59)	46 (36)	26 (20)				39 (30)			77/89 (86)	56/89 (63)	40/89 (45)
	Guselkumab 100 mg Q8W	127		66 (52)	38 (30)	15 (12)				29 (23)			62/82 (76)	41/82 (50)	21/82 (26)
Mease 2020a / 2021b	Placebo	246	24	81 (33)	35 (14)	10 (4)				15 (6)			42/183 (23)	18/183 (10)	5/183 (3)
	Guselkumab 100 mg Q4W	245		156 (64)	81 (33)	32 (13)				46 (19)			144/184 (78)	112/184 (61)	82/184 (45)
	Guselkumab 100 mg Q8W	248		159 (64)	78 (31)	46 (19)				62 (25)			139/176 (79)	121/176 (69)	80/176 (45)
Coates 2021a	Placebo	96	24	19 (20)	5 (5)	1 (1.0)	−5.7		2 (2.1)	3 (3.1)	0		5/53 (9.4)	4/53 (7.5)	2/53 (3.8)
	Guselkumab 100 mg Q8W	189		84 (44)	40 (21)	15 (7.9)	−14.5		10 (5.3)	28 (14.8)	7 (3.7)		79/133 (59.4)	68/133 (51.1)	41/133 (31)
Merola 2023	Placebo	133	16	21 (16)	9 (7)	1 (1)				8 (6)	3 (2)		9/88 (10)	6/88 (7)	4/88 (5)
	Bimekizumab 160mg Q4W	267		179 (67)	116 (43)	71 (27)				118 (44)	36 (13)		145/176 (82)	121/176 (69)	103/176 (59)
McInnes 2023	Placebo	281	16	67 (24)	28 (10)	12 (4)				37 (13)	3 (1)		18 (13) of 140	4 (3) of 140	3 (2) of 140
	Bimekizumab 160mg Q4W	431		268 (62)	189 (44)	105 (24)				194 (45)	63 (15)		168 (77) of 217	133 (61) of 217	103 (47) of 217
	Adalimumab 40mg Q2W	140		96 (69)	64 (46)	39 (28)				63 (45)	22 (16)		45 (66) of 68	28 (41) of 68	14 (21) of 68
Kristensen 2022	Placebo	481	24	161 (33.5)	54 (11.3)	23 (4.7)		108 (22.5)	16 (3.2)	49 (10.2)				27 (9.9)	

	Risankizumab 150 mg (wk0, wk4, wk16)	483		277 (57.3)	162 (33.4)	74 (15.3)		199 (41.2)	55 (11.3)	121 (25.0)				143 (52.3)	
Östör 2022a	Placebo	219	24	58 (26.5)	20 (9.3)	13 (5.9)		40 (18.4)	12 (5.3)	25 (11.4)	4 (1.8)			12 (10.2)	
	Risankizumab 150 mg (wk0, wk4, wk16)	224		115 (51.3)	59 (26.3)	27 (12.0)		83 (36.8)	21 (9.4)	57 (25.6)	18 (8.0)			68 (55.0)	
McInnes 2021	Placebo	423	12 / 24*	153 (36.2)	80/423 (13.2)	10/423 (2.4)				52 (12.3)			45/211 (21.3)	35/211 (16.6)*	21/211 (10.0)*
	Upadacitinib 15 mg QD	429		303 (70.6)	161/429 (37.5)	67/429 (15.6)				157 (36.6)			134/214 (62.6)	89/214 (41.6)*	57/214 (26.6)*
	Upadacitinib 30 mg QD	423		332 (78.5)	219/423 (51.8)	107/423 (25.3)				192 (45.4)			131/210 (62.4)	101/210 (48.1)*	80/210 (38.1)*
	Adalimumab 40mg Q2W	429		279 (65.0)	161/429 (37.5)	59/429 (13.8)				143 (33.3)			112/211 (53.1)	95/211 (45.0)*	58/211 (27.5)*
Mease 2021c	Placebo	212	12 / 24*	51 (24.1)	10 (4.7)	1 (0.5)	-11.5			6 (2.8)*			21/131 (16.0)	8/131 (6.1)	6/131 (4,6)
	Upadacitinib 15 mg QD	211		120 (56.9)	67 (31.8)	18 (8.5)	-27.2			53 (25.1)*			68/130 (52.3)	38/130 (29.2)	28/130 (21.5)
	Upadacitinib 30 mg QD	218		139 (63.8)	82 (37.6)	36 (16.5)	-31.0			63 (28.9)*			74/131 (56.5)	52/131 (39.7)	39/131 (29.8)
Mease 2021d	Placebo	322	16	20,9	7,2	3,4	–3,152					–0,325	10,4	6,1	3,9
	Brodalumab 140mg Q2W	318		45,8	24,8	11,3	–17,51					–1,526	52,4	38,5	20,7
	Brodalumab 210mg Q2W	322		47,9	26,1	12,2	–17,61					–1,913	75,5	58,8	40,8
Koem 2023	Ustekinumab + Placebo	79	24	51 (65%)	34 (43%)	16 (20%)	-20,5								
	Ustekinumab + MTX 15mg QW	87		53 (61%)	37 (43%)	15 (17%)	-18,7								
McInnes 2020	Adalimumab 40mg Q2W	427	52	427 (62%)	427 (45%)	427 (29%)			427 (24%)	427 (38%)	427 (17%)		202 (61%)	202 (43%)	202 (30%)
	Secukinumab 300mg	426		426 (67%)	426 (49%)	426 (33%)			426 (25%)	426 (43%)	426 (18%)		215 (79%)	215 (65%)	215 (46%)
Nguyen 2022	Placebo	52	16	12/52 (23.1)	3/52 (5.8)	1/52 (1.9)				2/52 (3.8)		-0.36	7/43 (16.3)	4/43 (9.3)	1/43 (2.3)
	Secukinumab 300mg	103		53/103 (51.5)	29/103 (28.2)	18/103 (17.5)				27/103 (26.2)		-1.04	51/79 (64.6)	39/79 (49.4)	20/79 (25.3)

	Secukinumab 150mg	103		38/103 (36.9)	25/103 (24.3)	11/103 (10.7)				27/103 (26.2)		-0.92	45/83 (54.2)	30/83 (36.1)	15/83 (18.1)
D'Agostino 2022	Placebo	83	16	32	8	1									
	Secukinumab (150mg/300mg)	83		68	46	22									
Baraliakos 2021	Placebo	166	12	19%											
	Secukinumab 300mg	167		52%											
	Secukinumab 150mg	165		57%											
Kivitz 2019	Placebo	114	16	18.4 (21)	6.1 (7)	0.9 (1)				2.6 (114)			8.1 (62)	1.6 (62)	
	Secukinumab 150mg load	114		41.2 (47)	22.8 (26)	7.9 (9)				14.0 (114)			52.7 (55)	36.4 (55)	
	Secukinumab 150mg no load	113		39.8 (45)	16.8 (19)	8.8 (10)				10.6 (113)			50.0 (54)	20.4 (54)	
Mease 2020b	Adalimumab 40mg Q2W	283	24	204/283 (72.1)	132/283 (46.6)	73/283 (25.8)	−30.10 (0.94)	171/283 (60.4)	51/283 (18.0)	100/283 (35.3)	29/283 (10.2)	−2.94 (0.10)	195/283 (68.9)	158/283 (55.8)	132/283 (46.6)
	Ixekizumab 80mg Q4W	283		195/283 (68.9)	143/283 (50.5)	90/283 (31.8)	−31.74 (0.94)	174/283 (61.5)	75/283 (26.5)	135/283 (47.7)	49/283 (17.3)	−3.08 (0.10)	227/283 (80.2)	203/283 (71.7)	170/283 (60.1)
Smolen 2020	Adalimumab 40mg Q2W	283	52	195 (68.9) (63.5 to 74.3)	141 (49.8) (44.0 to 55.6)	97 (34.3) (28.7 to 39.8)	−32.4 (0.9)	166 (58.7) (52.9 to 64.4)	80 (28.3) (23.0 to 33.5)	116 (41.0) (35.3 to 46.7)	54 (19.1) (14.5 to 23.7)		194 (68.6) (63.1 to 74.0)	153 (54.1) (48.3 to 59.9)	
	Ixekizumab 80mg Q4W	283		197 (69.6) (64.3 to 75.0)	141 (49.8) (44.0 to 55.6)	100 (35.3) (29.8 to 40.9)	−33.8 (0.9)	174 (61.5) (55.8 to 67.2)	85 (30.0) (24.7 to 35.4)	134 (47.3) (41.5 to 53.2)	66 (23.3) (18.4 to 28.2)		222 (78.4) (73.7 to 83.2)	206 (72.8) (67.6 to 78.0)	
Vieira-Sousa 2020	Placebo + MTX	23	24	12/19 (63.2)	7/21 (33.3)	5/22 (22.7)	-12.88			9/21 (42.9)		-1.76		8/20 (40.0)	
	Golimumab 50mg Q4W + MTX	21		15/16 (93.8)	12/17 (70.6)	8/19 (42.1)	-21.62			11/16 (68.8)		-3.27		5/20 (25.0)	
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	30												

	Infliximab TDM + csDMARD	20													
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	52				1.2 (5.0)								
	Infliximab TDM + csDMARD	28					-2.2 (8.1)								
Michielsens 2022	T2T with tapering	42	104							26 (62)					
	T2T without tapering	22								13 (60)					
Nash 2021	Tofacitinib 5 mg BID + placebo	90	24							44 (49%)					
	Tofacitinib 5 mg BID + MTX	89								41 (46%)					
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	24							12 (57)					
	Etanercept interval continuation (QW)	20								14 (70)					
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16	83/123 (67.5%, 59.2–75.8)	56/123 (45.5%, 36.7–54.3)	38/123 (30.9%, 22.7–39.1)	−28.2 (−31.6 to −24.9; n=114)		27/114 (23.7%, 15.9–31.5)	51/123 (41%)		−2.8 (−3.1 to −2.5; n=114)	57/78 (73.1%, 63.2–82.9)	45/78 (57.7%, 46.7–68.7)	23/78 (29.5%, 19.4–39.6)
	MTX escalation to 25mg QW	122		40/122 (32.8%, 24.5–41.1)	20/122 (16.4%, 9.8–23.0)	10/122 (8.2%, 3.3–13.1)	−12.1 (−15.6 to −8.7; n=108)		3/108 (2.8%, 0.0–5.9)	16/122 (13%)		−1.2 (−1.5 to −0.9; n=105)	27/87 (31.0%, 21.3–40.8)	16/87 (18.4%, 10.3–26.5)	8/87 (9.2%, 3.1–15.3)
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16	13/37 (35)	7/37 (19)	3/37 (11)	−10.0 (−23.8 to 0.0)	14 (37%)		12 (32%)					
	Methotrexate 25mg QW + Leflunomide 10mg QD	39		17/38 (45)	10/38 (26)	5/38 (13)	−10.7 (−24.5 to −3.5)	20 (51%)		23 (59%)					

Table S2.6: Efficacy outcomes (musculoskeletal, skin, nails, radiographic)

Study identifier	Treatment arm	n	Endpoint (week)	ΔSJC66	ΔTJC68	ΔEGA	ΔCRP (mg/L)	Resolution of dactylitis (%)	Resolution of enthesitis (%)	ΔmSvDHS	NAPSI 0
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16						10		
	Izokibep 40mg Q2W	44							63		
	Izokibep 80mg Q2W	47							88		
Mease ACR 2021 / Mease 2023	Placebo	67	16					8/21 (38.1)	15/35 (42.9)		
	Brepocitinib 10mg QD	31						8/9 (88.9)	6/18 (33.3)		
	Brepocitinib 30mg QD	60						11/19 (57.9)	16/28 (57.1)		
	Brepocitinib 60mg QD	59						11/14 (78.6)	18/28 (64.3)		
Mease 2021a	Placebo Q4W	79	24	−6.0 ± 0.56	−8.8 ± 1.1	−21.9 ± 2.1	0.79 ± 1.0				
	Tildrakizumab 200mg Q4W	78		−7.6 ± 0.56	−10.8 ± 1.1	−32.7 ± 2.1	−4.4 ± 1.1				
	Tildrakizumab 200mg Q12W	79		−7.2 ± 0.56	−11.8 ± 1.1	−36.2 ± 2.0	−2.8 ± 1.0				
	Tildrakizumab 100mg Q12W	77		−7.9 ± 0.57	−12.4 ± 1.1	−35.4 ± 2.1	−3.6 ± 1.0				
	Tildrakizumab 20mg Q12W	78		−6.8 ± 0.56	−10.7 ± 1.1	−32.5 ± 2.1	−2.4 ± 1.1				
Mease 2022a	Placebo	66	16	-4.3 ± 8.0	-4.6 ± 9.7	-19.9 ± 21.8	-3.3 ± 22.6	60.0 (40.8 to 79.2)	22.6 (7.9 to 37.3)		
	Deucravacitinib 6mg QD	70		-7.7 ± 5.8	-9.3 ± 9.7	-33.6 ± 23.0	-14.2 ± 24.5	76.7 (61.5 to 91.8)	51.3 (35.6 to 67.0)		
	Deucravacitinib 12mg QD	67		-8.5 ± 9.1	-12.2 ± 10.2	-32.2 ± 25.0	-10.9 ± 22.8	79.2 (62.9 to 95.4)	50.0 (30.8 to 69.2)		

Deodhar 2020	Placebo	126	24					27/55 (49)	21/77 (27)		
	Guselkumab 100 mg Q4W	128						24/38 (63)	35/73 (48)		
	Guselkumab 100 mg Q8W	127						32/49 (65)	29/72 (40)		
Mease 2020a	Placebo	246	24					38/99 (38)	21/77 (27)	0.95 (0.61 to 1.29)	
	Guselkumab 100 mg Q4W	245						77/121 (64)	35/73 (48)	0.29 (-0.05 to 0.63)	
	Guselkumab 100 mg Q8W	248						63/111 (57)	29/72 (40)	0.52 (0.18 to 0.86)	
Mease 2021b	Placebo	118	24								
	Guselkumab 100 mg Q4W	103									
	Guselkumab 100 mg Q8W	91									
Coates 2021a	Placebo	96	24					9/36 (25.0)	12/64 (18.8)		
	Guselkumab 100 mg Q8W	189						30/67 (44.8)	50/126 (39.7)		
Merola 2023	Placebo	133	16								12/83 (14)
	Bimekizumab 160mg Q4W	267									73/159 (46)
McInnes 2023	Placebo	281	16					24 (51) of 47	37 (35) of 106	0.31 ± 0.09 (n=269)	
	Bimekizumab 160mg Q4W	431						68 (76) of 90	124 (50) of 249	0.01 ± 0.04 (n=420)	
	Adalimumab 40mg Q2W	140						9 (82) of 11	18 (50) of 36	−0.03 ± 0.07 (n=135)	

Kristensen 2022	Placebo	481	24	−6.2 (−6.7, −5.6)	−7.1 (−8.0, −6.1)	−21.1 (−23.2, −19.0)	−0.2 (−1.2, 0.8)	104/204 (51.0)	156/444 (34.8)	0.32 (0.11, 0.53)	
	Risankizumab 150 mg (wk0, wk4, wk16)	483		−8.4 (−8.9, −7.8)	−11.2 (−12.2, −10.3)	−33.9 (−35.9, −31.8)	−4.3 (−5.3, −3.3)	128/188 (68.1)	215/448 (48.4)	0.23 (0.02, 0.44)	
Östör 2022a	Placebo	219	24	−5.5 (−6.5, −4.6)	−6.3 (−7.9, −4.7)	−19.3 (−22.8, −15.9)	0.3 (−1.4, 1.9)	24/57 (42.1)	48/158 (30.4)		
	Risankizumab 150 mg (wk0, wk4, wk16)	224		−8.6 (−9.4, −7.7)	−11.6 (−13.1, −10.1)	−32.4 (−35.6, −29.1)	−1.1 (−2.7, 0.4)	29/40 (72.5)	63/147 (42.9)		
McInnes 2021	Placebo	423	12 / 24*					50/126 (39.7)	78/241 (32.4)	0.25 (0.13 to 0.36) [372]*	
	Upadacitinib 15 mg QD	429						104/136 (76.5)	145/270 (53.7)	−0.04 (−0.16 to 0.07) [391]*	
	Upadacitinib 30 mg QD	423						101/127 (79.5)	154/267 (57.7)	0.03 (−0.08 to 0.15) [383]*	
	Adalimumab 40mg Q2W	429						94/127 (74.0)	125/265 (47.2)	0.01 (−0.11 to 0.13) [384]*	
Mease 2021c	Placebo	212	12 / 24*					23/64 (35.9)	29/144 (20.1)		
	Upadacitinib 15 mg QD	211						35/55 (63.6)	52/133 (39.1)		
	Upadacitinib 30 mg QD	218						38/50 (76.0)	73/152 (48.0)		
Mease 2021d	Placebo	322	16					24,2	23,7		
	Brodalumab 140mg Q2W	318						40,9	42,3		

	Brodalumab 210mg Q2W	322						50,8	39,1		
Koem 2023	Ustekinumab + Placebo	79	24	-6,7	-8,5	-38,2					
	Ustekinumab + MTX 15mg QW	87		-6,4	-8,6	-35,5					
McInnes 2020	Adalimumab 40mg Q2W	427	52	−8.06 ± 0.20	−13.90 ± 0.45	−43.63 ± 0.84		137 (70%)	264 (54%)		
	Secukinumab 300mg	426		−8.41 ± 0.19	−14.27 ± 0.44	−46.24 ± 0.80		130 (75%)	234 (61%)		
Nguyen 2022	Placebo	52	16					4/23 (17.4)	7/39 (17.9)		
	Secukinumab 300mg	103						20/49 (40.8)	28/74 (37.8)		
	Secukinumab 150mg	103						20/52 (38.5)	30/76 (39.5)		
D'Agostino 2022	Placebo	83	16	-3	-4	-18					
	Secukinumab (150mg/300mg)	83		-6	-7	-35					
Baraliakos 2021	Placebo	166	12								
	Secukinumab 300mg	167									
	Secukinumab 150mg	165									
Kivitz 2019	Placebo	114	16					31.8 (44)	21.1 (76)		
	Secukinumab 150mg load	114						32.5 (40)	32.4 (74)		
	Secukinumab 150mg no load	113						42.1 (38)	39.4 (66)		
Mease 2020b	Adalimumab 40mg Q2W	283	24					54/58 (93.1)	77/171 (45.0)		88/177 (49.7)
	Ixekizumab 80mg Q4W	283						37/42 (88.1)	107/189 (56.6)		111/191 (58.1)
Smolen 2020	Adalimumab 40mg Q2W	283	52						84 (57.1) (49.1 to 65.1)		

	Ixekizumab 80mg Q4W	283							98 (61.6) (54.1 to 69.2)		
Vieira-Sousa 2020	Placebo + MTX	23	24	-4	-5			4/22 (18.1)	9/11 (90.0)		
	Golimumab 50mg Q4W + MTX	21		-7	-7.5			6/20 (30.0)	11/11 (100.0)		
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	30			-28.9 ± 22.2	-10.7 ± 14.5				
	Infliximab TDM + csDMARD	20				-23.3 ± 27.7	-6.5 ± 13.8				
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	52								
	Infliximab TDM + csDMARD	28									
Nash 2021	Tofacitinib 5 mg BID + placebo	90	24	0.1 ± 0.2	0.5 ± 0.4	1.8 ± 1.7	−0.3 ± 0.8	87 (100%); n2=87	68 (94%); n2=72		
	Tofacitinib 5 mg BID + MTX	89		0.1 ± 0.2	0.5 ± 0.4	−0.2 ± 1.7	0.5 ± 0.8	78 (100%); n2=78	63 (91%); n2=69		
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16					48/65 (73.8%)	58/97 (59.8%)		
	MTX escalation to 25mg QW	122						27/74 (36.5%)	36/101 (35.6%)		
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16	−2.0 (−4.0 to 0.0)	−2.0 (−5.0 to 0.0)	−12.2 (19.7)	−0.5 (−7.0 to 1.0)				
	Methotrexate 25mg QW + Leflunomide 10mg QD	39		−3.0 (−5.0 to −2.0)	−2.0 (−4.0 to 0.0)	−22.0 (21.9)	0.0 (−4.0 to 1.0)				

Table S2.7: Efficacy outcomes (PROs, Fatigue)

Study identifier	Treatment arm	Endpoint (week)	ΔPGA	ΔPain	ΔHAQ-DI	ΔSF36-PCS	ΔFACIT-F
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44					
	Izokibep 40mg Q2W	44					
	Izokibep 80mg Q2W	47					
Mease ACR 2021 / Mease 2023	Placebo	67		–13.1 (–18.0, –8.23)	-0.18 (-0.28, -0.08)	1.73 (0.06, 3.40)	3.84 (2.02 to 5.65)
	Brepocitinib 10mg QD	31		–23.4 (–30.7, –16.1)	-0.32 (-0.47, -0.17)	5.04 (2.56, 7.52)	4.60 (1.89,7.31)
	Brepocitinib 30mg QD	60		–24.9 (–30.1, –19.8)	-0.50 (-0.61, -0.39)	6.76 (4.99, 8.53)	7.13 (5.23 to 9.04)
	Brepocitinib 60mg QD	59		–30.5 (–35.6, –25.3)	-0.50 (-0.61, -0.40)	6.57 (4.80, 8.34)	5.89 (3.99 to 7.79)
Mease 2021a	Placebo Q4W	79	–20.0 ± 2.3	–20.6 ± 2.6	–0.2 ± 0.05		
	Tildrakizumab 200mg Q4W	78	–31.3 ± 2.3	–31.7 ± 2.7	–0.3 ± 0.05		
	Tildrakizumab 200mg Q12W	79	–30.9 ± 2.3	–30.4 ± 2.6	–0.3 ± 0.05		
	Tildrakizumab 100mg Q12W	77	–31.1 ± 2.4	–30.3 ± 2.7	–0.3 ± 0.05		
	Tildrakizumab 20mg Q12W	78	–26.9 ± 2.3	–25.7 ± 2.7	–0.2 ± 0.05		
Mease 2022a	Placebo	66	-13.4 ± 23.5	-13.8 ± 21.5	–0.1 (–0.2 to 0.0)	2.3 (0.4 to 4.2)	
	Deucravacitinib 6mg QD	70	-28.7 ± 23.1	-25.3 ± 26.1	–0.4 (–0.5 to –0.2)	5.6 (3.8 to 7.5)	

	Deucravacitinib 12mg QD	67	-27.6 ± 25.8	-27.5 ± 25.0	−0.4 (−0.5 to −0.3)	5.8 (3.9 to 7.7)	
Deodhar 2020	Placebo	126			−0.07 (−0.16 to 0.01)	1.96 (0.69 to 3.24)	
	Guselkumab 100 mg Q4W	128			−0.40 (−0.48 to −0.31)	6.87 (5.60 to 8.14)	
	Guselkumab 100 mg Q8W	127			−0.32 (−0.41 to −0.24)	6.10 (4.83 to 7.37)	
Mease 2020a	Placebo	246			−0.13 (−0.19 to −0.07)	3.42 (2.53 to 4.32)	
	Guselkumab 100 mg Q4W	245			−0.40 (−0.46 to −0.34)	7.04 (6.14 to 7.94)	
	Guselkumab 100 mg Q8W	248			−0.37 (−0.43 to −0.31)	7.39 (6.50 to 8.29)	
Mease 2021b	Placebo	118					
	Guselkumab 100 mg Q4W	103					
	Guselkumab 100 mg Q8W	91					
Coates 2021a	Placebo	96			-0.01	-0.39	
	Guselkumab 100 mg Q8W	189			-0.22	3.51	
Merola 2023	Placebo	133		−4.5 (2.1)	−0.07 (0.04)	1.4 (0.7)	0.1 (0.7)
	Bimekizumab 160mg Q4W	267		−27.7 (1.7)	−0.38 (0.03)	7.3 (0.5)	5.5 (0.6)
McInnes 2023	Placebo	281		−6.2 ± 1.5	−0.09 ± 0.03	2.3 ± 0.5	1.5 ± 0.5
	Bimekizumab 160mg Q4W	431		−23.6 ± 1.3	−0.26 ± 0.02	6.3 ± 0.4	3.9 ± 0.4
	Adalimumab 40mg Q2W	140		−25.7 ± 2.5	−0.33 ± 0.04	6.8 ± 0.8	5.0 ± 0.7
Kristensen 2022	Placebo	481	−10.5 (−12.8, −8.3)	−10.2 (−12.5, −8.0)	−0.11 (−0.16,–0.06)	3.2 (2.5, 3.9)	3.9 (3.1, 4.7)

	Risankizumab 150 mg (wk0, wk4, wk16)	483	−21.6 (−23.9, −19.4)	−21.0 (−23.2, −18.8)	−0.31 (−0.36,–0.27)	6.5 (5.8, 7.2)	6.5 (5.6, 7.3)
Östör 2022a	Placebo	219	−7.7 (−11.1, −4.2)	−6.5 (−9.9, −3.1)	−0.05 (−0.12 to 0.02)	2.0 (0.9 to 3.1)	2.6 (1.4 to 3.9)
	Risankizumab 150 mg (wk0, wk4, wk16)	224	−16.5 (−19.7, −13.3)	−14.7 (−17.8, −11.5)	−0.22 (−0.28 to –0.15)	5.9 (4.9 to 6.9)	4.9 (3.7 to 6.0)
McInnes 2021	Placebo	423		−0.9 (−1.2 to −0.7) [392]	−0.14 (−0.18 to −0.09) [392]	3.2 (2.4 to 4.0) [394]	2.8 (1.9 to 3.7) [394]
	Upadacitinib 15 mg QD	429		−2.3 (−2.5 to −2.0) [404]	−0.42 (−0.47 to −0.37) [404]	7.9 (7.1 to 8.6) [405]	6.3 (5.4 to 7.2) [404]
	Upadacitinib 30 mg QD	423		−2.7 (−2.9 to −2.5) [398]	−0.47 (−0.52 to −0.42) [398]	8.9 (8.1 to 9.7) [398]	7.1 (6.2 to 8.0) [398]
	Adalimumab 40mg Q2W	429		−2.3 (−2.5 to −2.1) [406]	−0.34 (−0.38 to −0.29) [406]	6.8 (6.1 to 7.6) [410]	5.7 (4.8 to 6.6) [410]
Mease 2021c	Placebo	212			−0.10 (−0.16 to −0.03)	1.6 (0.6 to 2.7)	1.3 (0.1 to 2.5)
	Upadacitinib 15 mg QD	211			−0.30 (−0.37 to −0.24)	5.2 (4.1 to 6.2)	5.0 (3.8 to 6.1)
	Upadacitinib 30 mg QD	218			−0.41 (−0.47 to −0.35)	7.1 (6.1 to 8.1)	6.1 (4.9 to 7.2)
Mease 2021d	Placebo	322			–0,154		
	Brodalumab 140mg Q2W	318			–0,321		
	Brodalumab 210mg Q2W	322			–0,385		
Koem 2023	Ustekinumab + Placebo	79	-26,0		-0,3		
	Ustekinumab + MTX 15mg QW	87	-18,1		-0,2		

McInnes 2020	Adalimumab 40mg Q2W	427	−31.61 ± 1.19	−29.44 ± 1.23	−0.56 (0.03) [318]	8,3	
	Secukinumab 300mg	426	−33.81 ± 1.14	−30.21 ± 1.18	−0.58 (0.03) [363]	5,2	
Nguyen 2022	Placebo	52			-0.11		
	Secukinumab 300mg	103			-0.32		
	Secukinumab 150mg	103			-0.24		
D'Agostino 2022	Placebo	83	-7	-6	-0.2 (0.1)		
	Secukinumab (150mg/300mg)	83	-34	-31	-0.7 (0.1)		
Baraliakos 2021	Placebo	166			−0.2 (0.04)		4.2 (0.7)
	Secukinumab 300mg	167			−0.4 (0.04)		7.6 (0.7)
	Secukinumab 150mg	165			−0.3 (0.04)		8.0 (0.7)
Kivitz 2019	Placebo	114				0.63 (0.59)	− 0.05 (0.89)
	Secukinumab 150mg load	114				3.42 (0.58)	2.81 (0.87)
	Secukinumab 150mg no load	113				3.44 (0.58)	4.23 (0.87)
Mease 2020b	Adalimumab 40mg Q2W	283					
	Ixekizumab 80mg Q4W	283					
Smolen 2020	Adalimumab 40mg Q2W	283				9.6 (0.5)	
	Ixekizumab 80mg Q4W	283				10.1 (0.5)	
Vieira-Sousa 2020	Placebo + MTX	23	-16.5		-0.188		
	Golimumab 50mg Q4W + MTX	21	-34		-0.375		
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	-28.1 ± 25.1				
	Infliximab TDM + csDMARD	20	-18.6 ± 29.2				
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25					

	Infliximab TDM + csDMARD	28					
Nash 2021	Tofacitinib 5 mg BID + placebo	90	4.5 ± 1.7			−1.4 ± 0.5	−2.0 ± 0.6
	Tofacitinib 5 mg BID + MTX	89	3.2 ± 1.7			−0.7 ± 0.5	−1.3 ± 0.6
Coates 2022	Adalimumab 40mg Q2W + MTX	123			−0.5 (−0.6 to −0.4)	8.9 (7.6–10.2)	
	MTX escalation to 25mg QW	122			−0.3 (−0.4 to −0.2)	4.4 (3.1–5.7)	
Mulder 2022	Placebo + Methotrexate 25mg QW	39	−13.9 (28.3)	4.1 ± 1.7	−0.1 (0.4)		
	Methotrexate 25mg QW + Leflunomide 10mg QD	39	−20.9 (24.4)	3.1 ± 1.7	−0.2 (0.4)		

Table S2.8: Outcomes of trials investigating DMARD dose reduction and discontinuation.

Study identifier	Treatment arm	n	Tapering: Primary Outcome	Tapering: Definition of primary outcome / flare	Tapering: Primary Endpoint (week)	Tapering: Result	non-inferiority margin	P / 95% CI
Michielsens 2022	T2T with tapering	42	PASDAS LDA	PASDAS >3.2 or increase of ≥0.8; important worsening of mBSA or active extra-musculoskeletal symptoms	104	30 (71%)	20%	8% (-14% to 30%)
	T2T without tapering	22				16 (73%)		
Coates 2021b	Ixekizumab withdrawal	79	median time to relapse (loss of MDA) in weeks	loss of MDA	104	22.3 (95% CI: 16.1-28.3); 85% relapse rate		p<0.001
	Ixekizumab 80mg Q2W	79				time to relapse not estimateable; 38% relapse rate		
Nash 2021	Tofacitinib 5 mg BID + placebo	90	ΔPASDAS + ΔHAQ	HAQ: Δ0.18; PASDAS: Δ0.47	24	ΔPASDAS: 0.23 (SE 0.08); ΔHAQ: 0.04 (SE 0.03)		Treatment difference: 0.03 (95% CI – 0.05 to 0.10)
	Tofacitinib 5 mg BID + MTX	89				ΔPASDAS: 0.14 (SE 0.08); ΔHAQ: 0.02 (SE 0.03)		
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	sustained MDA	MDA	24	57%		NR
	Etanercept interval continuation (QW)	20				70%		

Section 3: Safety

Table S3.1: Safety: Details of articles and abstracts selected for inclusion.

PICO	Study	Comparison	Outcome	Database type	Database	Analysis type	Population	Comparator arms
2, 3, 5	Winthrop 2023	TOFA vs. ADA vs. PBO	Influenza	RCT	TOFA trial database	RCT safety	csDMARD iR	Placebo + csDMARD (PBO controlled period)
								Tofacitinib 5mg BID + csDMARD (PBO controlled period)
								Tofacitinib 10mg BID + csDMARD (PBO controlled period)
								Tofacitinib 5mg BID + csDMARD (active controlled period)
								Tofacitinib 10mg BID + csDMARD (active controlled period)
								Adalimumab 40mg Q2W + csDMARD (active controlled period)
2, 5	Glintborg 2023	TNFi vs. IL17i	infection	registry	DANBIO, ROB-FIN, NOR-DMARD, ARTIS/SRQ	cohort		Secukinumab
								Adalimumab
								Certolizumab pegol
								Etanercept
								Golimumab
								Infliximab
2, 5	Jin & Lee 2021	IL12/23i vs. TNFi vs. IL17A vs. PDE4i	serious infection	claims	IBM MarketScan, Optums Data Mart	cohort		Ustekinumab
								Adalimumab
								Apremilast
								Certolizumab
								Etanercept
								Golimumab
								Infliximab
								Ixekizumab
								Secukinumab
2	Krabbe 2021	TNFi vs. GP	serious infection	registry	DANBIO	cohort	first bDMARD	bDMARD
								General population (matched)

2, 5	Li 2019	TNFi vs. IL17i vs IL12/23i	serious infection	claims	Optum's Data Mart	cohort		all bDMARDs
								TNFi
								IL-17i
								IL-12/23i
2	Elewski 2020	IL17i vs. Placebo	tbc/ltbi	RCT	Secukinumab trial database	cohort		All Secukinumab treated patients
								Secukinumab treated patients with +LTBI
2	Rotar 2019	TNFi vs. GP	tbc	registry	biorx.si	cohort		TNFi
2	Hellgren 2021	TNFi vs. bDMARD naive/GP	solid cancer	registry	DANBIO, ROB-FIN, NOR-DMARD, ARTIS/SRQ, ICEBIO	cohort		TNFi vs bDMARD naive/GP
2	Lebwohl 2021	IL17i vs. GP	malignancy	RCT	Secukinumab trial database, SEER	RCT safety		IL17i
2	Fagerli 2019	TNFi vs. GP	malignancy	registry	British Society for Rheumatology Biologics Register	cohort		TNFi
2	Cordtz 2022	TNFi vs. Biologic naive vs. GP	hematologic malignancy	registry	DANBIO, ROB-FIN, NOR-DMARD, ARTIS/SRQ	cohort	first TNFi vs. bDMARD naive	TNFi
								bDMARD naive
2	Stovall 2021	TNFi vs. csDMARD	myocardial infarction	claims	Optum's Data Mart	case-control		MI Cases
								Controls
2	Pina Vegas 2022	TNFi vs. IL12/23i vs. IL17i vs. PDE4i	mace	claims	Frech national health insurance database (SNDS)	cohort	bDMARD naive; no previous CVD	TNFi
								IL12/23i
								IL17i
								PDE4i
2	Persson 2021	bDMARD vs. csDMARDs	myocardial infarction	claims	Market scan	cohort		Apremilast mono
								csDMARD mono
								TNFi mono
								IL17/12/23i inhibition mono
								GC mono

								Apremilast + csDMARDs
								csDMARD + GC
								TNFi + csDMARDs
								IL17/12/23i + csDMARDs
								Unexposed
2, 3	Mease 2020b	TOFA vs. Placebo	VTE + ATE	RCT	Tofacitinib trial database	RCT safety		Average tofacitinib 5 mg
								Average tofacitinib 10 mg twice daily
								Placebo
								Adalimumab 40mg Q2W
2	Tang 2020	TNFi vs. Non	liver disease	claims	IBM MarketScan	cohort		TNFi
								no TNFi
2	Vasilakis-Scaramozza 2020	csDMARDs vs. bDMARDs vs. PDE4i	anxiety and depression	claims	IBM MarketScan	cohort		Treated anxiety + depression
								DMARDs only
								Apremilast only
								TNF-i biologics only
								IL-i biologics only
								Corticosteroids only
								Apremilast + any non-steroid
								TNF-i with DMARDs
								IL-i with DMARDs
								Corticosteroids + any other‡
								Unexposed
2	Ghosh 2019	Ustekinumab vs. Placebo	AE, infection, mace, malignancies	RCT	Ustekinumab trial database	RCT safety		Placebo
2	Gossec 2023	Ustekinumab vs. TNFi	AE, infection, mace, malignancies	observational study				Ustekinumab
								TNFi
2	Meng ACR 2022	TNFi vs. Non-TNFi	mace	registry	Hong Kong citywide database	cohort		

2	Strober ACR 2022	Guselkumab vs. Placebo	AE, infection, mace, malignancies	RCT	Guselkumab trial database	RCT safety		Placebo
								Guselkumab 100mg Q8W
								Guselkumab 100mg Q4W
2	Mease ACR 2022b	Apremilast vs. Placebo	AE, infection, mace, malignancies	RCT	Apremilast trial database	RCT safety		Placebo
								Apremilast
2, 3, 5	Rubbert-Roth ACR 2022	Upadacitinib vs. Adalimumab	malignancy, nmsc, lymphoma	RCT	Upadacitinib trial database	RCT safety		Upadacitinib 15mg OD
								Adalimumab 40mg Q2W
2, 3, 5	Charles-Schoeman ACR 2022	Upadacitinib vs. Adalimumab	mace, vte	RCT	Upadacitinib trial database	RCT safety		Adalimumab 40mg Q2W
								Upadacitinib 15mg OD
								Upadacitinib 30mg OD

Table S3.2: Safety: Risk of bias analysis of cohort studies (Newcastle-Ottawa scale)

Study	Selection bias			Comparability of cohorts (design/analysis)			Outcome			Overall	Comment
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Study controls for most important factor	Study controls for any additional factor	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts		
Winthrop 2023	*	*	*	*	*	*	*	*	*	**low**	trial database: adverse event of special interest
Glintborg 2023	*	*	*		*	*	*	*	*	**low**	
Jin & Lee 2021	*			*	*	*		*	*	**high**	PsA cohort as small subpopulation, baseline characteristics for PsA patients not reported
Li 2019	*	*		*	*	*		*	*	**high**	claims data
Elewski 2020	*	*	*	*	*	*	*	*	*	**low**	trial database: adverse event of special interest
Rotar 2019	*	*	*	*	*	*	*	*	*	**low**	

Hellgren 2021	*	*		*	*		*	*	*	**unclear**	not adjusted for smoking status; baseline characteristics for overall population / control not reported
Lebwohl 2021	*		*	*			*		*	**high**	not adjusted for risk factors on malignancy, short follow-up, trial database: adverse event of special interest
Fagerli 2019	*	*					*	*	*	**high**	not adjusted for risk factors
Cordtz 2022	*	*	*		*	*	*	*	*	**low**	
Pina Vegas 2022	*	*		*		*		*	*	**high**	not adjusted for smoking status (not assessed), claims data
Persson 2021	*	*		*		*		*	*	**high**	not adjusted for smoking status (not assessed), claims data
Mease 2020b	*	*	*	*	*		*			**high**	follow-up time not long enough, small sample size, trial database: adverse

											event of special interest
Tang 2020	*				*			*	*	**high**	non-exposed cohort heterogenous, claims data
Vasilakis-Scaramozza 2020	*	*		*		*	*	*	*	**high**	
Ghosh 2019	*	*	*	*	*	*	*	*	*	**low**	RCT database: integrated safety analysis
Gossec 2021	*	*	*	*	*	*	*	*	*	**low**	
Each category can be rated with a star (*), based on the respective assessment. This leads to a possible maximum of 4 stars for selection, 2 stars for comparability and 3 stars for exposure.											

Table S3.3: Safety: Risk of bias analysis of case-control studies (Newcastle-Ottawa scale)

Study	**Selection bias**				**Comparability of cases and controls (design/analysis)**		**Exposure**			**Overall**	**Comment**
	Case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls	Study controls for most important factor	Study controls for any additional factor	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate		
Krabbe 2021	*	*	*		*	*	*	*		unclear	
Stovall 2021	*	*	*	*	*	*		*		high	claims data

Table S3.4: Baseline characteristics of safety studies.

Study	Comparator arms	No. of patients (n)	Mean age (years)	prev TNFi (%)	concom. MTX	concom. csDMARD	concom. Steroids (%)	PsA disease duration (years)	Male (%)	Female (%)	BMI (kg/m²)
Winthrop 2023	Placebo + csDMARD (PBO controlled period)	236	NR	NR			NR	NR		NR	NR
	Tofacitinib 5mg BID + csDMARD (PBO controlled period)	238	48.7 (12.0)	377 (48.1)			171 (21.8)	7.7 (7.2)		428 (54.7)	29.6 (6.0)
	Tofacitinib 10mg BID + csDMARD (PBO controlled period)	236									
	Tofacitinib 5mg BID + csDMARD (active controlled period)	347									
	Tofacitinib 10mg BID + csDMARD (active controlled period)	344									
	Adalimumab 40mg Q2W + csDMARD (active controlled period)	106	NR	NR			NR	NR		NR	NR
Glintborg 2023	Secukinumab	1142	52 (12)		114 (15)	144 (18)	148 (19)	9.5 (8.8)	455 (40)		
	Adalimumab	1303	50 (13)		83 (10)	114 (14)	114 (14)	7.3 (9.0)	612 (47)		
	Certolizumab pegol	674	49 (12)		147 (29)	191 (38)	72 (14)	8.2 (8.8)	268 (40)		
	Etanercept	2726	50 (13)		218 (11)	271 (14)	251 (13)	6.5 (7.8)	1213 (45)		
	Golimumab	549	49 (13)		68 (17)	84 (22)	50 (13)	9.2 (8.6)	250 (46)		
	Infliximab	1390	49 (13)		388 (36)	463 (43)	124 (11)	7.6 (8.2)	619 (45)		
Jin & Lee 2021	Ustekinumab	NR									
	Adalimumab	NR									

	Apremilast	NR									
	Certolizumab	NR									
	Etanercept	NR									
	Golimumab	NR									
	Infliximab	NR									
	Ixekizumab	NR									
	Secukinumab	NR									
Krabbe 2021	bDMARD	2429	47.8 (38.4–56.2)		50.5		19.2	2.8 (0.9–7.5)	45.6	54.4	
	General population (matched)	24288	47.8 (38.4–56.2)				1.0		45.6	54.4	
Li 2019	all bDMARDs	5517									
	TNFi	3685									
	IL-17i	944									
	IL-12/23i	888									
Elewski 2020	All Secukinumab treated patients	2523	48.8 (12.1)						1200 (47.6)		
	Secukinumab treated patients with +LTBI	152	50.6 (12.9)						73 (48.0)		
Rotar 2019	TNFi	413	40.4 (33.2–49.0)		0,53	0,68	0,07			46.2	
Hellgren 2021	TNFi vs bDMARD naive/GP	9655									
Lebwohl 2021	IL17i	2523									
Fagerli 2019	TNFi	709	45.7 (11)		427 (60)		168 (24)	12.7 (8.7)		378 (53)	
Cordtz 2022	TNFi	10621									
	bDMARD naive										
Stovall 2021	MI Cases	404	61.5 (11.2)							167 (41.3%)	
	Controls	1596	61.4 (11.2)							660 (41.4%)	
Pina Vegas 2022	TNFi	7289	48.2 (12.8)			2992 (41.0)	747 (10.2)		3002 (41.2)		

	IL12/23i	1058	49.8 (12.8)			305 (28.8)	72 (6.8)		475 (44.9)		
	IL17i	1163	49.2 (12.2)			336 (28.9)	102 (8.8)		482 (41.4)		
	PDE4i	1885	54.0 (12.5)			653 (34.6)	160 (8.5)		835 (44.3)		
Persson 2021	Apremilast mono	2881	53					0.2	1287 (44.7)	1594 (55.3)	
	csDMARD mono	12248	53					0.1	5393 (44.0)	6855 (56.0)	
	TNFi mono	23818	51					0.3	13185 (55.4)	10633 (44.6)	
	IL17/12/23i inhibition mono	3598	49					0.2	1857 (51.6)	1741 (48.4)	
	GC mono	11941	53					0.0	4972 (41.6)	6969 (58.4)	
	Apremilast + csDMARDs	782	54					0.0	307 (39.3)	475 (60.7)	
	csDMARD + GC	4054	54					0.0	1590 (39.2)	2464 (60.8)	
	TNFi + csDMARDs	8472	53					0.3	3723 (43.9)	4749 (56.1)	
	IL17/12/23i + csDMARDs	884	51					0.0	390 (44.1)	494 (55.9)	
	Unexposed	27180									
Mease 2020b	Average tofacitinib 5 mg	458	49.2 (11.9)	190 (41.5)	432 (94.3)	205 (44.8)	109 (23.8)			258 (56.3)	29.5 (5.9) (458)
	Average tofacitinib 10 mg twice daily	325	48.0 (12.2)	187 (57.5)	293 (90.2)	165 (50.8)	62 (19.1)			170 (52.3)	29.8 (6.2) (325)
	Placebo	236									
	Adalimumab 40mg Q2W										
Tang 2020	TNFi	5015	48 (19–65)		25.6		9.2			50.9	

	no TNFi	13330	51 (19–65)		14.5		4.3			54.3	
Vasilakis-Scaramozza 2020	Treated anxiety + depression	30426	52.9						17 159 (56.4)	13 267 (43.6)	
	DMARDs only	5484									
	Apremilast only	1293									
	TNF-i biologics only	10986									
	IL-i biologics only	1541									
	Corticosteroids only	5376									
Ghosh 2019	Placebo	379									
	Ustekinumab	1018	47.6 (11.87)	20.5 (220/1073)	482 (44.9)	482 (44.9)	100 (9.3)		560 (52.2)		31.0 (7.13)
Gossec 2023	Ustekinumab	438	51.0 (12.5) (49.9; 52.2)		131 (29.9) (25.7; 34.4)	173 (39.5) (34.9; 44.2)	143 (32.6) (28.3; 37.3)	7.5 (8.1) (6.7; 8.3)		246 (56.2) (51.4; 60.9)	28.6 (6.2) (27.9; 29.2)
	TNFi	455	48.5 (12.5) (47.3; 49.7)		191 (42.0) (37.4; 46.7)	251 (55.2) (50.5; 59.8)	156 (34.3) (29.9; 38.8)	6.2 (6.6) (5.6; 6.9)		248 (54.5) (49.8; 59.1)	27.7 (5.3) (27.2; 28.2)
Meng ACR 2022		1672	51.0 (12.8)		918 (54.9)		176 (10.5)	0.3 (1)	942 (56.3)		
Strober ACR 2022	Placebo	517									
	Guselkumab 100mg Q8W	664									
	Guselkumab 100mg Q4W	373									
Mease ACR 2022b	Placebo	780									
	Apremilast	781									
Rubbert-Roth ACR 2022	Upadacitinib 15mg OD	907									
	Adalimumab 40mg Q2W	429									

Charles-Schoeman ACR 2022	Adalimumab 40mg Q2W	429									
	Upadacitinib 15mg OD	907									
	Upadacitinib 30mg OD	921									

Table S3.4.1: Safety of RCTs: AE, serious AE, discontinuations, deaths

Study identifier	Treatment arm	No. of patients (n)	Safety Endpoint	Any AE	Serious TEAEs	Discontinuations due to TEAEs	Deaths
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16				
	Izokibep 40mg Q2W	44					
	Izokibep 80mg Q2W	47					
Mease ACR 2021	Placebo	67	16	32 (47.8)	1 (1.5)	3 (4.5)	0 (0.0)
	Brepocitinib 10mg QD	31		14 (45.2)	0 (0.0)	0 (0.0)	0 (0.0)
	Brepocitinib 30mg QD	60		33 (55.0)	3 (5.0)	2 (3.3)	0 (0.0)
	Brepocitinib 60mg QD	59		40 (66.7)	1 (1.7)	3 (5.0)	0 (0.0)
Mease 2021a	Placebo Q4W	79	24	34 (43.0)	2 (2.5)	0	0
	Tildrakizumab 200mg Q4W	78		39 (50.0)	2 (2.6)	0	0
	Tildrakizumab 200mg Q12W	79		39 (49.4)	2 (2.5)	0	0
	Tildrakizumab 100mg Q12W	77		44 (57.1)	2 (2.6)	0	0
	Tildrakizumab 20mg Q12W	78		34 (43.6)	1 (1.3)	0	0
Mease 2022a	Placebo	66	16	28 (42.4)	1 (1.5)	1 (1.5)	0
	Deucravacitinib 6mg QD	70		46 (65.7)	0	3 (4.3)	0
	Deucravacitinib 12mg QD	67		44 (65.7)	0	4 (6.0)	0

Deodhar 2020	Placebo	126	24	75 (60)	5 (4)	3 (2)	1 (1)
	Guselkumab 100 mg Q4W	128		71 (55)	0	1 (1)	0
	Guselkumab 100 mg Q8W	127		68 (54)	4 (3)	3 (2)	0
Mease 2020a	Placebo	246	24	100 (41)	7 (3)	4 (2)	
	Guselkumab 100 mg Q4W	245		113 (46)	8 (3)	6 (2)	
	Guselkumab 100 mg Q8W	248		114 (46)	3 (1)	2 (1)	
Mease 2021b	Placebo	118	24				
	Guselkumab 100 mg Q4W	103					
	Guselkumab 100 mg Q8W	91					
Coates 2021a	Placebo	96	24	46 (47.9)	3 (3.1)	2 (2.1)	
	Guselkumab 100 mg Q8W	189		80 (42.3)	7 (3.7)	4 (2.1)	
Merola 2023	Placebo	133	16	44 (33)	0	0	0
	Bimekizumab 160mg Q4W	267		108 (40)	5 (2)	2 (1)	0
McInnes 2023	Placebo	281	16	139 (49)	3 (1)	3 (1)	0
	Bimekizumab 160mg Q4W	431		258 (60)	7 (2)	8 (2)	0
	Adalimumab 40mg Q2W	140		83 (59)	2 (1)	3 (2)	0
Kristensen 2022	Placebo	481	24	186 (38.7)	18 (3.7)	4 (0.8)	0
	Risankizumab 150 mg (wk0, wk4, wk16)	483		195 (40.4)	12 (2.5)	4 (0.8)	1 (0.2)
Östör 2022a	Placebo	219	24	120 (54.8)	12 (5.5)	5 (2.3)	0

	Risankizumab 150 mg (wk0, wk4, wk16)	224		124 (55.4)	9 (4.0)	2 (0.9)	0
McInnes 2021	Placebo	423	24	252 (59.6)	13 (3.1)	13 (3.1)	1 (0.2)
	Upadacitinib 15 mg QD	429		287 (66.9)	14 (3.3)	13 (3.0)	0
	Upadacitinib 30 mg QD	423		306 (72.3)	26 (6.1)	21 (5.0)	0
	Adalimumab 40mg Q2W	429		278 (64.8)	16 (3.7)	22 (5.1)	0
Mease 2021c	Placebo	212	24	139 (65.6)	4 (1.9)	11 (5.2)	1 (0.5)
	Upadacitinib 15 mg QD	211		135 (64.0)	12 (5.7)	15 (7.1)	0
	Upadacitinib 30 mg QD	218		170 (78.0)	18 (8.3)	20 (9.2)	0
Mease 2021d	Placebo	322	16	174 (54.4)	9 (2.8)	7 (2.2)	0,00
	Brodalumab 140mg Q2W	318		164 (51.6)	6 (1.9)	3 (0.9)	0
	Brodalumab 210mg Q2W	322		175 (54.5)	11 (3.4)	4 (1.2)	0
Koem 2023	Ustekinumab + Placebo	79	24	71 (90%)			
	Ustekinumab + MTX 15mg QW	87		76 (87%)			
McInnes 2020	Adalimumab 40mg Q2W	427	52	338 (79%)	28 (7%)	32 (7%)	0
	Secukinumab 300mg	426		330 (77%)	32 (8%)	17 (4%)	1
Nguyen 2022	Placebo	52	16	27 (51.9)	2 (3.8)	0	1 (1.9)
	Secukinumab 300mg	103		59 (57.3)	2 (1.9)	1 (1.0)	0
	Secukinumab 150mg	103		61 (59.2)	2 (1.9)	1 (1.0)	0
D'Agostino 2022	Placebo	83	16	47 (57%)	2 (2.4%)	2 (2.4%)	0

	Secukinumab (150mg/300mg)	83		48 (58%)	0	0	0
Baraliakos 2021	Placebo	166	16	80 (48.2.)	4 (2.4)	1 (0.6)	0
	Secukinumab 300mg	167		67 (40.1)	4 (2.4)	1 (0.6)	0
	Secukinumab 150mg	165		61 (37.0)	1 (0.6)	3 (1.8)	0
Kivitz 2019	Placebo	114					
	Secukinumab 150mg load	114					
	Secukinumab 150mg no load	113					
Mease 2020b	Adalimumab 40mg Q2W	283	24	173 (61.1)	24 (8.5)	13 (4.6)	0
	Ixekizumab 80mg Q4W	283		197 (69.6)	10 (3.5)	7 (2.5)	0
Smolen 2020	Adalimumab 40mg Q2W	283	52	194 (68.6)	35 (12.4)	21 (7.4)	0
	Ixekizumab 80mg Q4W	283		209 (73.9)	12 (4.2)	12 (4.2)	0
Vieira-Sousa 2020	Placebo + MTX	23	NR				
	Golimumab 50mg Q4W + MTX	21					
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	NR				
	Infliximab TDM + csDMARD	20					
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	NR				
	Infliximab TDM + csDMARD	28					
Michielsens 2022	T2T with tapering	42					
	T2T without tapering	22					

Coates 2021b	Ixekizumab withdrawal	79	104	40 (50.6)	2 (2.5)	1 (1.3)	0 (0)
	Ixekizumab 80mg Q2W	79		40 (50.6)	1 (1.3)	0 (0)	0 (0)
Nash 2021	Tofacitinib 5 mg BID + placebo	90	104	43 (48%)	4 (4%)	3 (3%)	0
	Tofacitinib 5 mg BID + MTX	89		41 (46%)	3 (3%)	4 (4%)	0
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	NR				
	Etanercept interval continuation (QW)	20					
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16	76 (62%)	2 (2%)	3 (2%)	0
	MTX escalation to 25mg QW	122		70 (57%)	0	2 (2%)	0
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16		0	3 (8%)	0
	Methotrexate 25mg QW + Leflunomide 10mg QD	39			3 (8%)	10 (25.6%)	0

Table S3.4.2: Safety of RCTs: Infections, serious infections, URTI, urinary infections

Study identifier	Treatment arm	n	week	Infections and infestations	Serious infections	Upper respiratory tract infection	Bronchitis	Nasopharyngitis	Urinary tract infection
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16						
	Izokibep 40mg Q2W	44							
	Izokibep 80mg Q2W	47							
Mease ACR 2021	Placebo	67	16	16 (23.9)	0 (0.0)				
	Brepocitinib 10mg QD	31		9 (29.0)	0 (0.0)				
	Brepocitinib 30mg QD	60		21 (35.0)	2 (3.3)				
	Brepocitinib 60mg QD	59		21 (35.0)	0 (0.0)				
Mease 2021a	Placebo Q4W	79	24		0	1 (1.3)			3 (3.8)
	Tildrakizumab 200mg Q4W	78			0	2 (2.6)			0
	Tildrakizumab 200mg Q12W	79			0	4 (5.1)			1 (1.3)

	Tildrakizumab 100mg Q12W	77			0	3 (3.9)			3 (3.9)
	Tildrakizumab 20mg Q12W	78			1 (1.3)	2 (2.6)			1 (1.3)
Mease 2022a	Placebo	66	16		0	0		5 (7.6)	
	Deucravacitinib 6mg QD	70			0	4 (5.7)		4 (5.7)	
	Deucravacitinib 12mg QD	67			0	1 (1.5)		12 (17.9)	
Deodhar 2020	Placebo	126	24	32 (25)	2 (2)	8 (6)		8 (6)	
	Guselkumab 100 mg Q4W	128		31 (24)	0	11 (9)		7 (5)	
	Guselkumab 100 mg Q8W	127		33 (26)	0	7 (6)		16 (13)	
Mease 2020a	Placebo	246	24	45 (18)	1 (<1)	8 (3)	3 (1)	9 (4)	
	Guselkumab 100 mg Q4W	245		49 (20)	3 (1)	12 (5)	10 (4)	12 (5)	
	Guselkumab 100 mg Q8W	248		40 (16)	1 (<1)	6 (2)	1 (<1)	10 (4)	
Mease 2021b	Placebo	118	24						
	Guselkumab 100 mg Q4W	103							
	Guselkumab 100 mg Q8W	91							
Coates 2021a	Placebo	96	24	19 (19.8)	0			5 (5.2)	3 (3.1)
	Guselkumab 100 mg Q8W	189		40 (21.2)	1 (0.5)			10 (5.3)	7 (3.7)
Merola 2023	Placebo	133	16		0			1 (1)	2 (2)

	Bimekizumab 160mg Q4W	267			2 (1)			10 (4)	6 (2)
McInnes 2023	Placebo	281	16	56 (20)	0	18 (6)		13 (5)	4 (1)
	Bimekizumab 160mg Q4W	431		131 (30)	1 (<1)	21 (5)		40 (9)	9 (2)
	Adalimumab 40mg Q2W	140		35 (25)	1 (1)	3 (2)		7 (5)	3 (2)
Kristensen 2022	Placebo	481	24		6 (1.2)	20 (4.2)		14 (2.9)	
	Risankizumab 150 mg (wk0, wk4, wk16)	483			5 (1.0)	12 (2.5)		16 (3.3)	
Östör 2022a	Placebo	219	24		5 (2.3)	12 (5.5)	4 (1.8)	8 (3.7)	
	Risankizumab 150 mg (wk0, wk4, wk16)	224			2 (0.9)	17 (7.6)	5 (2.2)	9 (4.0)	
McInnes 2021	Placebo	423	24	140 (33.1)	4 (0.9)				
	Upadacitinib 15 mg QD	429		169 (39.4)	5 (1.2)				
	Upadacitinib 30 mg QD	423		183 (43.3)	11 (2.6)				
	Adalimumab 40mg Q2W	429		146 (34.0)	3 (0.7)				
Mease 2021c	Placebo	212	24	73 (34.4)	1 (0.5)				
	Upadacitinib 15 mg QD	211		71 (33.6)	1 (0.5)				
	Upadacitinib 30 mg QD	218		108 (49.5)	6 (2.8)				
Mease 2021d	Placebo	322	16	91 (28.4)					

	Brodalumab 140mg Q2W	318		75 (23.6)					
	Brodalumab 210mg Q2W	322		96 (29.9)					
Koem 2023	Ustekinumab + Placebo	79	24	51 (65%)		11 (14%)	5 (6%)	21 (27%)	
	Ustekinumab + MTX 15mg QW	87		47 (54%)		7 (8%)	5 (6%)	18 (21%)	
McInnes 2020	Adalimumab 40mg Q2W	427	52	234 (55%)	6 (1%)	49 (11%)	23 (5%)	80 (19%)	
	Secukinumab 300mg	426		237 (56%)	7 (2%)	41 (10%)	14 (3%)	81 (19%)	
Nguyen 2022	Placebo	52	16			0		1 (1.9)	
	Secukinumab 300mg	103				6 (5.8)		3 (2.9)	
	Secukinumab 150mg	103				2 (1.9)		4 (3.9)	
D'Agostino 2022	Placebo	83	16		0			5 (6%)	
	Secukinumab (150mg/300mg)	83			0			7 (8%)	
Baraliakos 2021	Placebo	166	16					11 (6.6)	5 (3.0)
	Secukinumab 300mg	167						9 (5.4)	3 (1.8)
	Secukinumab 150mg	165						4 (2.4)	5 (3.0)
Kivitz 2019	Placebo	114							
	Secukinumab 150mg load	114							

	Secukinumab 150mg no load	113							
Mease 2020b	Adalimumab 40mg Q2W	283	24	87 (30.7)	8 (2.8)				
	Ixekizumab 80mg Q4W	283		102 (36.0)	4 (1.4)				
Smolen 2020	Adalimumab 40mg Q2W	283	52	111 (39.2)	8 (2.8)				
	Ixekizumab 80mg Q4W	283		119 (42)	5 (1.8)				
Vieira-Sousa 2020	Placebo + MTX	23	NR						
	Golimumab 50mg Q4W + MTX	21							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	NR						
	Infliximab TDM + csDMARD	20							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	NR						
	Infliximab TDM + csDMARD	28							
Michielsens 2022	T2T with tapering	42							
	T2T without tapering	22							
Coates 2021b	Ixekizumab withdrawal	79	104	20 (25.3)	1 (1.3)	4 (5.1)	1 (1.3)	4 (5.1)	3 (3.8)
	Ixekizumab 80mg Q2W	79		29 (36.7)	0 (0)	9 (11.4)	4 (5.1)	11 (13.9)	1 (1.3)
Nash 2021	Tofacitinib 5 mg BID + placebo	90	104		0	4 (4%)	3 (3%)	3 (3%)	4 (4%)

	Tofacitinib 5 mg BID + MTX	89			2 (2%)	6 (7%)	2 (2%)	1 (1%)	3 (3%)
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	NR						
	Etanercept interval continuation (QW)	20							
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16	41 (33%)	1 (1%)	10 (8%)	0	0	
	MTX escalation to 25mg QW	122		25 (20%)	0	11 (9%)	0	0	
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16			2 (5%)			
	Methotrexate 25mg QW + Leflunomide 10mg QD	39				2 (5%)			

Table S3.4.3: Safety of RCTs: Herpes zoster, Opportunistic infections, Candida/fungal infections, Tbc, COVID-19

Study identifier	Treatment arm	n	Week	Herpes zoster	opportunistic infections	Candida infection	Fungal infection	Active tuberculosis	COVID-19 infections
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16						
	Izokibep 40mg Q2W	44							
	Izokibep 80mg Q2W	47							
Mease ACR 2021	Placebo	67	16	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)
	Brepocitinib 10mg QD	31		1 (3.2)	0 (0.0)			0 (0.0)	0 (0.0)
	Brepocitinib 30mg QD	60		1 (1.7)	0 (0.0)			0 (0.0)	0 (0.0)
	Brepocitinib 60mg QD	59		0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)
Mease 2021a	Placebo Q4W	79	24			0			
	Tildrakizumab 200mg Q4W	78				2 (2.6)			
	Tildrakizumab 200mg Q12W	79				0			
	Tildrakizumab 100mg Q12W	77				0			
	Tildrakizumab 20mg Q12W	78				0			
Mease 2022a	Placebo	66	16	0				0	
	Deucravacitinib 6mg QD	70		0				0	

	Deucravacitinib 12mg QD	67		0				0	
Deodhar 2020	Placebo	126	24			0			
	Guselkumab 100 mg Q4W	128				1 (<1)			
	Guselkumab 100 mg Q8W	127				0			
Mease 2020a	Placebo	246	24			0			
	Guselkumab 100 mg Q4W	245				0			
	Guselkumab 100 mg Q8W	248				0			
Mease 2021b	Placebo	118	24						
	Guselkumab 100 mg Q4W	103							
	Guselkumab 100 mg Q8W	91							
Coates 2021a	Placebo	96	24						
	Guselkumab 100 mg Q8W	189							
Merola 2023	Placebo	133	16		0	0	0	0	6 (5)
	Bimekizumab 160mg Q4W	267			0	7 (3)	4 (1)	0	5 (2)
McInnes 2023	Placebo	281	16		0	2 (1)	4 (1)	0	0
	Bimekizumab 160mg Q4W	431			0	11 (3)	20 (5)	0	0
	Adalimumab 40mg Q2W	140			1 (1)	0	1 (1)	0	0
Kristensen 2022	Placebo	481	24	1 (0.2)	0	0		0	2 (0.4)
	Risankizumab 150 mg (wk0, wk4, wk16)	483		2 (0.4)	0	0		0	1 (0.2)

Östör 2022a	Placebo	219	24	1 (0.5)	0	0		0	0
	Risankizumab 150 mg (wk0, wk4, wk16)	224		0	0	0		0	1 (0.4)
McInnes 2021	Placebo	423	24	3 (0.7)	0			0	
	Upadacitinib 15 mg QD	429		4 (0.9)	1 (0.2)			0	
	Upadacitinib 30 mg QD	423		5 (1.2)	2 (0.5)			0	
	Adalimumab 40mg Q2W	429		0	0			0	
Mease 2021c	Placebo	212	24	2 (0.9)	0			0	
	Upadacitinib 15 mg QD	211		3 (1.4)	0			0	
	Upadacitinib 30 mg QD	218		8 (3.7)	2 (0.9)			0	
Mease 2021d	Placebo	322	16						
	Brodalumab 140mg Q2W	318							
	Brodalumab 210mg Q2W	322							
Koem 2023	Ustekinumab + Placebo	79	24						
	Ustekinumab + MTX 15mg QW	87							
McInnes 2020	Adalimumab 40mg Q2W	427	52			7 (2%)			
	Secukinumab 300mg	426				16 (4%)			
Nguyen 2022	Placebo	52	16			0			
	Secukinumab 300mg	103				1 (1.0)			
	Secukinumab 150mg	103				2 (1.9)			

D'Agostino 2022	Placebo	83	16			0	1 (1.2%)		
	Secukinumab (150mg/300mg)	83				1 (1.2%)	3 (4%)		
Baraliakos 2021	Placebo	166	16			1 (0.6)			
	Secukinumab 300mg	167				3 (1.8)			
	Secukinumab 150mg	165				2 (1.2)			
Kivitz 2019	Placebo	114							
	Secukinumab 150mg load	114							
	Secukinumab 150mg no load	113							
Mease 2020b	Adalimumab 40mg Q2W	283	24			2 (0.7)			
	Ixekizumab 80mg Q4W	283				7 (2.5)			
Smolen 2020	Adalimumab 40mg Q2W	283	52			3 (1.1)			
	Ixekizumab 80mg Q4W	283				7 (2.5)			
Vieira-Sousa 2020	Placebo + MTX	23	NR						
	Golimumab 50mg Q4W + MTX	21							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	NR						
	Infliximab TDM + csDMARD	20							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	NR						
	Infliximab TDM + csDMARD	28							
Michielsens 2022	T2T with tapering	42							

	T2T without tapering	22							
Coates 2021b	Ixekizumab withdrawal	79	104						
	Ixekizumab 80mg Q2W	79							
Nash 2021	Tofacitinib 5 mg BID + placebo	90	104	1 (1%)	0				
	Tofacitinib 5 mg BID + MTX	89		2 (2%)	1 (1%)§				
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	NR						
	Etanercept interval continuation (QW)	20							
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16	2 (2%)					
	MTX escalation to 25mg QW	122		0					
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16						
	Methotrexate 25mg QW + Leflunomide 10mg QD	39							

Table S3.4.4: Safety of RCTs: Malignancies, NMSC, MACE, VTE

Study identifier	**Treatment arm**	**n**	**week**	**Malignancy**	**NMSC**	**MACE**	**VTE**
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16				
	Izokibep 40mg Q2W	44					
	Izokibep 80mg Q2W	47					
Mease ACR 2021	Placebo	67	16	0 (0.0)		0 (0.0)	0 (0.0)
	Brepocitinib 10mg QD	31		0 (0.0)		0 (0.0)	0 (0.0)
	Brepocitinib 30mg QD	60		0 (0.0)		0 (0.0)	0 (0.0)
	Brepocitinib 60mg QD	59		2 (3.3)		0 (0.0)	0 (0.0)
Mease 2021a	Placebo Q4W	79	24			0	
	Tildrakizumab 200mg Q4W	78				0	
	Tildrakizumab 200mg Q12W	79				0	
	Tildrakizumab 100mg Q12W	77				0	
	Tildrakizumab 20mg Q12W	78				0	
Mease 2022a	Placebo	66	16	0			1 (1.5)
	Deucravacitinib 6mg QD	70		0			0
	Deucravacitinib 12mg QD	67		0			0
Deodhar 2020	Placebo	126	24	0		1 (1)	

	Guselkumab 100 mg Q4W	128		0		0	
	Guselkumab 100 mg Q8W	127		1 (1)		0	
Mease 2020a	Placebo	246	24	1 (<1)		0	
	Guselkumab 100 mg Q4W	245		0		1 (<1)	
	Guselkumab 100 mg Q8W	248		1 (<1)		0	
Mease 2021b	Placebo	118	24				
	Guselkumab 100 mg Q4W	103					
	Guselkumab 100 mg Q8W	91					
Coates 2021a	Placebo	96	24	0			
	Guselkumab 100 mg Q8W	189		1 (0.5)			
Merola 2023	Placebo	133	16	1 (1)	1	0	
	Bimekizumab 160mg Q4W	267		0	0	0	
McInnes 2023	Placebo	281	16	1 (<1)	0	0	
	Bimekizumab 160mg Q4W	431		1 (<1)	1 (<1)	0	
	Adalimumab 40mg Q2W	140		0	0	0	
Kristensen 2022	Placebo	481	24	2 (0.4)		0	
	Risankizumab 150 mg (wk0, wk4, wk16)	483		0		0	
Östör 2022a	Placebo	219	24	1 (0.5)		0	
	Risankizumab 150 mg (wk0, wk4, wk16)	224		1 (0.4)		1 (0.4)	

McInnes 2021	Placebo	423	24	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)
	Upadacitinib 15 mg QD	429		1 (0.2)	0	0	0
	Upadacitinib 30 mg QD	423		3 (0.7)	2 (0.5)	0	1 (0.2)
	Adalimumab 40mg Q2W	429		3 (0.7)	0	2 (0.5)	2 (0.5)
Mease 2021c	Placebo	212	24	0	0	0	0
	Upadacitinib 15 mg QD	211		3 (1.4)	1 (0.5)	1 (0.5)	1 (0.5)
	Upadacitinib 30 mg QD	218		3 (1.4)	1 (0.5)	0	0
Mease 2021d	Placebo	322	16	0,00		2 (0.6)	
	Brodalumab 140mg Q2W	318		1 (0.3)		0	
	Brodalumab 210mg Q2W	322		1 (0.3)		0	
Koem 2023	Ustekinumab + Placebo	79	24				
	Ustekinumab + MTX 15mg QW	87					
McInnes 2020	Adalimumab 40mg Q2W	427	52	3 (1%)		0	
	Secukinumab 300mg	426		2 (<1%)		2 (<1%)	
Nguyen 2022	Placebo	52	16			1 (1.9)	
	Secukinumab 300mg	103				0	
	Secukinumab 150mg	103				1 (1.0)	
D'Agostino 2022	Placebo	83	16			0	
	Secukinumab (150mg/300mg)	83				0	

Baraliakos 2021	Placebo	166	16	0		0	
	Secukinumab 300mg	167		0		1 (0.6)	
	Secukinumab 150mg	165		0		0	
Kivitz 2019	Placebo	114					
	Secukinumab 150mg load	114					
	Secukinumab 150mg no load	113					
Mease 2020b	Adalimumab 40mg Q2W	283	24	3 (1.1)		5 (1.8)	
	Ixekizumab 80mg Q4W	283		0		3 (1.1)	
Smolen 2020	Adalimumab 40mg Q2W	283	52	4 (1.4)			
	Ixekizumab 80mg Q4W	283		0			
Vieira-Sousa 2020	Placebo + MTX	23	NR				
	Golimumab 50mg Q4W + MTX	21					
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	NR				
	Infliximab TDM + csDMARD	20					
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	NR				
	Infliximab TDM + csDMARD	28					
Michielsens 2022	T2T with tapering	42					
	T2T without tapering	22					
Coates 2021b	Ixekizumab withdrawal	79	104	0 (0)		0 (0)	

	Ixekizumab 80mg Q2W	79		0 (0)		0 (0)	
Nash 2021	Tofacitinib 5 mg BID + placebo	90	104	1 (1%)	0	0	0
	Tofacitinib 5 mg BID + MTX	89		1 (1%)	0	0	0
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	NR				
	Etanercept interval continuation (QW)	20					
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16				
	MTX escalation to 25mg QW	122					
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16				
	Methotrexate 25mg QW + Leflunomide 10mg QD	39					

Table S3.4.5: Safety of RCTs: Adverse Events of special interest

Study identifier	Treatment arm	n	Week	IBD	Diarrhoea	Uveitis	Suicidal ideation	Depression	Injection site reaction
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16						
	Izokibep 40mg Q2W	44							
	Izokibep 80mg Q2W	47							
Mease ACR 2021	Placebo	67	16						
	Brepocitinib 10mg QD	31							
	Brepocitinib 30mg QD	60							
	Brepocitinib 60mg QD	59							
Mease 2021a	Placebo Q4W	79	24	0		0		0	
	Tildrakizumab 200mg Q4W	78		0		0		0	
	Tildrakizumab 200mg Q12W	79		0		0		0	
	Tildrakizumab 100mg Q12W	77		0		0		0	
	Tildrakizumab 20mg Q12W	78		0		0		1 (1.3)	
Mease 2022a	Placebo	66	16		0				
	Deucravacitinib 6mg QD	70			4 (5.7)				
	Deucravacitinib 12mg QD	67			0				
Deodhar 2020	Placebo	126	24				1 (1)		0

	Guselkumab 100 mg Q4W	128					0		1 (1)
	Guselkumab 100 mg Q8W	127					1 (1)		2 (2)
Mease 2020a	Placebo	246	24				1 (<1)		1 (<1)
	Guselkumab 100 mg Q4W	245					1 (<1)		3 (1)
	Guselkumab 100 mg Q8W	248					0		3 (1)
Mease 2021b	Placebo	118	24						
	Guselkumab 100 mg Q4W	103							
	Guselkumab 100 mg Q8W	91							
Coates 2021a	Placebo	96	24						1 (1.0)
	Guselkumab 100 mg Q8W	189							4 (2.1)
Merola 2023	Placebo	133	16	0			0		0
	Bimekizumab 160mg Q4W	267		0			0		3 (1)
McInnes 2023	Placebo	281	16	0	7 (2)		0		3 (1)
	Bimekizumab 160mg Q4W	431		0	16 (4)		0		5 (1)
	Adalimumab 40mg Q2W	140		0	5 (4)		0		7 (5)
Kristensen 2022	Placebo	481	24						0
	Risankizumab 150 mg (wk0, wk4, wk16)	483							3 (0.6)
Östör 2022a	Placebo	219	24		5 (2.3)				1 (0.5)
	Risankizumab 150 mg (wk0, wk4, wk16)	224			5 (2.2)				3 (1.3)
McInnes 2021	Placebo	423	24						

	Upadacitinib 15 mg QD	429							
	Upadacitinib 30 mg QD	423							
	Adalimumab 40mg Q2W	429							
Mease 2021c	Placebo	212	24						
	Upadacitinib 15 mg QD	211							
	Upadacitinib 30 mg QD	218							
Mease 2021d	Placebo	322	16	0,00			0,00		
	Brodalumab 140mg Q2W	318		0			1 (0.3)§		
	Brodalumab 210mg Q2W	322		0			0		
Koem 2023	Ustekinumab + Placebo	79	24	1 (1%)	4 (5%)				11 (14%)
	Ustekinumab + MTX 15mg QW	87		0	10 (11%)				12 (14%)
McInnes 2020	Adalimumab 40mg Q2W	427	52	0	35 (8%)				47 (11%)
	Secukinumab 300mg	426		2 (<1%)	31 (7%)				17 (4%)
Nguyen 2022	Placebo	52	16		1 (1.9)				
	Secukinumab 300mg	103			6 (5.8)				
	Secukinumab 150mg	103			6 (5.8)				
D'Agostino 2022	Placebo	83	16	0	6 (7%)				1 (1.2%)
	Secukinumab (150mg/300mg)	83		0	3 (4%)				3 (4%)
Baraliakos 2021	Placebo	166	16	0	4 (2.4)				
	Secukinumab 300mg	167		0	4 (2.4)				

	Secukinumab 150mg	165		0	2 (1.2)				
Kivitz 2019	Placebo	114							
	Secukinumab 150mg load	114							
	Secukinumab 150mg no load	113							
Mease 2020b	Adalimumab 40mg Q2W	283	24	0				7 (2.5)	9 (3.2)
	Ixekizumab 80mg Q4W	283		2 (0.7)				3 (1.1)	27 (9.5)
Smolen 2020	Adalimumab 40mg Q2W	283	52	0				9 (3.2)	10 (3.5)
	Ixekizumab 80mg Q4W	283		2 (0.7)				5 (1.8)	30 (10.6)
Vieira-Sousa 2020	Placebo + MTX	23	NR						
	Golimumab 50mg Q4W + MTX	21							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	NR						
	Infliximab TDM + csDMARD	20							
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	NR						
	Infliximab TDM + csDMARD	28							
Michielsens 2022	T2T with tapering	42							
	T2T without tapering	22							
Coates 2021b	Ixekizumab withdrawal	79	104	0 (0)				0 (0)	0 (0)
	Ixekizumab 80mg Q2W	79		0 (0)				0 (0)	2 (2.5)
Nash 2021	Tofacitinib 5 mg BID + placebo	90	104		3 (3%)				
	Tofacitinib 5 mg BID + MTX	89			0				

Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	NR						
	Etanercept interval continuation (QW)	20							
Coates 2022	Adalimumab 40mg Q2W + MTX	123	16						13 (11%)
	MTX escalation to 25mg QW	122							3 (2%)
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16						
	Methotrexate 25mg QW + Leflunomide 10mg QD	39							

Table S3.4.6: Safety of RCTs: Laboratory / hematologic abnormalities

Study identifier	Treatment arm	n	week	Hepatic disorder	ALT increase	AST increase	Lymphopenia	Neutropenia	Anemia	Elevated CK
Behrens EULAR/ACR 2022; de Vlam ACR 2022	Placebo	44	16							
	Izokibep 40mg Q2W	44								
	Izokibep 80mg Q2W	47								
Mease ACR 2021	Placebo	67	16							
	Brepocitinib 10mg QD	31								
	Brepocitinib 30mg QD	60								
	Brepocitinib 60mg QD	59								
Mease 2021a	Placebo Q4W	79	24		3 (3.8)	1 (1.3)				
	Tildrakizumab 200mg Q4W	78			0	0				
	Tildrakizumab 200mg Q12W	79			1 (1.3)	1 (1.3)				
	Tildrakizumab 100mg Q12W	77			1 (1.3)	1 (1.3)				
	Tildrakizumab 20mg Q12W	78			0	0				
Mease 2022a	Placebo	66	16							
	Deucravacitinib 6mg QD	70								
	Deucravacitinib 12mg QD	67								
Deodhar 2020	Placebo	126	24		3 (2)	3 (2)				
	Guselkumab 100 mg Q4W	128			5 (4)	3 (2)				
	Guselkumab 100 mg Q8W	127			8 (6)	9 (7)				
Mease 2020a	Placebo	246	24		11 (4)	6 (2)				
	Guselkumab 100 mg Q4W	245			25 (10)	11 (4)				
	Guselkumab 100 mg Q8W	248			15 (6)	14 (6)				
Mease 2021b	Placebo	118	24							
	Guselkumab 100 mg Q4W	103								
	Guselkumab 100 mg Q8W	91								
Coates 2021a	Placebo	96	24		4 (4.2)					

	Guselkumab 100 mg Q8W	189			5 (2.6)					
Merola 2023	Placebo	133	16		0	0		0		
	Bimekizumab 160mg Q4W	267			2 (1)	4 (1)		4 (1)		
McInnes 2023	Placebo	281	16		0	0		1 (<1)		
	Bimekizumab 160mg Q4W	431			5 (1)	5 (1)		5 (1)		
	Adalimumab 40mg Q2W	140			2 (1)	3 (2)		1 (1)		
Kristensen 2022	Placebo	481	24		10 (2.1)	7 (1.5)				
	Risankizumab 150 mg (wk0, wk4, wk16)	483			13 (2.7)	10 (2.1)				
Östör 2022a	Placebo	219	24							
	Risankizumab 150 mg (wk0, wk4, wk16)	224								
McInnes 2021	Placebo	423	24	16 (3.8)			5 (1.2)	1 (0.2)	4 (0.9)	6 (1.4)
	Upadacitinib 15 mg QD	429		39 (9.1)			6 (1.4)	4 (0.9)	3 (0.7)	38 (8.9)
	Upadacitinib 30 mg QD	423		52 (12.3)			15 (3.5)	21 (5.0)	20 (4.7)	41 (9.7)
	Adalimumab 40mg Q2W	429		67 (15.6)			1 (0.2)	10 (2.3)	1 (0.2)	24 (5.6)
Mease 2021c	Placebo	212	24	3 (1.4)			0	1 (0.5)	2 (0.9)	4 (1.9)
	Upadacitinib 15 mg QD	211		4 (1.9)			2 (0.9)	2 (0.9)	4 (1.9)	4 (1.9)
	Upadacitinib 30 mg QD	218		18 (8.3)			2 (0.9)	6 (2.8)	14 (6.4)	12 (5.5)
Mease 2021d	Placebo	322	16					0,00		
	Brodalumab 140mg Q2W	318						3 (0.9)		
	Brodalumab 210mg Q2W	322						3 (0.9)		
Koem 2023	Ustekinumab + Placebo	79	24							
	Ustekinumab + MTX 15mg QW	87								
McInnes 2020	Adalimumab 40mg Q2W	427	52							
	Secukinumab 300mg	426								
Nguyen 2022	Placebo	52	16					0		
	Secukinumab 300mg	103						1 (1.0)		
	Secukinumab 150mg	103						0		
D'Agostino 2022	Placebo	83	16					0		

	Secukinumab (150mg/300mg)	83						0		
Baraliakos 2021	Placebo	166	16							
	Secukinumab 300mg	167								
	Secukinumab 150mg	165								
Kivitz 2019	Placebo	114								
	Secukinumab 150mg load	114								
	Secukinumab 150mg no load	113								
Mease 2020b	Adalimumab 40mg Q2W	283	24							
	Ixekizumab 80mg Q4W	283								
Smolen 2020	Adalimumab 40mg Q2W	283	52							
	Ixekizumab 80mg Q4W	283								
Vieira-Sousa 2020	Placebo + MTX	23	NR							
	Golimumab 50mg Q4W + MTX	21								
Syversen 2021a	Infliximab 5mg/kg + csDMARD	22	NR							
	Infliximab TDM + csDMARD	20								
Syversen 2021a	Infliximab 5mg/kg + csDMARD	25	NR							
	Infliximab TDM + csDMARD	28								
Michielsens 2022	T2T with tapering	42								
	T2T without tapering	22								
Coates 2021b	Ixekizumab withdrawal	79	104	3 (3.8)						
	Ixekizumab 80mg Q2W	79		6 (7.6)						
Nash 2021	Tofacitinib 5 mg BID + placebo	90	104		0	0				
	Tofacitinib 5 mg BID + MTX	89			5 (6%)	3 (3%)				
Ruwaard 2023	Etanercept interval prolongation (Q2W)	21	NR							
	Etanercept interval continuation (QW)	20								

Coates 2022	Adalimumab 40mg Q2W + MTX	123	16		5 (4%)	5 (4%)				
	MTX escalation to 25mg QW	122			6 (5%)	3 (2%)				
Mulder 2022	Placebo + Methotrexate 25mg QW	39	16		7 (18%)					
	Methotrexate 25mg QW + Leflunomide 10mg QD	39			12 (31%)					

Table S3.5: Results of long term extension and cohort/case control studies.

Study	Comparator arms	PY	Outcome definition	Frequency n (%)	IR (95% CI)	aHR (95% CI)	aOR (95% CI)	IRR (95% CI)
Winthrop 2023	Placebo + csDMARD (PBO controlled period)	52.3	Influenza and Influenza-like illness AE (combined	2 (0.8)	3.36 (0.45-13.27)			
	Tofacitinib 5mg BID + csDMARD (PBO controlled period)	54		0	0 (0-6.78)			
	Tofacitinib 10mg BID + csDMARD (PBO controlled period)	53.4		1 (0.4)	1.86 (0.05-10.38)			
	Tofacitinib 5mg BID + csDMARD (active controlled period)	196.2		5 (1.4)	2.51 (0.81-5.85)			
	Tofacitinib 10mg BID + csDMARD (active controlled period)	192.2		5 (1.5)	2.56 (0.83-5.97)			
	Adalimumab 40mg Q2W + csDMARD (active controlled period)	91		0	0 (0-3.98)			
Glintborg 2023	Secukinumab	820	Serious infection	46 (4.0%)	5.6 (4.1, 7.5)	Reference		
	Adalimumab	940		23 (1.8%)	2.5 (1.6, 3.7)	0.59 (0.34, 1.03)		
	Certolizumab pegol	500		21 (3.1%)	4.2 (2.6, 6.4)	1.07 (0.60, 1.92)		
	Etanercept	1980		52 (1.9%)	2.6 (2.0, 3.4)	0.59 (0.37, 0.93)		
	Golimumab	430		11 (2.0%)	2.5 (1.3, 4.6)	0.57 (0.28, 1.20)		
	Infliximab	1030		41 (3.0%)	4.0 (2.8, 5.4)	0.88 (0.54, 1.42)		
Jin & Lee 2021	Ustekinumab	NR	Serious infection			Reference		
	Adalimumab	NR				1.67 (0.55–5.07)		
	Apremilast	NR				1.72 (0.68–4.30)		
	Certolizumab	NR				1.28 (0.74–2.20)		

	Etanercept	NR				1.41 (0.40–4.98)		
	Golimumab	NR				1.62 (0.18–14.41)		
	Infliximab	NR				2.89 (1.26–6.63)		
	Ixekizumab	NR				15.05 (4.27–53.04)		
	Secukinumab	NR				1.93 (0.97–3.87)		
Krabbe 2021	bDMARD	NR	Serious infection	89/2428 (3.6%)		3.4 (2.7, 4.3)		
	General population (matched)	NR		262/24288 (1.1%)		Reference		
Li 2019	all bDMARDs	4159	Serious infection	105 (2)	2.5 (2.1 to 3.1)	-		
	TNFi	2907		78 (2)	2.7 (2.1 to 3.3)	Reference		
	IL-17i	605		14 (1)	2.3 (1.3 to 3.7)	0.67 (0.25 to 1.73)		
	IL-12/23i	647		13 (1)	2.0 (1.1 to 3.3)	0.74 (0.40 to 1.36)		
Elewski 2020	All Secukinumab treated patients	4943.5	active TB / LTBI	0 / 1	NE / 0.02 (95% CI: 0.00-0.11)			
	Secukinumab treated patients with +LTBI			0 / 2	NR			
Rotar 2019	TNFi	1849	active TB	2	SIR: 5.8 (0.3 - 112)			
Hellgren 2021	TNFi vs bDMARD naive/GP	55 850	solid cancer		SIR: 1.0 (0.9-1.1)	1.0 (0.9-1.2)		
Lebwohl 2021	IL17i	4902	malignancy (excluding NMSC)	51/4902 (0.8%)	SIR: 1.16 (0.80–1.62)			
Fagerli 2019	TNFi	5956.5	malignancy (excluding NMSC)	32/709 (4%)	SIR: 0.94 (0.65, 1.34)			
			nmsc	15/709 (2%)	SIR: 2.12 (1.19, 3.50)			
Cordtz 2022	TNFi	59 827	hematological cancer	40	IRR: 0.96 (0.68-1.35)			

	bDMARD naive		hematological cancer	63	Ref			
Stovall 2021	MI Cases	43,734	myocardial infarction (DMARD vs. TNFi)	404			1.09 (0.74–1.60)	
	Controls			1596				
Pina Vegas 2022	TNFi	519.3	MACE	30/7289	2.8 (1.8, 3.9)	Reference		
	IL12/23i	1627.5		5/1058	3.1 (0.4, 5.8)	2.0 (1.3-3.0)		
	IL17i	1354.9		8/1163	5.9 (1.8, 9.9)	1.9 (1.2-3.0)		
	PDE4i	1523.9		1/1885	5.2 (1.6, 8.9)	1.3 (0.8-2.2)		
Persson 2021	Apremilast mono	4466	myocardial infarction	8	1.8 (0.8, 3.5)			-
	csDMARD mono	14058		37	2.6 (1.9, 3.6)			Reference
	TNFi mono	39604		55	1.4 (1.0, 1.8)			0.63 (0.41, 0.96)
	IL17/12/23i inhibition mono	7794		18	2.3 (1.4, 3.7)			1.15 (0.65, 2.02)
	GC mono	7579		27	3.6 (2.3, 5.2)			1.46 (0.89, 2.40)
	Apremilast + csDMARDs	2849		10	3.5 (1.7, 6.5)			-
	csDMARD + GC	3642		14	3.8 (2.1, 6.4)			1.49 (0.80, 2.75)
	TNFi + csDMARDs	18570		45	2.4 (1.8, 3.2)			1.10 (0.71, 1.70)
	IL17/12/23i + csDMARDs	2740		7	2.6 (1.0, 5.3)			
	Unexposed	27180		71	2.6 (2.0, 3.3)			1.16 (0.78, 1.73)
Mease 2020b	Average tofacitinib 5 mg	54.6	DVT / PE / VTE / ATE (Pbo controlled period	0/0/0/1	0/0/0/1.83 (0.05 - 10.22)			
	Average tofacitinib 10 mg twice daily	54.4		0/0/0/0	0/0/0/0			
	Placebo	53.7		0/0/0/0	0/0/0/0			
	Adalimumab 40mg Q2W							

Tang 2020	TNFi		liver disease (per 10000 PY)		79.0	1.25 (0.88 - 1.76)		
	no TNFi				72.7			
Vasilakis-Scaramozza 2020	Treated anxiety + depression	60 497	anxiety + depression (per 1000 PY)	341	5.6 (5.1–6.3)			
	DMARDs only	7291		28	3.8 (2.6–5.6)			Reference
	Apremilast only	2089		10	4.8 (2.3–8.8)			1.0 (0.5–2.1)
	TNF-i biologics only	19 994		107	5.4 (4.4–6.5)			1.3 (0.9–2.0)
	IL-i biologics only	3538		21	5.9 (3.7–9.1)			1.2 (0.7–2.2)
	Corticosteroids only	3161		23	7.3 (4.6–10.9)			1.5 (0.8–2.6)
	Apremilast + any non-steroid	574		4	7.0 (1.9–17.8)			–
	TNF-i with DMARDs	4456		25	5.6 (3.6–8.3)			1.5 (0.9–2.5)
	IL-i with DMARDs	384		0	0 (0–9.5)			–
	Corticosteroids + any other‡	6281		46	7.3 (5.4–9.8)			1.7 (1.1–2.7)
	Unexposed	12 729		77	6.0 (4.8–7.6)			1.2 (0.8–1.9)
Ghosh 2019	Placebo	145	infections		102.8 (86.9–120.6)			
	Ustekinumab	850			78.0 (72.2–84.2)			
Gossec 2023	Ustekinumab		malignancy	3 (0.6)				
	TNFi			4 (0.7)				
Meng ACR 2022		TNFi	MACE			0.7 (0.27-1.82)		
		non-TNFi						
Strober ACR 2022	Placebo	230	infections (per 100PY)		64.0 (54.1-75.2)			
	Guselkumab 100mg Q8W	305			59.0 (50.7-68.2)			

	Guselkumab 100mg Q4W	172			62.6 (51.4-75.6)			
Mease ACR 2022b	Placebo	269.4	serious opportunistic infections (per 100 PY)		0			
	Apremilast	327.0			0.31			
Rubbert-Roth ACR 2022	Upadacitinib 15mg OD	1872.3	malignancy (excl. Nmsc) per 100PY	11	0.6 (0.3-1.1)			
	Adalimumab 40mg Q2W	903.7		4	0.4 (0.1-1.1)			
Charles-Schoeman ACR 2022	Adalimumab 40mg Q2W	903.7	MACE	3	0.1 (0.1-1.0)			
	Upadacitinib 15mg OD	1872.3		5	0.3 (0.1-0.6)			
	Upadacitinib 30mg OD	1867.5		6	0.3 (0.1-0.7)			

Section 4: List of abbreviations

Δ	Change from baseline
ABA	Abatacept
ACR	American College of Rheumatology
ADA	Adalimumab
ANA	Anakinra
BARI	Baricitinib
bDMARD	Biological disease-modifying anti-rheumatic drug
BID	Twice daily
BLM	Brodalumab
boDMARD	Biooriginator disease-modifying anti-rheumatic drug
bsDMARD	Biosimilar disease-modifying anti-rheumatic drug
CD	Cluster of differentiation
CDAI	Clinical Disease Activity Index
csDMARD	Conventional synthetic disease-modifying anti-rheumatic drug
CZK	Clazakizumab
CZP	Certolizumab pegol
DAS28	Disease Activity Score of 28 Joints
DEC	Decernotinib
ETN	Etanercept
FILGO	Filgotinib
FOSTA	Fostamatinib
GC	Glucocorticoids
GKM	Guselkumab
GLM	Golimumab
GM-CSF	Granulocyte-macrophage colony-stimulating factor
HAQ	Health Assessment Questionnaire Disability Index
HCQ	Hydroxychloroquine
IL	Interleukin
IR	Insufficient responder
JAK	Janus Kinase
LEF	Leflunomide
mTSS	Modified total Sharp Score
MTX	Methotrexate
MVM	Mavrilimumab
NR	Not reported
NS	Not significant
OD	Once daily
OKM	Olokizumab
PEF	Peficitinib
QNW	Every N weeks
R	receptor
RA	Rheumatoid Arthritis
RoB	Risk of bias
RTX	Rituximab
SAR	Sarilumab
SDAI	Simplified Disease Activity Index
SEC	Secukinumab
SKM	Sirukumab
SZP/SSZ	Sulfasalazine

TBM	Tabalumab
TCZ	Tocilizumab
TLM	Tregalizumab
TNF	Tumor necrosis factor alpha
TOFA	Tofacitinib
tsDMARD	Targeted synthetic disease-modifying anti-rheumatic drug
UKM	Ustekinumab
UPA	Upadacitinib