BMJ Open Effects of bDMARDs on quality of life in patients with psoriatic arthritis: metaanalysis

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ABSTRACT

Objectives To determine the effects of biological diseasemodifying anti-rheumatic drugs (bDMARDs) on the quality of life (QoL) among patients with psoriatic arthritis (PsA). Design Meta-analysis.

Data sources and eligibility criteria PubMed, Web of Science, Cochrane Library, China National Knowledge Infrastructure, WanFang and VIP databases were searched to collect randomised controlled trials (RCTs), which were conducted to evaluate the effect of bDMARDs in the treatment of patients with PsA and reported QoL-related outcomes, from inception to November 2020 and updated on 19 February 2022.

Data extraction and synthesis Outcomes about Health Assessment Questionnaire Disability Index (HAQ-DI). Dermatology Life Quality Index, physical component summary and mental component summary of the Short Form 36, EuroQol Visual Analogue Scale, Psoriasis Area Severity Index (PASI) 50/75/90/100 were extracted by two reviewers independently. Data were pooled using the fixed or random effects methods and considered as mean difference (MD) or risk ratio with 95% Cl.

Results Out of 3190 articles screened, 37 RCTs (with 47 articles reported) were included. Pooled estimates showed that bDMARDs were superior versus placebo on all outcomes. Against methotrexate (MTX) and tofacitinib, bDMARDs showed no statistically significant advantages or significant disadvantages. Similar results were found for bDMARDs+MTX versus MTX. For HAQ-DI, the results of the subgroups of bDMARDs versus placebo, bDMARDs+MTX versus MTX, bDMARDs versus tofacitinib and bDMARDs versus MTX were -0.21 (MD, 95% Cl, -0.23 to -0.18), -0.22 (MD, 95% Cl, -0.58 to 0.14), -0.01 (MD, 95% CI, -0.05 to 0.04) and -0.03 (MD, 95% CI, -0.04 to -0.02), respectively.

Conclusions Compared with placebo, bDMARDs taken by patients with PsA appear to significantly improve the QoL. Compared with other therapeutic agents, more studies are required to confirm the effect of single and combined bDMARDs use further.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease that can lead to structural damage and disability, resulting in impaired quality of life (QoL), physical function and working ability. 1-3 Scotti et al analysed the results of 28 studies and found that

Strengths and limitations of this study

- ► This is the first meta-analysis focusing on the effects of biological disease-modifying anti-rheumatic drugs (bDMARDs) on the quality of life among patients with psoriatic arthritis (PsA).
- Subgroup analyses with the specific hierarchical structure were conducted to determine the source of heterogeneity, according to the experimental groups and control groups first, then category of bDMARDs, variety of bDMARDs, duration of PsA.
- Meta-analysis was not performed for the outcomes reported in less than 3 randomised controlled trials (RCTs), and funnel charts were not drawn for the outcomes reported in less than 10 RCTs.
- The results of Egger's test indicated the presence of publication bias, but the trim and fill method was not used to explore publication bias.
- There was a lack of stratification for countries or regions and long-term effects (exceeding 24 weeks) of bDMARDs for specific analysis due to the limited clinical data.

the prevalence and incidence rates of PsA are respectively 133 per 100000 subjects and 83 per 100 000 person-years. PsA develops in up to 30% of patients with psoriasis. Rosen et al reported that the QoL of patients with PsA is significantly lower than that of patients with psoriasis. Therefore, one of the main objectives of treating PsA is to improve the QoL of patients. Currently, the QoL of patients with PsA can be measured by questionnaires including the Short Form 36 (SF-36) Questionnaire, Health Assessment Questionnaire (HAO), Nottingham Health Profile (NHP), EuroQoL 5 domains (EQ-5D), Psoriasis Area and Severity Index (PASI), Disease Activity for Psoriatic Arthritis (DAPSA), Psoriasis Disability Index (PDI), Dermatology Life Quality Index (DLQI), Skindex-29, Skindex-17, Psoriasis Arthritis Quality of Life (PsAQoL). 7-10 Among these questionnaires, the higher scores of SF-36 and EQ-5D indicate higher levels of QoL, while others are the opposite.11-16





As a great advancement in the treatment of PsA, biological disease-modifying anti-rheumatic drugs (bDMARDs) have been proven to decrease inflammation and block structural progression effectively. 17 18 The bDMARDs are widely recommended by management guidelines, 119 including tumour necrosis factor inhibitors (TNFi, eg, etanercept, infliximab, adalimumab, golimumab, certolizumab pegol), interleukin-17 inhibitors (IL-17i, eg, ustekinumab, guselkumab, risankizumab) and interleukin-12/23 inhibitors (IL-12/23i, eg, secukinumab, ixekizumab, brodalumab). 1 20 Ruyssen-Witrand et al, 21 Lu et al^{22} and Lemos et al^{23} studied the efficacy and safety of bDMARDs in treating PsA, and found that the physical summarised component of SF-36 Score was improved, HAQ Score and PASI Score were decreased, but the change of mental summarised component of SF-36 Score was not significant. This indicated that the effects of bDMARDs on OoL in PsA need to be further evaluated.

The purpose of this study is to conduct a meta-analysis of randomised controlled trials (RCTs) related to bDMARDs in treating PsA, to comprehensively evaluate the effects of bDMARDs on QoL with multiple outcome indicators and to provide evidence for supporting pharmacists and physicians' clinical actions and decisions in treating PsA. The SF-36, HAQ, NHP and EQ-5D are generic instruments, scores measured by them are the primary outcomes of this study. The scores measured by other disease-specific instruments are the secondary outcomes.

MATERIALS AND METHODS

Search strategy and study selection

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.²⁴ To identify RCTs reporting the effects of bDMARDs on QoL, two independent authors (YqL and ZD) electronically conducted the searches in PubMed, Web of Science, the Cochrane Library, China National Knowledge Infrastructure, WanFang Database and VIP Datebase, from inception to November 2020 and updated on 19 February 2022. The keywords used for database searches were: patients, including "psoriatic arthritis"; intervention, including "etanercept" or "infliximab" or "adalimumab" or "golimumab" or "certolizumab" or "ustekinumab" or "guselkumab" or "risankizumab" or "tildrakizumab" or "secukinumab" or "ixekizumab" or "brodalumab" or "tumor necrosis factor inhibitor" or "TNFi" or "interleukin-12/23 inhibitor" or "IL-12/23i" or "interleukin-17 inhibitor" or "IL-17i" or "biologic"; and outcomes, including "health-related quality of life" or "HRQoL" or "Dermatology Life Quality Index" or "DLQI" or "disease activity index for psoriatic arthritis" or "DAPSA" or "psoriasis area and severity index" or "PASI" or "short form-36" or "SF-36" or "health assessment questionnaire" or "HAQ" or "Nottingham Health Profile" or "NHP" or "EuroQol-5D" or "EQ-5D" or "psoriasis disability index" or "PDI" or "Skindex-29" or "Skindex-17" or "PsAQoL" or "quality of life". To avoid

missing any related studies, the authors checked the reference citation sections of eligible articles as an additional level of searching. Research articles were limited to those regarding RCTs that were published in English or Chinese. The complete electronic search strategy for PubMed is provided in online supplemental table S1.

Inclusion and exclusion criteria

Studies were independently selected by two authors (YqL and ZD), and they achieved good agreement (κ =0.942). Studies were included if they met the following inclusion criteria: (1) the trial was a human study conducted on patients with PsA; (2) the experimental group was treated with bDMARDs or bDMARDs combined with other nonbDMARDs, while placebo and other non-bDMARDs were used as the control groups; (3) the study provided appropriate data (means and SD of continuous outcomes, the events number of dichotomous outcomes) for each group present at baseline and end of intervention for DLQI, DAPSA, PASI, SF-36, HAQ, NHP, EQ-5D, PDI, Skindex and PsAQoL. Other studies, including animal experiments, in vitro studies, case reports, observational studies, systematic reviews, duplicate publications, study protocols without findings, or congress abstracts without full texts were excluded.

Data extraction and quality assessment

Two authors (YqL and ZD) independently extracted data from each selected RCT using a standard abstraction Excel sheet (κ =0.959). The extracted data included trial name, sample size, characteristics of participants, duration of treatment and outcomes of interest. The methodological quality of the selected RCTs was evaluated by two independent investigators (YqL and ZD) using the Cochrane Collaboration risk-of-bias tool (κ =0.853).²⁵ The Cochrane Collaboration risk-of-bias tool used the following criteria for quality assessment: randomisation generation, allocation concealment, blinding of participants and outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias. Any disagreement between the reviewing authors was resolved by discussion and final consensus or when a third author (FC) approved the findings.

Data synthesis and statistical analysis

All statistical analyses were conducted using Review Manager V.5.3 software (Cochrane Collaboration, Copenhagen, Denmark) and STATA software V.16.0 (Stata Corp, College Station, Texas, USA). The risk ratio (RR) with 95% CI was used to evaluate dichotomous outcomes, and the mean difference (MD) with 95% CI was generated to evaluate continuous outcomes. Heterogeneity was assessed by using the I^2 estimate and the p value of the χ^2 -test. If the p value>0.10 and I^2 <50%, the assumption of homogeneity was made and the fixed effects model was used for analyses. Otherwise, heterogeneity was assumed, the random effects model was used to analyse and its source should be further determined by sensitivity

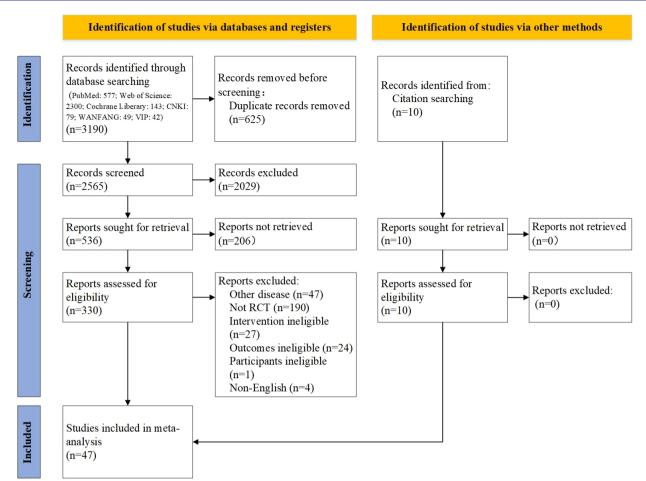


Figure 1 Flowchart of the study selection. RCT, randomised controlled trial.

analysis or subgroup analysis. Sensitivity analyses were conducted using a leave-one-out method to determine the effect of each trial on the reliability of overall pooled effect sizes. Further, subgroup analyses were carried out to determine the source of heterogeneity according to the potential moderator variables. First, the subgroup analyses were conducted according to the experimental groups and control groups (bDMARDs vs placebo, bDMARDs+methotrexate (MTX) vs MTX, bDMARDs vs tofacitinib, bDMARDs vs MTX), which were probably the biggest cause of heterogeneity. Then, each subgroup was analysed according to the following variables: category of bDMARDs (TNFi, IL-12/23i, IL-17i), variety of bDMARDs (etanercept, infliximab, adalimumab, etc), duration of PsA (<6 years, 6–9 years, ≥9 years, unclear), duration of treatment (<24 weeks, ≥24 weeks). The funnel plot, as well as Egger's test, was used to determine any possible publication bias.

RESULTS

Search results

The detailed step-by-step process of article identification and selection is presented in figure 1. In online searches, 3190 articles were identified initially. After duplicates and irrelevant articles were removed, 47 articles²⁶⁻⁷² (37 RCTs reported) were ultimately included in the meta-analysis. There was a total of 14115 participants in those RCTs. Overall, 25 RCTs have reported the effects of bDMARDs on HAQ Disability Index (HAQ-DI), 23 RCTs on SF-36 physical component summary (PCS), 18 RCTs on SF-36 mental component summary (MCS), 1 RCT on SF-36 Score, 8 RCTs on DLQI, 3 RCTs on EuroQol Visual Analogue Scale (EQ-VAS), 2 RCTs on PsAQoL, 2 RCT on DAPSA, 7 RCTs on the proportion of participants achieving 50% improvement from baseline in PASI (PASI 50), 2 RCTs on PASI 70, 27 RCTs on PASI 75, 26 RCTs on PASI 90, 10 RCTs on PASI 100 and 1 RCT on PASI Score. Among them, HAQ-DI, DLQI, PsAQoL, DAPSA and PASI scores are negative outcomes, and higher scores indicate worse health-related QoL, while the others are the opposite. The detailed characteristics of selected RCTs are summarised in online supplemental table S2. The methodological quality assessment of RCTs based on the Cochrane Collaboration risk-of-bias tool is shown in figure 2. Meta-analysis was not performed for the outcomes reported in less than three RCTs.

Main outcomes

Forest plots demonstrating the effects of bDMARDs on QoL are provided in online supplemental figures S1–S9. The pooled effect sizes of all outcomes are summarised in

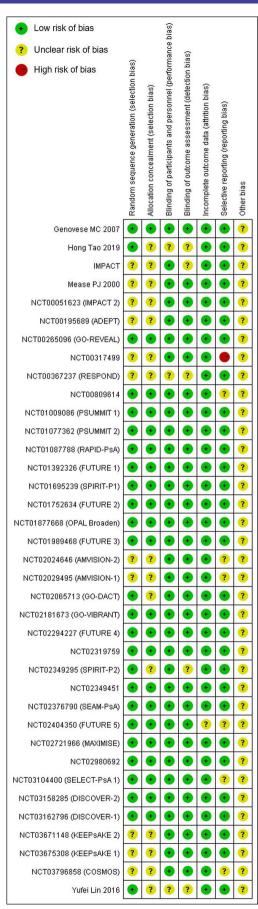


Figure 2 Quality assessment of included randomised controlled trials using Cochrane's risk-of-bias tool.

table 1. The results show that bDMARDs taken by patients with PsA can significantly decrease HAQ-DI (MD=-0.19; 95% CI, -0.22 to -0.17; p<0.00001; I²: 100%), DLQI (MD=-4.36; 95% CI, -5.76 to -2.96; p<0.00001; I²: 99%) and improve SF-36 PCS (MD=3.76; 95% CI, 3.42 to 4.10; p<0.00001; I²: 99%), SF-36 MCS (MD=1.76; 95% CI, 1.27 to 2.25; p<0.00001; I²: 99%), EQ-VAS (MD=5.27; 95% CI, 1.21 to 9.34; p<0.00001; I²: 99%), PASI 50 (RR=4.09; 95% CI, 2.71 to 6.16; p<0.00001; I²: 82%), PASI 75 (RR=4.72; 95% CI, 3.87 to 5.75; p<0.00001; I²: 81%), PASI 90 (RR=5.73; 95% CI, 4.73 to 6.95; p<0.00001; I²: 59%), PASI 100 (RR=9.57; 95% CI, 7.38 to 12.43; p<0.00001; I²: 13%). The changes in all outcomes mean that the bDMARDs can effectively improve the QoL of patients with PsA.

Sensitivity analysis

With the exclusion of any single study, the heterogeneity did not change materially in terms of any outcomes except PASI 90. After excluding Tao *et al*²⁷, the heterogeneity of PASI 90 decreased from 59% to 41%. After excluding NCT02181673 (GO-VIBRANT), postsensitivity pooled MD for EQ-VAS was 3.71 (95% CI, -0.58 to 7.99), which differed from presensitivity significantly. No statistically significant difference was found between presensitivity and postsensitivity pooled MDs or RRs for HAQ-DI, SF-36 PCS, SF-36 MCS, DLQI, PASI 50, PASI 75 and PASI 90. The detailed results of sensitivity analyses are presented in table 2.

Subgroup analysis

Following subgroup analyses, heterogeneity was changed among some of the strata of subgroups. Regarding the subgroup of bDMARDs versus placebo, there was a significant difference between presubgroup and postsubgroup analysis for HAQ-DI in strata of golimumab (MD=0.08; 95% CI, -0.53 to 0.69), SF-36 MCS in strata of adalimumab (MD=1.24; 95% CI, -0.11 to 2.59) and strata of <24 weeks (MD=-0.13; 95% CI, -0.39 to 0.13), DLQI in strata of adalimumab, ixekizumab, 6-9 years and <24 weeks. Similar results were found for HAQ-DI and SF-36 MCS in the subgroup of bDMARDs+MTX versus MTX, HAQ-DI, SF-36 MCS, EQ-VAS and PASI 75 in the subgroup of bDMARDs versus tofacitinib, SF-36 MCS in the subgroup of bDMARDs versus MTX. In general, bDMARDs had obvious advantages in improving the QoL of PsA compared with placebo, but bDMARDs+MTX compared with MTX, bDMARDs compared with tofacitinib and bDMARDs compared with MTX had no obvious advantages or disadvantages in improving the QoL of PsA. Taking the outcome of HAQ-DI as an example, the results of the subgroups of bDMARDs versus placebo, bDMARDs+MTX versus MTX, bDMARDs versus tofacitinib and bDMARDs versus MTX were -0.21 (MD, 95% CI, -0.23 to -0.18), -0.22 (MD, 95% CI, -0.58 to 0.14), -0.01(MD, 95% CI, -0.05 to 0.04) and -0.03 (MD, 95% CI, -0.04 to -0.02), respectively. The detailed results of the



Table 1 Meta-an	alysis of RCTs that exa	mined the effects	of bDMARDs on 0	QoL		
Outcomes	Number of trials	Effect model	Effect size	95% CI	l² (%)	P value
Primary outcomes	3					
HAQ-DI	25	RE	-0.19	-0.22 to -0.17	100	<0.00001
SF-36 PCS	23	RE	3.76	3.42 to 4.10	99	<0.00001
SF-36 MCS	18	RE	1.76	1.27 to 2.25	99	< 0.00001
EQ-VAS	3	RE	5.27	1.21 to 9.34	99	0.01
Secondary outcor	nes					
DLQI	8	RE	-4.36	−5.76 to −2.96	99	<0.00001
PASI 50	7	RE	4.09	2.71 to 6.16	82	< 0.00001
PASI 75	27	RE	4.72	3.87 to 5.75	81	<0.00001
PASI 90	26	RE	5.73	4.73 to 6.95	59	< 0.00001
PASI 100	10	FE	9.57	7.38 to 12.43	13	<0.00001

bDMARDs, biological disease-modifying anti-rheumatic drugs; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; FE, fixed effects model; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 MCS, mental component summary of the Short Form 36; PASI 50/75/90/100, the proportion of participants achieving 50%/75%/90%/100% improvement from baseline in Psoriasis Area Severity Index; SF-36 PCS, physical component summary of the Short Form 36; QoL, quality of life; RCTs, randomised controlled trials; RE, random effects model.

subgroup analysis are presented in online supplemental table S3.

Publication bias

Since the funnel chart requires a certain amount of literature, this part of the study was limited to outcomes that included at least 10 RCTs. As presented in figure 3, there was potential publication bias detected for the outcomes including HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, PASI 90 and PASI 100. The p value calculated by Egger's test based on these outcomes also suggested the presence of publication bias, which can likely be attributed to unpublished studies with negative findings.

DISCUSSION

This meta-analysis focused on the effects of bDMARDs on QoL in patients with PsA, involving a total of 29 RCTs and 9720 participants. Through the quantitative analysis of nine outcomes, it was found that bDMARDs could effectively improve the QoL of patients with PsA. By reviewing the studies on minimal clinically important differences related to PsA on PubMed and comparing the minimal results of concerned outcomes, it was found that the decrease of HAQ-DI (MD=-0.19; 95% CI, -0.22 to -0.17) was a probable clinically meaningful effect (<-0.131).^{73 74} Similar results were found for SF-36 PCS (MD=3.76; 95% CI, 3.42 to 4.10; >2.1),⁷⁵⁻⁷⁸ SF-36 MCS (MD=1.76; 95% CI, 1.27 to 2.25; >1.33),⁷⁶⁻⁷⁸ and DLQI (MD=-4.36; 95% CI, -5.76 to -2.96; <-2.24),⁷⁹ but not for EQ-VAS (MD=5.27; 95% CI, 1.21 to 9.34, <5.35).⁸⁰⁻⁸³

Since the medicines in experimental and control groups had large differences in the effects on QoL, subgroup analysis was conducted according to the experimental groups and control groups. The results showed that there was obvious dissimilarity in subgroups of

bDMARDs compared with placebo, tofacitinib and MTX, concerning HAQ-DI, SF-36 MCS, EQ-VAS and PASI 75. The bDMARDs had a significant effect on improving the QoL compared with placebo, but more experimental data were required to confirm the effects of bDMARDs compared with tofacitinib and MTX.

Looking specifically at the subgroup of bDMARDs versus placebo, the variety of bDMARDs and duration of treatment were probable sources of heterogeneity. Golimumab, adalimumab and ixekizumab had no significant difference from placebo concerning one or two of HAQ-DI, SF-36 MCS and DLQI, which might be due to the efficacy of these bDMARDs that cannot be reflected on the change of QoL. The bDMARDs had no significant difference from placebo in the subgroup of duration of the treatment <24 weeks, which might indicate that long-term use of bDMARDs can improve the QoL of patients.

In this meta-analysis, quantitative analysis was not performed on the outcomes that were reported in less than three RCTs, including SF-36 Score, PsAQoL, DAPSA, PASI 70 and PASI Score. According to NCT02376790 (SEAM-PsA), ^{61 62} etanercept or plus MTX could decrease DAPSA and improve SF-36 Score compared with MTX, but without statistical significance. The result of NCT02980692⁶⁵ showed that tildrakizumab could decrease DAPSA compared with placebo without statistical significance. The results of NCT01087788 (RAPID-PsA)⁴³ 44 and NCT01392326 (FUTURE 1) 45 46 showed that certolizumab pegol and secukinumab could significantly decrease PsAQoL compared with placebo. As for PASI 70, Tao et al²⁷ found that infliximab+MTX got more significant improvement than MTX, while NCT02065713 (GO-DACT)⁵⁴ found that golimumab+MTX had no difference from MTX. Additionally, Tao et al²⁷ found that the PASI Score of patients in the infliximab+MTX group was

Table 2 Sensitivity analysis of RCTs that examined the effects of bDMARDs on QoL

	Presensitivi	ty analysis		Upper and	Postsensiti	ivity analysis	
Outcomes	Number of trials	Pooled estimates	95% CI	lower of	Pooled estimates	95% CI	Excluded trials
HAQ-DI	25	-0.19	-0.22 to -0.17	Upper	-0.18	-0.20 to -0.15	Mease et al ²⁹
				Lower	-0.21	−0.24 to −0.19	NCT00265096 (GO- REVEAL)
SF-36 PCS	23	3.76	3.42 to 4.10	Upper	3.96	3.63 to 4.28	NCT01877668 (OPAL Broaden)
				Lower	3.65	3.31 to 4.00	NCT02349295 (SPIRIT-P2)
SF-36 MCS	18	1.76	1.27 to 2.25	Upper	2.12	1.62 to 2.61	NCT01877668 (OPAL Broaden)
				Lower	1.65	1.14 to 2.16	NCT02349295 (SPIRIT-P2)
EQ-VAS	3	5.27	1.21 to 9.34	Upper	9.66	5.34 to 13.98	NCT01877668 (OPAL Broaden)
				Lower	3.71	-0.58 to 7.99	NCT02181673 (GO- VIBRANT)
DLQI	8	-4.36	−5.76 to −2.96	Upper	-3.50	−5.00 to −2.00	NCT01392326 (FUTURE 1)
				Lower	-5.67	-6.71 to -4.62	NCT01695239 (SPIRIT-P1)
PASI 50	7	4.09	2.71 to 6.16	Upper	4.83	2.75 to 8.49	NCT01087788 (RAPID-PsA)
				Lower	3.30	2.29 to 4.78	NCT00265096 (GO- REVEAL)
PASI 75	27	4.72	3.87 to 5.75	Upper	5.01	4.30 to 5.83	NCT01877668 (OPAL Broaden)
				Lower	4.54	3.74 to 5.51	NCT00265096 (GO- REVEAL)
PASI 90	26	5.73	4.73 to 6.95	Upper	6.19*	5.53 to 6.93	Tao et al ²⁷
				Lower	5.50	4.54 to 6.67	NCT01392326 (FUTURE 1)

^{*}Fixed effect.

PASI 50/75/90, the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis Area Severity Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 MCS, mental component summary of the Short Form 36; SF-36 PCS, physical component summary of the Short Form 36; QoL, quality of life; RCTs, randomised controlled trials.

significantly lower than that in the MTX group. Taken together, the quantitative analysis results of the effects of bDMARDs on the QoL of patients with PsA are robust.

The patients who took bDMARDs showed an improvement in terms of SF-36 PCS, EQ-VAS, PASI 50 and PASI 90, which was consistent with the results of previous studies. However, our meta-analysis showed an improvement in terms of SF-36 MCS, which was inconsistent with the results reported by Lemos *et al.* This variance could be attributed to the differences in search strategies and inclusion criteria. For example, the study of Lemos *et al.* considered the effects of TNFi rather than bDMARDs. The articles included in that study concerned not only RCTs but also observational studies. Additionally, the new trials that appeared after August 2013 were

included in our study and could not have been reviewed by them. Furthermore, this meta-analysis comprehensively and specifically analysed the effects of bDMARDs on the QoL of patients with PsA, and quantitatively analysed some other outcomes that were not studied before, including HAQ-DI and DLQI. The results of this meta-analysis might be used to support the evidence-based clinical application of bDMARDs.

However, there were several limitations of this metaanalysis. First, all the included studies were published only in English or Chinese, and the results of Egger's test indicated the presence of some publication bias. Second, most of the included RCTs were multicentre studies. It was difficult to conduct subgroup analysis based on countries and regions to evaluate the effects of bDMARDs on the

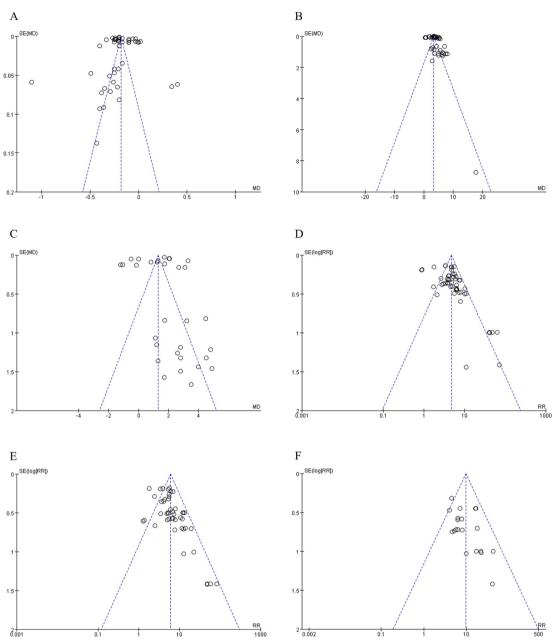


Figure 3 Funnel plots of (A) HAQ-DI, (B) SF-36 PCS, (C) SF-36 MCS, (D) PASI 75, (E) PASI 90 and (F) PASI 100. HAQ-DI, Health Assessment Questionnaire Disability Index: PASI 75/90/100, the proportion of participants achieving 75%/90%/100% improvement from baseline in Psoriasis Area Severity Index; SF-36 MCS, mental component summary of the Short Form 36; SF-36 PCS, physical component summary of the Short Form 36.

QoL of patients from different races and backgrounds. Third, the follow-up period for all included studies did not exceed 24 weeks, so the long-term effects were unable to be assessed. Thus, more studies that include longer follow-up periods of using bDMARDs in the treatment of PsA are required in the future to confirm the long-term effect of bDMARDs on the QoL of patients with PsA.

CONCLUSIONS

In summary, this meta-analysis demonstrated that the use of bDMARDs by patients with PsA appeared to significantly improve the QoL compared with a placebo. To

compare bDMARDs with other therapeutic agents, more extensive studies are still required to confirm the effect of single and combined bDMARDs.

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Contributors YqL substantially contributed to the conception and design of the research, and the acquisition, analysis and interpretation of data; was involved in drafting the manuscript and revising it critically for important intellectual content. ZD substantially contributed to the acquisition, analysis and interpretation of data; was involved in drafting the manuscript and revising it critically for important intellectual content. YL substantially contributed to the conception and design of the research; was involved in revising the manuscript critically for important



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Content

Table S1. Full electronic search strategy of PubMed
Table S2. Characteristics of included studies
Table S2. Subgroup analysis of RCTs that examined the effect of bDMARDs on QoL8
Figure S1 Forest plot of HAQ-DI
Figure S2. Forest plot of SF-36 PCS
Figure S3. Forest plot of SF-36 MCS
Figure S4. Forest plot of EQ-VAS.
Figure S5. Forest plot of DLQI.
Figure S6. Forest plot of PASI 50
Figure S7. Forest plot of PASI 75
Figure S8. Forest plot of PASI 90
Figure S9. Forest plot of PASI 100

Table S1. Full electronic search strategy of PubMed

#1 "arthritis, psoriatic" [MeSH Terms] #2 "etanercept"[Title/Abstract] OR "infliximab"[Title/Abstract] OR "adalimumab"[Title/Abstract] OR "golimumab"[Title/Abstract] OR OR "certolizumab"[Title/Abstract] "ustekinumab" [Title/Abstract] OR "guselkumab" [Title/Abstract] OR "risankizumab" [Title/Abstract] OR OR OR "tildrakizumab"[Title/Abstract] "secukinumab"[Title/Abstract] "ixekizumab"[Title/Abstract] OR "brodalumab"[Title/Abstract] OR "tumor necrosis factor inhibitor"[Title/Abstract] OR "TNFi"[Title/Abstract] OR "IL-12/23i"[Title/Abstract] "interleukin-12/23 inhibitor"[Title/Abstract] OR "IL-17i"[Title/Abstract] OR "interleukin-17 inhibitor"[Title/Abstract] OR "biologic"[Title/Abstract] #3 "health-related quality of life" [All Fields] OR "HRQoL" [All Fields] OR "Dermatology Life Quality Index"[All Fields] OR "DLQI"[All Fields] OR "disease activity index for psoriatic arthritis"[All Fields] OR "DAPSA"[All Fields] OR "psoriasis area and severity index"[All Fields] OR "PASI" [All Fields] OR "short form-36" [All Fields] OR "SF-36" [All Fields] OR "health assessment questionnaire"[All Fields] OR "HAQ"[All Fields] OR "Nottingham Health Profile"[All Fields] OR "NHP"[All Fields] OR "EuroQol-5D"[All Fields] OR "EQ-5D"[All Fields] OR "psoriasis disability index" [All Fields] OR "PDI" [All Fields] OR "Skindex-29" [All Fields] OR "Skindex-17" [All Fields] OR "quality of life" [All Fields] OR "PsAQoL" [All Fields] #4 #1 AND #2 AND #3

Table S2. Characteristics of included studies

T.::-1	T	Sample size	A	Duration of	Duration of	Presented
Trial name[Ref.]	Treatment arms and doses	(male, %)	Age, years	PsA, years	treatment	outcomes
Genovese MC 2007	Adalimumab 40 mg SC q2w	51 (56.9)	50.4±11.0	7.5±7.0	12 weeks	1235
[26]	Placebo	49 (51.0)	47.7±11.3	7.2 ± 7.0		
Hong Tao 2019 [27]	Infliximab 3mg /kg IV at weeks 0,2,6,14,22,24 +MTX	33 (57.58)	35.63±6.12	3.56±1.29	24 weeks	10(12)
	MTX 15.36±1.69 mg q1w	33 (54.55)	35.94 ± 6.25	3.52 ± 1.28		
IMPACT [28]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14	52 (57.7)	45.7±11.1	11.7±9.8	16 weeks	11)
	Placebo	52 (57.7)	45.2±9.7	11.0±6.6		
Mease PJ 2000 [29]	Etanercept 25 mg SC BIW	30 (53)	46.0*	9.0*	12 weeks	1111
	Placebo	30 (60)	43.5*	9.5*		
NCT00051623	Infliximab 5 mg/kg IV at weeks 0, 2, 6, 14, 22	100 (71)	47.1±12.8	8.4±7.2	24 weeks	123
(IMPACT 2) [30,31,32]	Placebo	100 (51)	46.5±11.3	7.5 ± 7.8		91112
NCT00195689	Adalimumab 40 mg SC at weeks 0, 2, 4, then q4w	151 (56.3)	48.6±12.5	9.8±8.3	24 weeks	1235
(ADEPT) [33,34,35]	Placebo	162 (54.9)	49.2±11.1	9.2 ± 8.7		9111213
NCT00265096 (GO-	Golimumab 50 mg SC q4w	146 (61)	45.7±10.7	7.2±6.8	24 weeks	123
REVEAL) [36,37]	Golimumab 100 mg SC q4w	146 (59)	48.2 ± 10.9	7.7±7.8		91112
	Placebo	113 (61)	47.0 ± 10.6	7.6 ± 7.9		
NCT00317499 [38]	Etanercept 25 mg SC BIW	101 (57)	47.6	9	24 weeks	911
	Placebo	104 (45)	47.3	9.2		
NCT00367237	Infliximab 5 mg/kg at weeks 0, 2, 6, 14 + MTX	56 (48.2)	40.1±12.3	2.8±2.6	16 weeks	1111
(RESPOND) [39]	MTX 15 mg q1w	54 (61.1)	42.3 ± 10.5	3.7±2.7		
NCT00809614 [40]	Secukinumab 10 mg/kg SC on days 1, 22	28 (32)	46.7±11.3	6.3±6.8	24 weeks	2
	Placebo	14 (43)	47.6±8.1	5.4±3.8		

NCT01009086	Ustekinumab 45 mg SC at weeks 0,2, then q12w	205 (51.7)	48.0 (39.0-55.0)*	3.4(1.2-9.2)*	24 weeks	1235
(PSUMMIT 1) [41]	Ustekinumab 90 mg SC at weeks 0,2, then q12w	204 (56.9)	47.0 (38.5-54.0)*	4.9(1.7-8.3)*		11)
	Placebo	206 (52.4)	48.0 (39.0-57.0)*	3.6(1.0-9.7)*		
NCT01077362	Ustekinumab 45 mg at weeks 0, 4, then q12w	103 (46.6)	49.0(40.0-56.0)*	5.3(2.3-12.2)*	24 weeks	1235
(PSUMMIT 2) [42]	Ustekinumab 90 mg at weeks 0, 4, then q12w	105 (46.7)	48.0(41.0-57.0)*	4.5(1.7-10.3)*		11)12)
	Placebo	104 (49.0)	48.0(38.5-56.0)*	5.5 (2.3-12.2)*		
NCT01087788	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 200	138 (46.4)	48.2±12.3	9.6±8.5	24 weeks	1235
(RAPID-PsA) [43,44]	mg q2w					791112
	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 400	135 (45.9)	47.1 ± 10.8	8.1 ± 8.3		
	mg q4w					
	Placebo	136 (41.9)	47.3±11.1	7.9 ± 7.7		
NCT01392326	Secukinumab 75 mg/kg IV at weeks 2, 4, then 75 mg	202 (41.6)	48.8 ± 12.2		24 weeks	1235
(FUTURE 1) [45,46]	SC q4w					7112
	Secukinumab 75 mg/kg IV at weeks 2, 4, then 150 mg	202 (47.5)	49.6±11.8			
	SC q4w					
	Placebo	202 (47.5)	48.5±11.2			
NCT01695239	Ixekizumab 80 mg SC q2w	107 (42.1)	49.1 ± 10.1	6.2 ± 6.4	24 weeks	1235
(SPIRIT-P1) [47,48]	Ixekizumab 80 mg SC q4w	103 (46.6)	49.8 ± 12.6	7.2 ± 8.0		6111213
	Adalimumab 40 mg SC q2w	101 (50.5)	48.6 ± 12.4	6.9 ± 7.5		
	Placebo	106(45.3)	50.6 ± 12.3	6.3 ± 6.9		
NCT01752634	Secukinumab 300 mg SC q1w to week 4 then q4w	100 (51)	46.9 ± 12.6		24 weeks	12112
(FUTURE 2) [49]	Secukinumab 150 mg SC q1w to week 4 then q4w	100 (55)	46.5±11.7			
	Secukinumab 75mg SC q1w to week 4 then q4w	99 (47)	48.6 ± 11.4			
	Placebo	98 (41)	49.9 ± 12.5			

NCT01877668	Adalimumab 40 mg SC q2w	106 (53)	47.4±11.3	5.3±5.3	3 months	1236
(OPAL Broaden)	Tofacitinib 5 mg orally BID	107 (47)	49.4 ± 12.6	7.3 ± 8.2		11)
[50][51]	Tofacitinib 10 mg orally BID	104 (40)	46.9 ± 12.4	5.4 ± 5.8		
	Placebo	105 (47)	47.7 ± 12.3	6.4 ± 6.4		
NCT01989468	Secukinumab 300 mg SC at weeks 1, 2, 3, 4, then q4w	139 (48.2)	49.3±12.9	8.3±9.2	24 weeks	121112
(FUTURE 3) [52]	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w	138 (44.2)	50.1±11.7	7.7 ± 8.5		
	Placebo	137 (43.1)	50.1 ± 12.6	6.6 ± 6.9		
NCT02024646	Brodalumab 140mg SC q2w	160 (50.0)	47.4±12.8	6.5±7.4	24 weeks	111213
(AMVISION-2) [53]	Brodalumab 210mg SC q2w	163 (48.5)	47.0 ± 12.6	6.4 ± 7.7		
	Placebo	161 (47.2)	48.3 ± 13.0	7.1 ± 7.5		
NCT02029495	Brodalumab 140mg SC q2w	158 (49.4)	49.9±12.8	8.1±8.1	24 weeks	11(12(13)
(AMVISION-1) [53]	Brodalumab 210mg SC q2w	159 (56.0)	49.1 ± 12.2	9.4 ± 9.3		
	Placebo	161 (50.3)	48.1±11.8	8.2 ± 8.2		
NCT02065713 (GO-	Golimumab 50 mg SC q4w + MTX	21 (81.0)	46.2 (15.5)*	3.8 (6.7)*	24 weeks	91012
DACT) [54]	MTX 15 mg orally q1w and increased 5 mg q4w until	22 (87.0)	44.1 (24.6)*	4.2 (6.1)*		
	25 mg q1w					
NCT02181673 (GO-	Golimumab 2 mg/kg IV at weeks 0, 4, then q8w	241 (50.6)	45.7 ± 11.3	6.2 ± 6.0	24 weeks	1235
VIBRANT) [55,56]	Placebo	239 (53.1)	46.7 ± 12.5	5.3 ± 5.9		6(1)(12(13)
NCT02294227	Secukinumab 150 mg SC q4w LD	114 (41.2)	48.3±12.2	5.6±7.3	16 weeks	21112
(FUTURE 4) [57]	Secukinumab 150 mg SC q4w no-LD	113 (45.1)	50.4±11.8	5.7±7.7		
	Placebo	114 (39.5)	48.5 ± 12.2	6.9 ± 7.6		
NCT02319759 [58]	Guselkumab 100 mg SC at weeks 0, 4, then q8w	100 (52)	47.4±12.8	7.0±7.2	24 weeks	1239
	Placebo	49 (49)	44.2±12.4	6.9 ± 7.2		111213
NCT02349295	Ixekizumab 80 mg SC q4w	122 (52)	52.6±13.6	11.0±9.6	24 weeks	123

(SPIRIT-P2) ^[59]	Ixekizumab 80 mg SC q2w	123 (41)	51.7±11.9	9.9±7.4		11)(12)(13)
	Placebo	118 (47)	51.5±10.4	9.2±7.3		
NCT02349451 [60]	Adalimumab 40 mg SC q1w	72 (54.2)	50.5±12.0	8.4±9.2	12 weeks	11)(12)
	Placebo	24 (50.0)	50.5±12.0	7.6±7.2		
NCT02376790	Etanercept 50 mg SC q1w	284 (53.2)	48.5±13.5	3.1±6.0	24 weeks	1234
(SEAM-PsA) [61,62]	Etanercept 50 mg SC + MTX orally q1w	283 (50.9)	48.1 ± 12.7	3.0 ± 6.0		8
	MTX 20 mg orally q1w	284 (43.7)	48.7±13.1	3.6 ± 6.8		
NCT02404350	Secukinumab 300 mg SC q4w LD	222 (48.6)	48.9 ± 12.8	6.7±8.3	16 weeks	11)(12)
(FUTURE 5) [63]	Secukinumab 150 mg SC q4w LD	220 (50.5)	48.4 ± 12.9	6.7 ± 7.1		
	Secukinumab 150 mg SC q4w no-LD	222 (54.1)	48.8 ± 11.8	6.2 ± 6.1		
	Placebo	332 (48.5)	49.0 ± 12.1	6.6 ± 7.6		
NCT02721966	Secukinumab 300 mg SC at weeks 1, 2, 3, 4, then q4w	167 (46.1)	46.2 ± 12.3		12 weeks	1
(MAXIMISE) [64]	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w	165 (49.1)	46.9 ± 11.5			
	Placebo	166 (53.0)	46.6 ± 11.5			
NCT02980692 ^[65]	Tildrakizumab 200 mg SC q4w	78 (41.0)	50.1 ± 13.3	7.5 ± 8.5	24 weeks	18
	Tildrakizumab 200 mg SC q12w	79 (53.2)	49.3 ± 11.2	6.2 ± 7.2		111213
	Tildrakizumab 100 mg SC q12w	77 (39.0)	49.2 ± 11.9	7.0 ± 6.6		
	Tildrakizumab 20 mg SC q12w	78 (47.4)	47.2 ± 13.4	6.6 ± 6.7		
	Placebo	79 (44.3)	48.1 ± 13.3	6.3 ± 6.1		
NCT03104400	Adalimumab 40 mg SC q2w	429 (48.3)	51.4 ± 12.0	5.9 ± 7.1	24 weeks	123
(SELECT-PsA 1) [66]	Placebo	423 (50.1)	50.4 ± 12.2	6.2 ± 7.0		
NCT03158285	Guselkumab 100mg SC at weeks 0,4, then q4w	245 (58)	45.9±11.5	5.5±5.9	24 weeks	123
(DISCOVER-2) [67]	Guselkumab 100mg SC at weeks 0,4, then q8w	248 (52)	44.9±11.9	5.1±5.5		111213
	Placebo	246 (48)	46.3±11.7	5.8 ± 5.6		

NCT03162796	Guselkumab 100 mg SC q4w	128 (52)	47.4±11.6	6.6±6.3	24 weeks	123
(DISCOVER-1) [68]	Guselkumab 100 mg SC at weeks 0, 4, then q8w	127 (54)	48.9±11.5	6.4 ± 5.9		111213
	Placebo	126 (48)	49.0±11.1	7.2±7.6		
NCT03671148	Risankizumab 150mg SC at weeks 0, 4, 16	224 (44.6)	53 (23–84)	8.2±8.2	24 weeks	1212
(KEEPsAKE 2) [69]	Placebo	219 (45.2)	52 (24-83)	8.2 ± 8.3		
NCT03675308	Risankizumab 150mg SC at weeks 0, 4, 16	483 (52.2)	52 (20–85)	7.1±7.0	24 weeks	1212
(KEEPsAKE 1) [71]	Placebo	481 (48.6)	52 (22–79)	7.1 ± 7.7		
NCT03796858	Guselkumab 100 mg SC at weeks 0, 4, then q8w	189 (46)	49±12	8.3±7.8	24 weeks	31112
(COSMOS)	Placebo	96 (54)	49±12	8.7±7.2		
Yufei Lin 2016 [72]	Infliximab 5mg /kg IV at weeks 0,2,6,12 + MTX	42 (61.90)	44.01 ± 10.33	3.62 ± 2.11	24 weeks	14)
	MTX 7.5-15 mg orally q1w and increased to 15-25 mg	42 (66.67)	43.59 ± 10.29	3.31 ± 2.12		
	qlw					

MTX: methotrexate; IV: intravenous; SC: subcutaneous; qXw: once every X weeks; BID: twice daily; BIW: twice weekly; LD: loading dose; ---: not reported; ① HAQ-DI, Health Assessment Questionnaire Disability Index; ②SF-36 PCS, physical component summary of the Short Form 36; ③SF-36 MCS, mental component summary of the Short Form 36; ④SF-36 score, the Short Form 36 score; ⑤DLQI, Dermatology Life Quality Index; ⑥EQ-VAS, EuroQol Visual Analogue Scale; ⑦PsAQoL, Psoriasis Arthritis Quality of Life; ⑧DAPSA, Disease Activity for Psoriatic Arthritis; ⑨PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index; ⑩PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index; ⑩PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index; ⑪PASI score, Psoriasis Area Severity Index score.

^{*} Data are reported as median (IQR);

Table S2. Subgroup analysis of RCTs that examined the effect of bDMARDs on QoL

Groups	Outcomes	K	Effect size	95% CI	I ² (%)	P-value
bDMARDs	HAQ-DI					
vs. Placebo	Total	40	-0.21	-0.23, -0.18	99	< 0.00001
	Category of bDMARD					
	TNFi	11	-0.25	-0.31, -0.18	98	< 0.00001
	IL-12/23i	9	-0.23	-0.27, -0.19	99	< 0.00001
	IL-17i	11	-0.17	-0.21, -0.14	99	< 0.00001
	Variety of bDMARD					
	Etanercept	1	-1.10	-1.22, -0.98		< 0.00001
	Infliximab	1	-0.40	-0.58, -0.22		< 0.0001
	Adalimumab	5	-0.20*	-0.20, -0.20	0	< 0.00001
	Golimumab	3	0.08	-0.53, 0.69	99	0.79
	Certolizumab pegol	2	-0.30*	-0.39, -0.21	1	< 0.00001
	Ustekinumab	4	-0.21*	-0.25, -0.17	0	< 0.00001
	Guselkumab	5	-0.27	-0.31, -0.24	98	< 0.00001
	Tildrakizumab	4	-0.07	-0.12, -0.03	97	0.003
	Risankizumab	2	-0.19	-0.21, -0.16	98	< 0.00001
	Secukinumab	9	-0.17	-0.22, -0.12	99	< 0.00001
	Ixekizumab	4	-0.32	-0.46, -0.18	98	< 0.00001
	Duration of PsA					
	< 6 years	8	-0.22	-0.25, -0.20	98	< 0.00001
	6-9 years	20	-0.16	-0.20, -0.13	99	< 0.00001
	\geq 9 years	5	-0.46	-0.65, -0.28	99	< 0.00001
	Unclear	7	-0.17	-0.23, -0.12	99	< 0.00001
	Duration of treatment					
	< 24 weeks	5	-0.32	-0.40, -0.24	99	< 0.00001
	≥ 24 weeks	35	-0.19	-0.22, -0.17	99	< 0.00001
	SF-36 PCS					
	Total	36	4.04	3.75, 4.32	99	< 0.00001
	Category of bDMARD					
	TNFi	11	4.96	4.37, 5.56	88	< 0.00001
	IL-12/23i	11	3.93	3.58, 4.28	98	< 0.00001
	IL-17i	14	3.78	3.05, 4.50	99	< 0.00001
	Variety of bDMARD					
	Infliximab	1	6.40	3.90, 8.90		< 0.00001
	Adalimumab	5	3.62	3.26, 3.98	73	< 0.00001
	Golimumab	3	7.06*	6.06, 8.05	0	< 0.00001
	Certolizumab pegol	2	5.85*	4.48, 7.22	0	< 0.00001
	Ustekinumab	4	3.47*	2.74, 4.22	6	< 0.00001
	Guselkumab	5	4.22	3.77, 4.67	98	< 0.00001
	Risankizumab	2	3.60	3.01, 4.19	99	< 0.00001
	Secukinumab	10	3.30	2.50, 4.11	99	< 0.00001
	Ixekizumab	4	5.22	4.67, 5.78	64	< 0.00001
			8			

Secukinumab	Duration of PsA					
≥ 9 years 4 5.58 4.84,6.31 79 <0.00001 Unclear 5 3.97 3.27,4.67 99 <0.00001 Duration of treatment < 24 weeks 4 3.04 2.62, 3.46 92 <0.00001 ≥ 24 weeks 32 4.19 3.88, 4.50 99 <0.00001 SF-36 MCS Total 27 2.11 1.76, 2.46 97 <0.00001 IL-12/23i 9 1.75 1.28, 2.22 96 <0.00001 IL-17i 7 2.37 1.51, 3.23 99 <0.00001 Variety of bDMARD Infliximab 1 3.50 0.24, 6.76 0.04 Adalimumab 5 1.24 -0.11, 2.59 98 0.07 Golimumab 3 4.47* 3.22, 5.72 0 <0.00001 Guselkumab 6 1.66 1.22, 2.10 98 <0.00001 Guselkumab 4 2.21* 1.27, 3.15 0 <0.00001 Secukinumab 4 2.21* 1.27, 3.15 0 <0.00001 Secukinumab 4 2.89* 2.67, 3.11 32 <0.00001 Duration of PsA < 6 years 8 1.57 1.13, 2.01 98 <0.00001 Duration of PsA < 6 years 13 2.00 1.49, 2.52 84 <0.00001 Duration of treatment < 24 weeks 2 -0.13* -0.39, 0.13 27 0.86 ≥ 9 years 4 2.90 2.40, 3.40 61 <0.00001 Duration of treatment < 24 weeks 2 -0.13* -0.39, 0.13 27 0.86 ≥ 24 weeks 2 5 2.24 1.91, 2.57 97 <0.00001 EQ-VAS Total 5 8.76 5.32, 12.20 71 <0.00001 Category of bDMARD TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.00001 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 <0.00001 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 <0.00001 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 <0.00001	< 6 years	10	3.39	3.09, 3.68	97	< 0.00001
Unclear 5 3.97 3.27, 4.67 99 < 0.00001 Duration of treatment < 24 weeks	6-9 years	17	4.44	3.81, 5.08	99	< 0.00001
Duration of treatment < 24 weeks	≥9 years	4	5.58	4.84, 6.31	79	< 0.00001
< 24 weeks	Unclear	5	3.97	3.27, 4.67	99	< 0.00001
≥ 24 weeks 32 4.19 3.88, 4.50 99 < 0.00001 SF-36 MCS Total 27 2.11 1.76, 2.46 97 < 0.00001	Duration of treatment					
SF-36 MCS Total 27 2.11 1.76, 2.46 97 < 0.00001	< 24 weeks	4	3.04	2.62, 3.46	92	< 0.00001
Total 27 2.11 1.76, 2.46 97 < 0.00001 Category of bDMARD TNFi 11 2.60 1.59, 3.60 95 < 0.00001	≥ 24 weeks	32	4.19	3.88, 4.50	99	< 0.00001
Category of bDMARD TNFi 11 2.60 1.59, 3.60 95 < 0.00001	SF-36 MCS					
TNFi 11 2.60 1.59, 3.60 95 <0.00001 IL-12/23i 9 1.75 1.28, 2.22 96 <0.00001 IL-17i 7 2.37 1.51, 3.23 99 <0.00001 Variety of bDMARD Infliximab 1 3.50 0.24, 6.76 0.04 Adalimumab 5 1.24 -0.11, 2.59 98 0.07 Golimumab 3 4.47* 3.22, 5.72 0 <0.00001 Certolizumab pegol 2 3.78* 2.11, 5.44 28 0.0002 Ustekinumab 4 2.21* 1.27, 3.15 0 <0.00001 Guselkumab 6 1.66 1.22, 2.10 98 <0.00001 Secukinumab 2 2.30 0.34, 4.26 100 0.02 Ixekizumab 4 2.89* 2.67, 3.11 32 <0.00001 Duration of PsA < 6 years 8 1.57 1.13, 2.01 98 <0.00001 6-9 years 13 2.00 1.49, 2.52 84 <0.00001 ≥ 9 years 4 2.90 2.40, 3.40 61 <0.00001 Unclear 2 2.30 0.34, 4.26 100 0.02 Duration of treatment < 24 weeks 2 -0.13* -0.39, 0.13 27 0.86 ≥ 24 weeks 25 2.24 1.91, 2.57 97 <0.00001 EQ-VAS Total 5 8.76 5.32, 12.20 71 <0.00001 Category of bDMARD TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 <0.00001 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 <0.00001	Total	27	2.11	1.76, 2.46	97	< 0.00001
IL-12/23i 9 1.75 1.28, 2.22 96 < 0.00001	Category of bDMARD					
IL-17i 7 2.37 1.51, 3.23 99 < 0.00001 Variety of bDMARD Infliximab 1 3.50 0.24, 6.76 0.04 Adalimumab 5 1.24 -0.11, 2.59 98 0.07 Golimumab 3 4.47* 3.22, 5.72 0 < 0.00001 Certolizumab pegol 2 3.78* 2.11, 5.44 28 0.0002 Ustekinumab 4 2.21* 1.27, 3.15 0 < 0.00001 Guselkumab 6 1.66 1.22, 2.10 98 < 0.00001 Secukinumab 2 2.30 0.34, 4.26 100 0.02 Ixekizumab 4 2.89* 2.67, 3.11 32 < 0.00001 Duration of PsA 8 1.57 1.13, 2.01 98 < 0.00001 6-9 years 8 1.57 1.13, 2.01 98 < 0.00001 6-9 years 4 2.90 2.40, 3.40 61 < 0.00001 Unclear 2 2.30 0.34, 4.26 100 0.02 Durati	TNFi	11	2.60	1.59, 3.60	95	< 0.00001
Variety of bDMARD Infliximab 1 3.50 0.24, 6.76 0.04 Adalimumab 5 1.24 -0.11, 2.59 98 0.07 Golimumab 3 4.47* 3.22, 5.72 0 < 0.00001	IL-12/23i	9	1.75	1.28, 2.22	96	< 0.00001
Infliximab 1 3.50 0.24, 6.76 0.04 Adalimumab 5 1.24 -0.11, 2.59 98 0.07 Golimumab 3 4.47* 3.22, 5.72 0 < 0.00001	IL-17i	7	2.37	1.51, 3.23	99	< 0.00001
Adalimumab 5 1.24 -0.11, 2.59 98 0.07 Golimumab 3 4.47* 3.22, 5.72 0 < 0.00001	Variety of bDMARD					
Golimumab 3 4.47* 3.22, 5.72 0 < 0.00001 Certolizumab pegol 2 3.78* 2.11, 5.44 28 0.0002 Ustekinumab 4 2.21* 1.27, 3.15 0 < 0.00001	Infliximab	1	3.50	0.24, 6.76		0.04
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Adalimumab	5	1.24	-0.11, 2.59	98	0.07
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Golimumab	3	4.47*	3.22, 5.72	0	< 0.00001
Guselkumab 6 1.66 1.22, 2.10 98 < 0.00001	Certolizumab pegol	2	3.78*	2.11, 5.44	28	0.0002
Secukinumab 2 2.30 0.34, 4.26 100 0.02 Ixekizumab 4 2.89* 2.67, 3.11 32 < 0.00001	Ustekinumab	4	2.21*	1.27, 3.15	0	< 0.00001
Ixekizumab 4 2.89* 2.67, 3.11 32 < 0.00001	Guselkumab	6	1.66	1.22, 2.10	98	< 0.00001
Duration of PsA < 6 years	Secukinumab	2	2.30	0.34, 4.26	100	0.02
< 6 years	Ixekizumab	4	2.89*	2.67, 3.11	32	< 0.00001
6-9 years 13 2.00 1.49, 2.52 84 < 0.00001 ≥ 9 years 4 2.90 2.40, 3.40 61 < 0.00001 Unclear 2 2.30 0.34, 4.26 100 0.02 Duration of treatment < 24 weeks 2 -0.13* -0.39, 0.13 27 0.86 ≥ 24 weeks 25 2.24 1.91, 2.57 97 < 0.00001 EQ-VAS Total 5 8.76 5.32, 12.20 71 < 0.00001 Category of bDMARD TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	Duration of PsA					
≥ 9 years 4 2.90 2.40, 3.40 61 < 0.00001 Unclear 2 2.30 0.34, 4.26 100 0.02 Duration of treatment < 24 weeks 2 -0.13* -0.39, 0.13 27 0.86 ≥ 24 weeks 25 2.24 1.91, 2.57 97 < 0.00001 EQ-VAS Total 5 8.76 5.32, 12.20 71 < 0.00001 Category of bDMARD TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	< 6 years	8	1.57	1.13, 2.01	98	< 0.00001
Unclear 2 2.30 0.34, 4.26 100 0.02 Duration of treatment 24 weeks 2 -0.13* -0.39, 0.13 27 0.86 ≥ 24 weeks 25 2.24 1.91, 2.57 97 < 0.00001	6-9 years	13	2.00	1.49, 2.52	84	< 0.00001
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	≥9 years	4	2.90	2.40, 3.40	61	< 0.00001
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Unclear	2	2.30	0.34, 4.26	100	0.02
≥ 24 weeks 25 2.24 1.91, 2.57 97 < 0.00001 EQ-VAS Total 5 8.76 5.32, 12.20 71 < 0.00001	Duration of treatment					
EQ-VAS Total 5 8.76 5.32, 12.20 71 < 0.00001	< 24 weeks	2	-0.13*	-0.39, 0.13	27	0.86
Total 5 8.76 5.32, 12.20 71 < 0.00001 Category of bDMARD TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	≥ 24 weeks	25	2.24	1.91, 2.57	97	< 0.00001
Category of bDMARD TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	EQ-VAS					
TNFi 3 9.05 3.75, 14.35 85 0.0008 IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	Total	5	8.76	5.32, 12.20	71	< 0.00001
IL-17i 2 8.31* 3.85, 12.77 0 0.0003 Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001	Category of bDMARD					
Variety of bDMARD Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	TNFi	3	9.05	3.75, 14.35	85	0.0008
Adalimumab 2 6.72* 6.13, 7.31 0 < 0.00001 Golimumab 1 14.70 10.44, 18.96 < 0.00001	IL-17i	2	8.31*	3.85, 12.77	0	0.0003
Golimumab 1 14.70 10.44, 18.96 < 0.00001	Variety of bDMARD					
•	Adalimumab	2	6.72*	6.13, 7.31	0	< 0.00001
T 11 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Golimumab	1	14.70	10.44, 18.96		< 0.00001
Ixekizumab 2 8.31* 3.85, 12.77 0 0.0003	Ixekizumab	2	8.31*	3.85, 12.77	0	0.0003
Duration of PsA	Duration of PsA					
< 6 years 1 6.73 6.14, 7.32 < 0.00001	< 6 years	1	6.73	6.14, 7.32		< 0.00001
	6-9 years	4	9.66	5.34, 13.98	58	< 0.0001
6-9 years 4 9.66 5.34, 13.98 58 < 0.0001	Duration of treatment					
6-9 years 4 9.66 5 34 13 98 58 < 0.0001	•	•	2.00	3.3 1, 13.70	55	0.0001
•						

< 24 weeks	1	6.73	6.14, 7.32		< 0.00001
≥ 24 weeks	4	9.66	5.34, 13.98	58	< 0.0001
DLQI					
Total	14	-4.36	-5.76, -2.96	99	< 0.00001
Category of bDMARD					
TNFi	6	-3.38	-5.53, -1.23	92	0.002
IL-12/23i	4	-5.39*	-6.15, -4.63	0	< 0.00001
IL-17i	4	-4.79	-6.81, -2.77	99	< 0.00001
Variety of bDMARD					
Adalimumab	3	-2.31	-5.60, 0.98	89	0.17
Golimumab	1	-6.20	-7.56, -4.84		< 0.00001
Certolizumab pegol	2	-3.46	-6.40, -0.53	90	0.02
Ustekinumab	4	-5.39*	-6.15, -4.63	0	< 0.00001
Secukinumab	2	-9.05	-9.93, -8.17	98	< 0.00001
Ixekizumab	2	-0.17*	-0.99, 0.65	0	0.69
Duration of PsA					
< 6 years	4	-5.39*	-6.15, -4.63	0	< 0.00001
6-9 years	6	-1.70	-3.59, 0.19	92	0.08
≥9 years	2	-5.12*	-6.35, -3.89	0	< 0.00001
Unclear	2	-9.05	-9.93, -8.17	98	< 0.00001
Duration of treatment					
< 24 weeks	1	-1.70	-4.21, 0.81		0.18
≥ 24 weeks	13	-4.53	-5.97, -3.10	99	< 0.00001
PASI 50					
Total	8	4.54	2.98, 6.91	81	< 0.00001
Category of bDMARD					
TNFi	7	4.92	3.00, 8.07	83	< 0.00001
IL-12/23i	1	2.97	1.90, 4.65		< 0.00001
Variety of bDMARD					
Etanercept	1	2.69	1.68, 4.30		< 0.0001
Infliximab	1	9.83	5.06, 19.09		< 0.00001
Adalimumab	1	6.50	3.34, 12.64		< 0.00001
Golimumab	2	9.59	5.55, 16.56	0	< 0.00001
Certolizumab pegol	2	2.63	2.03, 3.40	0	< 0.00001
Guselkumab	1	2.97	1.90, 4.65		< 0.00001
Duration of PsA			,		
6-9 years	4	6.93	3.33, 14.42	80	< 0.00001
≥ 9 years	4	3.06	2.20, 4.25	54	< 0.00001
PASI 75			·		
Total	47	5.29*	4.85, 5.76	45	< 0.00001
Category of bDMARD			,-		
TNFi	13	7.19	4.26, 12.16	74	< 0.00001
IL-12/23i	13	4.95*	4.30, 5.69	49	< 0.00001
IL-17i	21	4.94*	4.36, 5.60	5	< 0.00001
11/1	~ 1	1.2 T	1.50, 5.00	J	. 0.00001

Variety of bDMARD					
Etanercept	2	8.34*	2.83, 24.62	0	0.0001
Infliximab	2	65.64*	13.30, 322.82	0	< 0.00001
Adalimumab	4	4.58	1.72, 12.22	74	0.002
Golimumab	3	18.30	2.23, 149.96	84	0.007
Certolizumab pegol	2	4.06*	2.79, 5.91	0	< 0.00001
Ustekinumab	4	6.50*	4.79, 8.83	2	< 0.00001
Guselkumab	6	4.23*	3.56, 5.02	43	< 0.00001
Tildrakizumab	4	3.70*	2.59, 5.28	0	< 0.00001
Secukinumab	12	5.10*	4.41, 5.89	21	< 0.00001
Ixekizumab	4	5.03*	3.51, 7.22	2	< 0.00001
Brodalumab	4	6.16*	4.32, 8.80	0	< 0.00001
Duration of PsA					
< 6 years	9	4.68	3.57, 6.13	57	< 0.00001
6-9 years	26	5.68*	5.06, 6.38	26	< 0.00001
≥9 years	7	5.92	3.33, 10.51	57	< 0.00001
Unclear	5	4.23	2.43, 7.36	68	< 0.00001
Duration of treatment					
< 24 weeks	9	5.13*	4.37, 6.02	37	< 0.00001
≥ 24 weeks	38	5.34*	4.83, 5.91	48	< 0.00001
PASI 90					
Total	43	6.38*	5.68, 7.16	30	< 0.00001
Category of bDMARD					
TNFi	9	9.45*	6.62, 13.50	49	< 0.00001
IL-12/23i	11	7.47*	5.97, 9.35	0	< 0.00001
IL-17i	23	5.39*	4.66, 6.24	23	< 0.00001
Variety of bDMARD					
Infliximab	1	82.76	5.17, 1325.04		0.002
Adalimumab	3	7.64	1.43, 40.80	65	0.02
Golimumab	3	16.48	2 22 116 50		0.005
		10.10	2.33, 116.59	65	0.005
Certolizumab pegol	2	7.11*	2.33, 116.59 3.78, 13.36	65 0	< 0.0001
Certolizumab pegol Ustekinumab	2 2				
		7.11*	3.78, 13.36	0	< 0.00001
Ustekinumab	2	7.11* 9.93*	3.78, 13.36 4.42, 22.34	0 0	< 0.00001 < 0.00001
Ustekinumab Guselkumab	2	7.11* 9.93* 6.36*	3.78, 13.36 4.42, 22.34 4.96, 8.16	0 0 0	< 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab	2 6 4	7.11* 9.93* 6.36* 6.09*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76	0 0 0 0	< 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab	2 6 4 2	7.11* 9.93* 6.36* 6.09* 5.36*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42	0 0 0 0	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab Secukinumab	2 6 4 2 12	7.11* 9.93* 6.36* 6.09* 5.36* 5.12	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42 3.72, 7.03	0 0 0 0 0 0 51	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab Secukinumab Ixekizumab	2 6 4 2 12 4	7.11* 9.93* 6.36* 6.09* 5.36* 5.12 5.75*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42 3.72, 7.03 3.70, 8.93	0 0 0 0 0 51 39	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab Secukinumab Ixekizumab Brodalumab	2 6 4 2 12 4	7.11* 9.93* 6.36* 6.09* 5.36* 5.12 5.75*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42 3.72, 7.03 3.70, 8.93	0 0 0 0 0 51 39	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab Secukinumab Ixekizumab Brodalumab Duration of PsA	2 6 4 2 12 4 4	7.11* 9.93* 6.36* 6.09* 5.36* 5.12 5.75* 12.05*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42 3.72, 7.03 3.70, 8.93 6.80, 21.36	0 0 0 0 0 51 39	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab Secukinumab Ixekizumab Brodalumab Duration of PsA < 6 years	2 6 4 2 12 4 4	7.11* 9.93* 6.36* 6.09* 5.36* 5.12 5.75* 12.05*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42 3.72, 7.03 3.70, 8.93 6.80, 21.36 5.62, 10.07	0 0 0 0 0 51 39 0	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001
Ustekinumab Guselkumab Tildrakizumab Risankizumab Secukinumab Ixekizumab Brodalumab Duration of PsA < 6 years 6-9 years	2 6 4 2 12 4 4 6 28	7.11* 9.93* 6.36* 6.09* 5.36* 5.12 5.75* 12.05* 7.52* 6.10*	3.78, 13.36 4.42, 22.34 4.96, 8.16 3.44, 10.76 3.87, 7.42 3.72, 7.03 3.70, 8.93 6.80, 21.36 5.62, 10.07 5.31, 7.00	0 0 0 0 0 51 39 0	< 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001 < 0.00001

	< 24 weeks	6	4.60*	3.73, 5.67	44	< 0.00001
	≥ 24 weeks	37	7.04*	6.14, 8.08	14	< 0.00001
bDMARDs+	HAQ-DI	2	-0.22	-0.58, 0.14	86	0.23
MTX vs.	SF-36 PCS	1	2.00	1.90, 2.10		< 0.00001
MTX	SF-36 MCS	1	0.00	-0.10, 0.10		1.00
	PASI 50	1	1.76	1.06, 2.92		0.03
	PASI 75	1	1.79	1.31, 2.44		0.0002
	PASI 90	2	1.97	1.45, 2.70	0	< 0.0001
bDMARDs	HAQ-DI	2	-0.01	-0.05, 0.04	96	0.84
vs.	SF-36 PCS	2	0.63*	0.49, 0.77	36	< 0.00001
Tofacitinib	SF-36 MCS	2	-1.15*	-1.32, -0.97	0	< 0.00001
	EQ-VAS	2	-1.81	-3.61, -0.02	95	0.05
	PASI 75	2	0.90*	0.69, 1.17	0	0.43
bDMARDs	HAQ-DI	1	-0.03	-0.04, -0.02		< 0.00001
vs. MTX	SF-36 PCS	1	1.80	1.70, 1.90		< 0.00001
	SF-36 MCS	1	-0.50	-0.60, -0.40		< 0.00001

bDMARDs, the biological disease-modifying anti-rheumatic drugs; TNFi, the tumor necrosis factor inhibitor; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36, DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90, the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis Area Severity Index; K: Number of data reported in included studies;

^{*} fixed effect

Figure S1 Forest plot of HAQ-DI. HAQ-DI, Health Assessment Questionnaire Disability Index.

	Expe	rimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	-0.3	0.5	51	-0.1	0.3	49	1.3%	-0.20 [-0.36, -0.04]	
Mease PJ 2000	-1.2	0.23	30	-0.1	0.23	30	1.7%	-1.10 [-1.22, -0.98]	
NCT00051623 (IMPACT 2)	-0.4	0.66	100	0	0.66	100	1.2%	-0.40 [-0.58, -0.22]	
NCT00195689 (ADEPT)	-0.4	0.5	151	-0.1	0.4	162	1.9%	-0.30 [-0.40, -0.20]	
NCT00265096 (GO-REVEAL) A	0.33	0.55	146	-0.01	0.49	113	1.6%	0.34 [0.21, 0.47]	
NCT00265096 (GO-REVEAL) B	0.39	0.5	146	-0.01	0.49	113	1.7%	0.40 [0.28, 0.52]	
NCT00367237 (RESPOND)	-0.99	0.72	56	-0.56	0.72	54	0.7%	-0.43 [-0.70, -0.16]	
NCT01009086 (PSUMMIT 1) A	-0.3	0.47	205	-0.09	0.38	206	2.1%	-0.21 [-0.29, -0.13]	
NCT01009086 (PSUMMIT 1) B	-0.34	0.56	204	-0.09	0.38	206	2.0%	-0.25 [-0.34, -0.16]	
NCT01077362 (PSUMMIT 2) A	-0.17	0.29	103	0	0.2	104	2.2%	-0.17 [-0.24, -0.10]	-
NCT01077362 (PSUMMIT 2) B	-0.25	0.38	105	0	0.2	104	2.1%	-0.25 [-0.33, -0.17]	-
NCT01087788 (RAPID-PsA) A	-0.52	0.66	138	-0.17	0.43	136	1.6%	-0.35 [-0.48, -0.22]	
NCT01087788 (RAPID-PsA) B	-0.43	0.54	135	-0.17	0.43	136	1.7%	-0.26 [-0.38, -0.14]	
NCT01392326 (FUTURE 1) A	-0.41	0.04	202	-0.17	0.05	202	2.6%	-0.24 [-0.25, -0.23]	•
NCT01392326 (FUTURE 1) B		0.04				202	2.6%	-0.23 [-0.24, -0.22]	
NCT01695239 (SPIRIT-P1) A	-0.53		107	-0.15	0.5	106	1.5%	-0.38 [-0.52, -0.24]	
NCT01695239 (SPIRIT-P1) B	-0.44		103	-0.15	0.5	106	1.5%	-0.29 [-0.43, -0.15]	
NCT01695239 (SPIRIT-P1) C	-0.37		101	-0.15	0.5	106	1.6%	-0.22 [-0.35, -0.09]	
NCT01752634 (FUTURE 2) A	-0.56		100	-0.31		98	2.6%	-0.25 [-0.27, -0.23]	•
NCT01752634 (FUTURE 2) B	-0.48		100	-0.31		98	2.6%	-0.17 [-0.19, -0.15]	-
NCT01752634 (FUTURE 2) C	-0.32		99	-0.31		98	2.6%	-0.01 [-0.03, 0.01]	4
NCT01877668 (OPAL Broaden) A	-0.38		106	-0.35		107	2.6%	-0.03 [-0.04, -0.02]	<u>-</u>
NCT01877668 (OPAL Broaden) B	-0.38		106		0.05	104	2.6%	0.02 [0.01, 0.03]	-
NCT01877668 (OPAL Broaden) C	-0.38		106	-0.18		105	2.6%	-0.20 [-0.21, -0.19]	·
NCT01989468 (FUTURE 3) A	-0.38	0.04	139	-0.17		137	2.6%	-0.21 [-0.22, -0.20]	-
NCT01989468 (FUTURE 3) B	-0.27		138	-0.17		137	2.6%	-0.10 [-0.11, -0.09]	*
NCT02181673 (GO-VIBRANT)			237	-0.14	0.5	236	2.0%	-0.49 [-0.58, -0.40]	
NCT02319759	-0.42		100	-0.06		49	1.2%	-0.36 [-0.54, -0.18]	
NCT02349295 (SPIRIT-P2) A	-0.6	0.1	122	-0.2	0.33	118	2.6%	-0.40 [-0.43, -0.37]	÷
NCT02349295 (SPIRIT-P2) B	-0.4	0.1	123	-0.2	0.1	118	2.6%	-0.20 [-0.23, -0.17]	-
NCT02376790 (SEAM-PSA) A	-0.44		258	-0.41		252	2.6%	-0.03 [-0.04, -0.02]	
NCT02376790 (SEAM-PSA) B	-0.47		283	-0.41		252	2.6%	-0.06 [-0.07, -0.05]	
NCT02721966 (MAXIMISE) A		0.04	167		0.04	166	2.6%	-0.20 [-0.21, -0.19]	
NCT02721966 (MAXIMISE) B		0.04	165		0.04	166	2.6%	-0.10 [-0.11, -0.09]	
NCT02980692 A			78		0.05	79	2.6%	-0.10 [-0.12, -0.08]	•
NCT02980692 B		0.05	79		0.05	79	2.6%	-0.10 [-0.12, -0.08]	•
NCT02980692 C		0.05	77		0.05	79	2.6%	-0.10 [-0.12, -0.08]	•
NCT02980692 D		0.05	78		0.05	79	2.6%	0.00 [-0.02, 0.02]	<u> </u>
NCT02980092 D NCT03104400 (SELECT-PsA 1)	-0.39	0.04	391	-0.19		367	2.6%		
NCT03104400 (SELECT-PSAT) NCT03158285 (DISCOVER-2) A		0.04	245	-0.19		246	2.6%	-0.20 [-0.21, -0.19] -0.27 [-0.28, -0.26]	
	-0.4		245	-0.13		246	2.6%		
NCT03158285 (DISCOVER-2) B	-0.37		128	-0.13		126	2.6%	-0.24 [-0.25, -0.23]	
NCT03162796 (DISCOVER-1) A								-0.33 [-0.34, -0.32]	
NCT03162796 (DISCOVER-1) B	-0.32 -0.22		127 224	-0.07 -0.05		126 219	2.6% 2.6%	-0.25 [-0.26, -0.24]	
NCT03671148 (KEEPsAKE 2)								-0.17 [-0.18, -0.16]	
NCT03675308 (KEEPsAKE 1)	-0.31	0.02	483	-0.11	0.03	481	2.6%	-0.20 [-0.20, -0.20]	
Total (95% CI)			6792			6603	100.0%	-0.19 [-0.22, -0.17]	•
Heterogeneity: Tau2 = 0.01; Chi2 = 1	0182.80,	df = 4	4 (P < (0.00001); l ² = 1	00%			-1 -05 0 05 1
Test for overall effect: Z = 14.14 (P =									. 0.0 0 0.0 .
									Favours [experimental] Favours [control]

Figure S2. Forest plot of SF-36 PCS. SF-36 PCS, physical component summary of the Short Form 36.

	Experimental							Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	5.7	8.5	49	2.8	7.1	45	0.9%	2.90 [-0.26, 6.06]	
NCT00051623 (IMPACT 2)	7.7	9.8	100	1.3	8.2	100	1.2%	6.40 [3.90, 8.90]	
NCT00195689 (ADEPT)	9.3	10.1	140	1.4	9.6	152	1.3%	7.90 [5.64, 10.16]	
NCT00265096 (GO-REVEAL) A	7.42	9.17	146	0.67	8.72	113	1.4%	6.75 [4.56, 8.94]	-
NCT00265096 (GO-REVEAL) B	8.22	9.64	146	0.67	8.72	113	1.4%	7.55 [5.31, 9.79]	
NCT00809614	15.2	28.1	28	-2.61	26	14	0.0%	17.81 [0.67, 34.95]	
NCT01009086 (PSUMMIT 1) A	4.46	8.96	205	1.38	5.6	206	2.1%	3.08 [1.63, 4.53]	-
NCT01009086 (PSUMMIT 1) B		7.69	204	1.38	5.6	206	2.2%	4.38 [3.08, 5.68]	-
NCT01077362 (PSUMMIT 2) A	3.76	7.37	99	1.13	3.61	97	1.9%	2.63 [1.01, 4.25]	
NCT01077362 (PSUMMIT 2) B		7.75	97	1.13	3.61	97	1.8%	3.39 [1.69, 5.09]	-
NCT01087788 (RAPID-PsA) A	8.4	10.1	138	2.1	7.2	136	1.5%	6.30 [4.23, 8.37]	
NCT01087788 (RAPID-PsA) B	7.6	8.1	135	2.1	7.2	136	1.7%	5.50 [3.67, 7.33]	-
NCT01392326 (FUTURE 1) A	5.41	0.52	202	1.82	0.72	202	3.3%	3.59 [3.47, 3.71]	
NCT01392326 (FUTURE 1) B	5.91	0.53	202		0.72	202	3.3%	4.09 [3.97, 4.21]	
NCT01695239 (SPIRIT-P1) A	7.7	8.6	107	2.7	7.7	106	1.4%	5.00 [2.81, 7.19]	
NCT01695239 (SPIRIT-P1) B	7.7	9.8	103	2.7	7.7	106	1.3%	5.00 [2.61, 7.39]	
NCT01695239 (SPIRIT-P1) C	6.3	8.3	101	2.7	7.7	106	1.4%	3.60 [1.42, 5.78]	
NCT01752634 (FUTURE 2) A		0.74	100	1.95		98	3.2%	5.30 [5.06, 5.54]	
NCT01752634 (FUTURE 2) B		0.73	100		0.97	98	3.2%	4.44 [4.20, 4.68]	
NCT01752634 (FUTURE 2) C		0.75	99	1.95		98	3.2%	2.43 [2.19, 2.67]	
NCT01732634 (10161CE 2) C NCT01877668 (OPAL Broaden) A		0.75	106	5.51		107	3.3%	0.72 [0.52, 0.92]	
NCT01877668 (OPAL Broaden) B		0.75	106	5.69		104	3.3%	0.54 [0.34, 0.74]	,
NCT01877668 (OPAL Broaden) C		0.75	106	2.68		105	3.3%	3.55 [3.34, 3.76]	
NCT01989468 (FUTURE 3) A		0.79	139	2.94		137	3.3%	3.52 [3.35, 3.69]	
NCT01989468 (FUTURE 3) B	3.42	0.58	138	2.94		137	3.3%		<u> </u>
								0.48 [0.31, 0.65]	
NCT02181673 (GO-VIBRANT)	9.4	8.1	237	2.4	6.1	236	2.2%	7.00 [5.71, 8.29]	. '
NCT02294227 (FUTURE 4) A		0.58	114	0.63		114	3.3%	2.79 [2.64, 2.94]	l.
NCT02294227 (FUTURE 4) B		0.58	113		0.59	114	3.3%	2.81 [2.66, 2.96]	'
NCT02319759		7.47	100	0.46		49	1.3%	6.13 [3.79, 8.47]	-
NCT02349295 (SPIRIT-P2) A	8.9	1.3	122	3.3	1.4	118	3.2%	5.60 [5.26, 5.94]	l .
NCT02349295 (SPIRIT-P2) B	8.2	1.2	123	3.3	1.4	118	3.2%	4.90 [4.57, 5.23]	. *
NCT02376790 (SEAM-PsA) A	7.8	0.6	256	6	0.6	253	3.3%	1.80 [1.70, 1.90]	-
NCT02376790 (SEAM-PsA) B	8	0.6	257	6	0.6	253	3.3%	2.00 [1.90, 2.10]	'
NCT03104400 (SELECT-PsA 1)	7.8	0.41	391		0.43	367	3.3%	3.50 [3.44, 3.56]	•
NCT03158285 (DISCOVER-2) A	7.04	0.46	245		0.46	246	3.3%	3.62 [3.54, 3.70]	
NCT03158285 (DISCOVER-2) B		0.46	248		0.46	246	3.3%	3.97 [3.89, 4.05]	'
NCT03162796 (DISCOVER-1) A	6.87	0.65	128	1.96	0.65	126	3.3%	4.91 [4.75, 5.07]	
NCT03162796 (DISCOVER-1) B	6.1	0.65	127	1.96	0.65	126	3.3%	4.14 [3.98, 4.30]	
NCT03671148 (KEEPsAKE 2)	5.9	0.51	224		0.56	219	3.3%	3.90 [3.80, 4.00]	
NCT03675308 (KEEPsAKE 1)	6.5	0.36	483	3.2	0.36	481	3.3%	3.30 [3.25, 3.35]	•
Total (95% CI)			6264			6087	100.0%	3.76 [3.42, 4.10]	
Heterogeneity: Tau ² = 0.92; Chi ² = 5	847.58, 0	df = 39	(P < 0.	00001);	$ ^2 = 99$	1%			-20 -10 0 10 20
Test for overall effect: Z = 21.63 (P <	0.00001)							-20 -10 0 10 20 Favours [control] Favours [experimental]
									ravours (experimental)

14

Figure S3. Forest plot of SF-36 MCS. SF-36 MCS, mental component summary of the Short Form 36.

	Exp	eriment	al	(ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean		Total	Mean		Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	1.1	7.4	49	-0.6	7.8	45	1.6%	1.70 [-1.38, 4.78]	-
NCT00051623 (IMPACT 2)	3.9	11.9	100	0.4	11.6	100	1.5%	3.50 [0.24, 6.76]	
NCT00195689 (ADEPT)	1.8	9.3	140	0.6	10.4	152	2.3%	1.20 [-1.06, 3.46]	
NCT00265096 (GO-REVEAL) A	3.37	10.55	146		12.13	113	1.8%	3.97 [1.15, 6.79]	
NCT00265096 (GO-REVEAL) B	4.29	11.03	146	-0.6	12.13	113	1.8%	4.89 [2.03, 7.75]	
NCT01009086 (PSUMMIT 1) A	3.19	9.11	205	1.46	7.84	206	3.0%	1.73 [0.09, 3.37]	
NCT01009086 (PSUMMIT 1) B	4.68	9.26	204	1.46	7.84	206	2.9%	3.22 [1.56, 4.88]	
NCT01077362 (PSUMMIT 2) A	1.72	8.65	99	0.6	6.1	97	2.5%	1.12 [-0.97, 3.21]	
NCT01077362 (PSUMMIT 2) B	3.19	10.84	97	0.6	6.1	97	2.1%	2.59 [0.11, 5.07]	
NCT01087788 (RAPID-PsA) A	5.5	10.2	138	0.7	9.9	136	2.2%	4.80 [2.42, 7.18]	
NCT01087788 (RAPID-PsA) B	3.5	9.6	135	0.7	9.9	136	2.2%	2.80 [0.48, 5.12]	
NCT01392326 (FUTURE 1) A	3.7	0.6	202	2.4	0.9	202	4.4%	1.30 [1.15, 1.45]	•
NCT01392326 (FUTURE 1) B	5.7	0.6	202	2.4	0.9	202	4.4%	3.30 [3.15, 3.45]	•
NCT01695239 (SPIRIT-P1) A	3.1	10.4	107	1.8	9.5	106	1.9%	1.30 [-1.37, 3.97]	
NCT01695239 (SPIRIT-P1) B	4.6	11.9	103	1.8	9.5	106	1.7%	2.80 [-0.12, 5.72]	
NCT01695239 (SPIRIT-P1) C	4.6	9.5	101	1.8	9.5	106	2.0%	2.80 [0.21, 5.39]	
NCT01877668 (OPAL Broaden) A	3.13	0.94	106	4.35	0.91	107	4.4%	-1.22 [-1.47, -0.97]	+
NCT01877668 (OPAL Broaden) B	3.13	0.94	106	4.2	0.91	104	4.4%	-1.07 [-1.32, -0.82]	+
NCT01877668 (OPAL Broaden) C	3.13	0.94	106	3.27	0.98	105	4.4%	-0.14 [-0.40, 0.12]	*
NCT02181673 (GO-VIBRANT)	5.3	10.2	237	0.8	7.4	236	3.0%	4.50 [2.89, 6.11]	
NCT02319759	4.95	9.06	100	0.42	6.74	49	2.0%	4.53 [1.94, 7.12]	
NCT02349295 (SPIRIT-P2) A	3.6	1.2	122	0.9	1.3	118	4.3%	2.70 [2.38, 3.02]	-
NCT02349295 (SPIRIT-P2) B	4	1.2	123	0.9	1.3	118	4.3%	3.10 [2.78, 3.42]	-
NCT02376790 (SEAM-PsA) A	2.8	0.6	256	3.3	0.6	253	4.4%	-0.50 [-0.60, -0.40]	•
NCT02376790 (SEAM-PsA) B	3.3	0.6	257	3.3	0.6	253	4.4%	0.00 [-0.10, 0.10]	†
NCT03104400 (SELECT-PsA 1)	4.1	0.43	391	2.4	0.48	367	4.4%	1.70 [1.63, 1.77]	•
NCT03158285 (DISCOVER-2) A	4.22	0.55	245	2.14	0.55	246	4.4%	2.08 [1.98, 2.18]	•
NCT03158285 (DISCOVER-2) B	4.17	0.54	248	2.14	0.55	246	4.4%	2.03 [1.93, 2.13]	•
NCT03162796 (DISCOVER-1) A	3.6	0.73	128	2.37	0.73	126	4.4%	1.23 [1.05, 1.41]	•
NCT03162796 (DISCOVER-1) B	3.2	0.73	127	2.37	0.73	126	4.4%	0.83 [0.65, 1.01]	+
NCT03796858 (COSMOS)	2.1	0.79	189	0.36	0.96	96	4.4%	1.74 [1.52, 1.96]	*
Total (95% CI)			4915			4673	100.0%	1.76 [1.27, 2.25]	•
Heterogeneity: Tau ² = 1.43; Chi ² = 4			P < 0.0	0001); I	²= 99%				-4 -2 0 2 4
Test for overall effect: Z = 7.01 (P < 0	1.00001)								Favours [control] Favours [experimental]

Figure S4. Forest plot of EQ-VAS. EQ-VAS, EuroQol Visual Analogue Scale.

	Expe	rimen	tal	Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
NCT01695239 (SPIRIT-P1) A	11.9	25	107	3.3	21.1	106	12.0%	8.60 [2.39, 14.81]	
NCT01695239 (SPIRIT-P1) B	11.3	25.8	103	3.3	21.1	106	11.8%	8.00 [1.60, 14.40]	
NCT01695239 (SPIRIT-P1) C	9.1	22.1	101	3.3	21.1	106	12.3%	5.80 [-0.09, 11.69]	
NCT01877668 (OPAL Broaden) A	13.1	2.14	106	14	2.1	107	16.6%	-0.90 [-1.47, -0.33]	•
NCT01877668 (OPAL Broaden) B	13.1	2.14	106	15.83	2.09	104	16.6%	-2.73 [-3.30, -2.16]	*
NCT01877668 (OPAL Broaden) C	13.1	2.14	106	6.37	2.24	105	16.6%	6.73 [6.14, 7.32]	-
NCT02181673 (GO-VIBRANT)	20.2	24.2	237	5.5	23.1	236	14.1%	14.70 [10.44, 18.96]	
Fotal (95% CI)			866			870	100.0%	5.27 [1.21, 9.34]	-
Heterogeneity: Tau² = 25.86; Chi² =	619.38, d	df=6 (P < 0.0	0001); F	= 999	%		_	-10 -5 0 5 10
Fest for overall effect: $Z = 2.54$ (P = 0	0.01)								Favours (control) Favours (experimental)

Figure S5. Forest plot of DLQI. DLQI, Dermatology Life Quality Index.

			•	•	,			- ·	•
	Expe	erimen	ıtal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	-3.4	4.5	32	-1.7	5.3	28	6.2%	-1.70 [-4.21, 0.81]	
NCT00195689 (ADEPT)	-6.1	6.3	66	-0.7	6.7	66	6.5%	-5.40 [-7.62, -3.18]	
NCT01009086 (PSUMMIT 1) A	-6.35	6.75	129	-1.35	5.25	132	7.1%	-5.00 [-6.47, -3.53]	
NCT01009086 (PSUMMIT 1) B	-7.05	6.74	134	-1.35	5.25	132	7.1%	-5.70 [-7.15, -4.25]	
NCT01077362 (PSUMMIT 2) A	-6.35	8.27	103	-0.7	4.51	104	6.8%	-5.65 [-7.47, -3.83]	
NCT01077362 (PSUMMIT 2) B	-6	6.01	105	-0.7	4.51	104	7.1%	-5.30 [-6.74, -3.86]	
NCT01087788 (RAPID-PsA) A	-6.3	7.5	138	-1.3	4.7	136	7.1%	-5.00 [-6.48, -3.52]	
NCT01087788 (RAPID-PsA) B	-3.3	5.1	135	-1.3	4.7	136	7.3%	-2.00 [-3.17, -0.83]	
NCT01392326 (FUTURE 1) A	-7.9	0.6	108	0.7	0.8	109	7.7%	-8.60 [-8.79, -8.41]	*
NCT01392326 (FUTURE 1) B	-8.8	0.6	108	0.7	0.8	109	7.7%	-9.50 [-9.69, -9.31]	•
NCT01695239 (SPIRIT-P1) A	-0.5	0.52	107	-0.3	6.1	106	7.3%	-0.20 [-1.37, 0.97]	
NCT01695239 (SPIRIT-P1) B	-0.44	0.53	103	-0.3	6.1	106	7.3%	-0.14 [-1.31, 1.03]	
NCT01695239 (SPIRIT-P1) C	-0.37	0.44	101	-0.3	6.1	106	7.3%	-0.07 [-1.23, 1.09]	
NCT02181673 (GO-VIBRANT)	-8.1	7.7	194	-1.9	5.9	195	7.2%	-6.20 [-7.56, -4.84]	
Total (95% CI)			1563			1569	100.0%	-4.36 [-5.76, -2.96]	•
Heterogeneity: Tau2 = 6.63; Chi2	= 954.91	1, df = 1	13 (P <	0.0000	1); 2 =	99%			+ + + + + +
Test for overall effect: Z = 6.09 (F									-10 -5 0 5 10
,									Favours [experimental] Favours [control]

Figure S6. Forest plot of PASI 50. PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index.

	Experime	ntal	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
NCT00051623 (IMPACT 2)	75	83	8	87	10.3%	9.83 [5.06, 19.09]	
NCT00195689 (ADEPT)	52	69	8	69	10.3%	6.50 [3.34, 12.64]	
NCT00265096 (GO-REVEAL) A	77	102	6	73	9.4%	9.18 [4.23, 19.93]	
NCT00265096 (GO-REVEAL) B	87	106	6	73	9.4%	9.99 [4.62, 21.60]	
NCT00317499	47	101	18	104	11.9%	2.69 [1.68, 4.30]	_ -
NCT01087788 (RAPID-PsA) A	67	90	24	86	12.7%	2.67 [1.86, 3.83]	
NCT01087788 (RAPID-PsA) B	55	76	24	86	12.6%	2.59 [1.80, 3.74]	
NCT02065713 (GO-DACT)	16	20	10	22	11.6%	1.76 [1.06, 2.92]	
NCT02319759	85	98	14	48	12.0%	2.97 [1.90, 4.65]	
Total (95% CI)		745		648	100.0%	4.09 [2.71, 6.16]	•
Total events	561		118				
Heterogeneity: Tau ² = 0.31; Chi ² =		8 (P < 0	0.00001)	; I² = 80	2%	-	0.05 0.2 1 5 20
Test for overall effect: Z = 6.72 (P	< 0.00001)						Favours [control] Favours [experimental]

Figure S7. Forest plot of PASI 75. PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index.

	Experim		Contr			Risk Ratio	Risk Ratio
tudy or Subgroup	Events					M-H, Random, 95% CI	M-H, Random, 95% CI
IPACT	35	52	0	52	0.4%	71.00 [4.47, 1127.60]	
lease PJ 2000	5	19	0	19	0.4%	11.00 [0.65, 186.02]	
ICT00051623 (IMPACT 2)	60	83	1	87	0.8%	62.89 [8.92, 443.47]	
ICT00195689 (ADEPT)	41	69	1	69	0.8%	41.00 [5.80, 289.75]	
ICT00265096 (GO-REVEAL) A	57	102	1	73	0.8%	40.79 [5.78, 287.91]	
ICT00265096 (GO-REVEAL) B	70	106	1	73	0.8%	48.21 [6.85, 339.27]	
ICT00317499	23	101	3	104	1.4%	7.89 [2.45, 25.48]	
ICT00367237 (RESPOND)	33	34	19	35	2.7%	1.79 [1.31, 2.44]	-
ICT01009086 (PSUMMIT 1) A	83	145	16	146	2.5%	5.22 [3.22, 8.47]	_
ICT01009086 (PSUMMIT 1) B	93	149	16	146	2.5%	5.70 [3.53, 9.19]	_
ICT01077362 (PSUMMIT 2) A	41	80	4	80	1.7%	10.25 [3.85, 27.28]	
ICT01077362 (PSUMMIT 2) B	45	81	4	80	1.7%	11.11 [4.19, 29.45]	
ICT01087788 (RAPID-PsA) A	56	90	13	86	2.4%	4.12 [2.43, 6.97]	—
ICT01087788 (RAPID-PsA) B	46	76	13	86	2.4%	4.00 [2.35, 6.82]	
ICT01392326 (FUTURE 1) A	70	108	9	109	2.2%	7.85 [4.13, 14.90]	
ICT01392326 (FUTURE 1) B	66	108	9	109	2.2%	7.40 [3.89, 14.09]	
ICT01695239 (SPIRIT-P1) A	37	52	4	41	1.7%	7.29 [2.83, 18.80]	
ICT01695239 (SPIRIT-P1) B	33	41	4	41	1.7%	8.25 [3.21, 21.18]	
ICT01695239 (SPIRIT-P1) C	20	37	4	41	1.7%	5.54 [2.09, 14.72]	
ICT01752634 (FUTURE 2) A	26	41	7	43	2.1%	3.90 [1.90, 7.98]	
ICT01752634 (FUTURE 2) B	28	58	7	43	2.1%	2.97 [1.43, 6.14]	
ICT01752634 (FUTURE 2) C	14	50	7	43	2.0%	1.72 [0.76, 3.87]	
ICT01877668 (OPAL Broaden) A	30	77	35	82	2.6%	0.91 [0.63, 1.33]	-
ICT01877668 (OPAL Broaden) B	30	77	31	70	2.6%	0.88 [0.60, 1.29]	-
ICT01877668 (OPAL Broaden) C	30	77	12	82	2.3%	2.66 [1.47, 4.82]	
ICT01989468 (FUTURE 3) A	29	62	6	59	2.0%	4.60 [2.06, 10.27]	
ICT01989468 (FUTURE 3) B	34	68	6	59	2.0%	4.92 [2.22, 10.88]	
ICT02024646 (AMVISION-2) A	34	73	10	90	2.2%	4.19 [2.22, 7.90]	
ICT02024646 (AMVISION-2) B	54	83	10	90	2.3%	5.86 [3.20, 10.73]	
ICT02024040 (AMVISION-1) A	36	73	5	65	1.9%	6.41 [2.68, 15.36]	
ICT02029495 (AMVISION-1) B	47	60	5	65	1.9%		
			26	239	2.6%	10.18 [4.34, 23.89]	
ICT02181673 (GO-VIBRANT)	127	241				4.84 [3.31, 7.10]	
ICT02294227 (FUTURE 4) A	29	55	5	62	1.8%	6.54 [2.72, 15.71]	
ICT02294227 (FUTURE 4) B	27	54	5	62	1.8%	6.20 [2.57, 14.97]	
ICT02319759	77	98	6	48	2.0%	6.29 [2.95, 13.38]	
ICT02349295 (SPIRIT-P2) A	38	68	10	67	2.3%	3.74 [2.04, 6.89]	
ICT02349295 (SPIRIT-P2) B	41	68	10	67	2.3%	4.04 [2.21, 7.39]	
ICT02349451	19	33	3	11	1.7%	2.11 [0.77, 5.79]	T
ICT02404350 (FUTURE 5) A	155	222	41	332	2.7%	5.65 [4.19, 7.63]	
ICT02404350 (FUTURE 5) B	132	220	41	332	2.7%	4.86 [3.58, 6.60]	
ICT02404350 (FUTURE 5) C	129	222	41	332	2.7%	4.71 [3.46, 6.40]	<u>-</u>
ICT02980692 A	34	53	7	42	2.1%	3.85 [1.90, 7.79]	
ICT02980692 B	35	44	7	42	2.1%	4.77 [2.39, 9.54]	—
ICT02980692 C	31	55	7	42	2.1%	3.38 [1.65, 6.91]	
ICT02980692 D	19	41	7	42	2.0%	2.78 [1.31, 5.90]	
ICT03158285 (DISCOVER-2) A	144	184	42	183	2.8%	3.41 [2.59, 4.49]	-
CT03158285 (DISCOVER-2) B	139	176	42	183	2.8%	3.44 [2.61, 4.54]	-
ICT03162796 (DISCOVER-1) A	77	89	11	78	2.4%	6.13 [3.53, 10.67]	—
ICT03162796 (DISCOVER-1) B	62	82	11	78	2.4%	5.36 [3.06, 9.40]	
ICT03796858 (COSMOS)	79	133	5	53	1.9%	6.30 [2.70, 14.67]	
otal (95% CI)		4470		4563	100.0%	4.72 [3.87, 5.75]	•
otal events	2700		590				
eterogeneity: Tau ² = 0.35; Chi ² = 2	59.40 df-	40 /P <	0.000043	· [2 - 91	196		0.001 0.1 1 10 1

Figure S8. Forest plot of PASI 90. PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Hong Tao 2019	29	33	16	33	4.0%	1.81 [1.25, 2.63]	-
NCT00051623 (IMPACT 2)	39	83	0	87	0.4%	82.76 [5.17, 1325.04]	
NCT00195689 (ADEPT)	29	69	0	69	0.4%	59.00 [3.68, 946.75]	
NCT00265096 (GO-REVEAL) A	33	102	0	73	0.4%	48.14 [3.00, 773.11]	
NCT00265096 (GO-REVEAL) B	34	106	0	73	0.4%	47.72 [2.97, 766.16]	
NCT00367237 (RESPOND)	24	34	10	35	3.3%	2.47 [1.40, 4.36]	-
NCT01077362 (PSUMMIT 2) A	24	80	3	80	1.7%	8.00 [2.51, 25.51]	
NCT01077362 (PSUMMIT 2) B	36	81	3	80	1.8%	11.85 [3.80, 36.93]	
NCT01087788 (RAPID-PsA) A	42	90	5	86	2.4%	8.03 [3.33, 19.33]	
NCT01087788 (RAPID-PsA) B	27	76	5	86	2.3%	6.11 [2.48, 15.07]	
NCT01392326 (FUTURE 1) A	53	108	4	109	2.1%	13.37 [5.01, 35.66]	
NCT01392326 (FUTURE 1) B	49	108	4	109	2.1%	12.36 [4.62, 33.07]	
NCT01695239 (SPIRIT-P1) A	29	52	2	41	1.4%	11.43 [2.90, 45.13]	
NCT01695239 (SPIRIT-P1) B	28	41	2	41	1.4%	14.00 [3.57, 54.97]	
NCT01695239 (SPIRIT-P1) C	14	37	2	41	1.476	7.76 [1.89, 31.88]	l ——
NCT01752634 (FUTURE 2) A	20	41	4	43	2.1%	5.24 [1.96, 14.04]	
NCT01752634 (FUTURE 2) B	19	58	4	43	2.1%		
	19	58 50	4	43		3.52 [1.29, 9.61]	
NCT01752634 (FUTURE 2) C				43 59	1.7%	1.29 [0.39, 4.27]	
NCT01989468 (FUTURE 3) A	21	62	4		2.0%	5.00 [1.82, 13.69]	
NCT01989468 (FUTURE 3) B	25	68	4	59	2.1%	5.42 [2.00, 14.68]	
NCT02024646 (AMVISION-2) A	24	73	4	90	2.0%	7.40 [2.69, 20.36]	
NCT02024646 (AMVISION-2) B	45	83	4	90	2.1%	12.20 [4.59, 32.44]	
NCT02029495 (AMVISION-1) A	29	73	2	65	1.4%	12.91 [3.20, 52.01]	
NCT02029495 (AMVISION-1) B	36	60	2	65	1.4%	19.50 [4.91, 77.51]	
NCT02065713 (GO-DACT)	5	20	4	22	1.7%	1.38 [0.43, 4.42]	
NCT02181673 (GO-VIBRANT)	84	241	15	239	3.5%	5.55 [3.30, 9.34]	
NCT02294227 (FUTURE 4) A	20	55	1	62	0.8%	22.55 [3.13, 162.52]	
NCT02294227 (FUTURE 4) B	11	54	1	62	0.8%	12.63 [1.68, 94.67]	
NCT02319759	65	98	3	48	1.8%	10.61 [3.52, 32.03]	
NCT02349295 (SPIRIT-P2) A	30	68	8	67	2.9%	3.69 [1.83, 7.46]	
NCT02349295 (SPIRIT-P2) B	34	68	8	67	2.9%	4.19 [2.10, 8.37]	
NCT02349451	15	33	2	11	1.5%	2.50 [0.68, 9.25]	+
NCT02404350 (FUTURE 5) A	119	222	31	332	4.0%	5.74 [4.02, 8.20]	-
NCT02404350 (FUTURE 5) B	81	220	31	332	3.9%	3.94 [2.70, 5.75]	-
NCT02404350 (FUTURE 5) C	70	222	31	332	3.9%	3.38 [2.29, 4.97]	-
NCT02980692 A	25	53	3	42	1.8%	6.60 [2.14, 20.38]	
NCT02980692 B	22	44	3	42	1.8%	7.00 [2.26, 21.66]	
NCT02980692 C	22	55	3	42	1.8%	5.60 [1.80, 17.47]	
NCT02980692 D	15	41	3	42	1.7%	5.12 [1.60, 16.38]	
NCT03158285 (DISCOVER-2) A	112	184	18	183	3.7%	6.19 [3.93, 9.74]	-
NCT03158285 (DISCOVER-2) B	121	176	18	183	3.7%	6.99 [4.46, 10.96]	-
NCT03162796 (DISCOVER-1) A	56	89	9	78	3.1%	5.45 [2.89, 10.29]	
NCT03162796 (DISCOVER-1) B	41	82	9	78	3.0%	4.33 [2.26, 8.31]	
NCT03671148 (KEEPsAKE 2)	143	483	27	481	3.9%	5.27 [3.57, 7.80]	-
NCT03675308 (KEEPSAKE 1)	68	224	12	219	3.3%	5.54 [3.09, 9.94]	
NCT03796858 (COSMOS)	68	133	4	53	2.2%	6.77 [2.60, 17.64]	
			_				
Total (95% CI)		4533		4617	100.0%	5.73 [4.73, 6.95]	•
Total events	1942		332				
Heterogeneity: Tau² = 0.21; Chi² =			< 0.0000	1); l²=	59%		0.001 0.1 1 10 100
Test for overall effect: Z = 17.73 (P	< 0.00001	١					0.001 0.1 1 10 100

Figure S9. Forest plot of PASI 100. PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Contr	ol		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% CI	
NCT00195689 (ADEPT)	20	69	0	69	0.8%	41.00 [2.53, 664.71]				
NCT01695239 (SPIRIT-P1) A	22	52	1	41	1.9%	17.35 [2.44, 123.36]			-	
NCT01695239 (SPIRIT-P1) B	22	41	1	41	1.7%	22.00 [3.11, 155.67]			-	
NCT01695239 (SPIRIT-P1) C	9	37	1	41	1.6%	9.97 [1.33, 75.00]				_
NCT02024646 (AMVISION-2) A	18	73	1	90	1.5%	22.19 [3.03, 162.32]			-	
NCT02024646 (AMVISION-2) B	39	83	1	90	1.6%	42.29 [5.94, 300.94]				-
NCT02029495 (AMVISION-1) A	18	73	2	65	3.6%	8.01 [1.93, 33.22]				
NCT02029495 (AMVISION-1) B	33	60	2	65	3.2%	17.88 [4.48, 71.30]				_
NCT02181673 (GO-VIBRANT)	50	241	11	239	18.6%	4.51 [2.41, 8.44]			-	
NCT02319759	39	98	3	48	6.8%	6.37 [2.07, 19.56]				
NCT02349295 (SPIRIT-P2) A	24	68	3	67	5.1%	7.88 [2.49, 24.94]				
NCT02349295 (SPIRIT-P2) B	19	68	3	67	5.1%	6.24 [1.94, 20.11]				
NCT02980692 A	16	53	2	42	3.8%	6.34 [1.54, 26.05]				
NCT02980692 B	11	44	2	42	3.4%	5.25 [1.24, 22.29]				
NCT02980692 C	15	55	2	42	3.8%	5.73 [1.38, 23.69]				
NCT02980692 D	9	41	2	42	3.3%	4.61 [1.06, 20.06]			-	
NCT03158285 (DISCOVER-2) A	82	184	5	183	8.4%	16.31 [6.77, 39.30]				•
NCT03158285 (DISCOVER-2) B	80	176	5	183	8.2%	16.64 [6.90, 40.09]			_	
NCT03162796 (DISCOVER-1) A	40	89	5	78	9.0%	7.01 [2.91, 16.88]			-	
NCT03162796 (DISCOVER-1) B	21	82	5	78	8.6%	4.00 [1.58, 10.07]			-	
Fotal (95% CI)		1687		1613	100.0%	9.57 [7.38, 12.43]			•	
Fotal events	587		57			,				
Heterogeneity: Chi² = 21.77, df = 1): I ² = 13					+	<u></u>		
Test for overall effect: Z = 16.99 (P							0.002	0.1 1 Favours (control)	10	50