Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α inhibitors: a randomised, double-blind, placebo-controlled, phase 3 trial (BE COMPLETE)

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Summary

Background Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F and IL-17A. This study compared the efficacy and safety of bimekizumab with placebo over 16 weeks in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α (TNFα) inhibitors.

Methods BE COMPLETE was a phase 3, multicentre, randomised, double-blind, placebo-controlled trial conducted across 92 sites (including hospitals, clinics, and research centres) in 11 countries (Australia, Canada, Czech Republic, Germany, Hungary, Italy, Japan, Poland, Russia, the UK, and the USA). Eligible patients were aged 18 years or older with adult-onset psoriatic arthritis (meeting the Classification Criteria for Psoriatic Arthritis for at least 6 months before screening) with a history of inadequate response or intolerance to treatment with one or two TNFα inhibitors for either psoriatic arthritis or psoriasis. We stratified patients with active psoriatic arthritis by region and previous TNFα inhibitor use. Patients were randomly assigned (2:1) to receive subcutaneous bimekizumab 160 mg every 4 weeks or placebo by an interactive-voice and web-response system on the basis of a predetermined randomisation schedule. The primary endpoint was the proportion of patients with 50% or greater improvement in American College of Rheumatology criteria (ACR50) at week 16 (non-responder imputation). Efficacy analyses were done in the randomised population. The safety analysis set comprised patients who received one or more doses of study treatment. This trial was registered at ClinicalTrials.gov, NCT03896581, and is completed.

Findings Between March 28, 2019, and Feb 14, 2022, 556 patients were screened and 400 patients were randomly assigned to bimekizumab 160 mg every 4 weeks (n=267) or placebo (n=133). The primary and all hierarchical secondary endpoints were met at week 16. 116 (43%) of 267 patients receiving bimekizumab reached ACR50, compared with nine (7%) of 133 patients receiving placebo (adjusted odds ratio [OR] 11·1 [95% CI 5·4–23·0], p<0·0001). 121 (69%) of 176 patients with psoriasis affecting at least 3% body surface area at baseline who received bimekizumab reached 90% or greater improvement in the Psoriasis Area and Severity Index (PASI90), compared with six (7%) of 88 patients who received placebo (adjusted OR 30·2 [12·4–73·9], p<0·0001). Treatment-emergent adverse events up to week 16 were reported in 108 (40%) of 267 patients receiving bimekizumab and 44 (33%) of 132 patients receiving placebo. There were no new safety signals and no deaths.

Interpretation Bimekizumab treatment led to superior improvements in joint and skin efficacy outcomes at week 16 compared with placebo in patients with psoriatic arthritis and inadequate response or intolerance to TNFα inhibitors. The safety profile of bimekizumab was consistent with previous phase 3 studies in patients with plaque psoriasis, and studies of IL-17A inhibitors.

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Introduction

Psoriatic arthritis is a chronic, immune-mediated inflammatory disease with a range of musculoskeletal and dermatological manifestations, including arthritis, axial inflammation, enthesitis, dactylitis, and psoriasis of skin and nails.[1]

International guidelines emphasise the need to reduce disease activity as much as possible across all active domains of the disease.[2] Treatment of both musculoskeletal and skin components is required to maximise patient wellbeing and health-related quality of life.[3] Despite the range of treatment options available for psoriatic arthritis,

Research in context

Evidence before this study

We searched PubMed with the terms "arthritis, psoriatic" or "psoriatic arthritis" and screened by title to identify industry-sponsored clinical trials and systematic literature reviews of biologic agents in patients with psoriatic arthritis. Manuscripts published between June 28, 2015, and Dec 30, 2021, were extracted. Despite the range of treatments available for psoriatic arthritis, patients often report residual symptoms, including joint pain, skin disease, fatigue, and suboptimal quality of life, suggesting new therapeutic options are needed. Patients who have previously inadequately responded or lost response to a biologic agent are a population of clinical interest as they often do not reach the high-threshold treatment targets of low disease activity or remission; thus, there is still a substantial unmet need in this patient population. Dual neutralisation of interleukin (IL)-17F and IL-17A with bimekizumab has shown efficacy and tolerability when used to treat patients with psoriatic arthritis in a phase 2b study and might represent a new treatment option for management of psoriatic arthritis in patients with inadequate response or intolerance to biologic treatment.

Added value of this study

BE COMPLETE is the first phase 3 randomised, placebo-controlled study to assess the efficacy and safety of subcutaneous bimekizumab treatment in patients with active psoriatic arthritis, who have inadequate response or intolerance to one or two tumour necrosis factor-α (TNFα) inhibitors. In this study, patients receiving bimekizumab had significantly higher response rates compared with placebo at week 16 for the primary and all ranked secondary endpoints, which span joint and skin outcomes. The safety profile of bimekizumab was consistent with that reported in a phase 2b study of patients with psoriatic arthritis and studies of bimekizumab for other indications.

Implications of all the available evidence

The results presented here support findings from previous studies showing the clinical efficacy and tolerability of inhibition of IL-17A and IL-17F with bimekizumab treatment in patients with active psoriatic arthritis. BE COMPLETE demonstrates consistent efficacy and tolerability of bimekizumab treatment in patients with inadequate response or intolerance to TNFα inhibitors, a subgroup of clinical interest. Bimekizumab 160 mg every 4 weeks showed greater improvements in joint and skin responses at week 16 compared with placebo, and a safety profile consistent with previous reports. These results, alongside other published reports, provide evidence for the clinical efficacy of bimekizumab across multiple domains of psoriatic arthritis.

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many patients continue to have residual symptoms that negatively impact their physical wellbeing and quality of life.[4,5] Furthermore, patients often lose response or develop intolerance to therapies; in clinical practice, the mechanisms underpinning such resistance are unclear and probably multifactorial.[1,6] There is an urgent need to analyse the varied causes of this loss of response and apply this understanding to treatment selection. Additionally, the development of new agents with diverse modes of action is important to provide efficacious therapeutic options for patients who lose response to treatments that are currently available.

Patients with psoriatic arthritis and inadequate response or intolerance to tumour necrosis factor-α (TNFα) inhibitors are of particular clinical interest. Treatment responses are usually lower when switching to a subsequent TNFα inhibitor or a different therapeutic class. Thus, reaching treatment targets in this patient group might be more difficult than in patients who are naive to biologic treatment.[7,8] A systematic review of seven randomised controlled trials found that the efficacy of interleukin (IL)-17A and IL-12/23 inhibitors was lower in patients who had inadequately responded or lost response to TNFα inhibitor treatment compared with patients who were naive to TNFα inhibitors. Efficacy was assessed using American College of Rheumatology (ACR) response criteria, Psoriasis Area and Severity Index (PASI) responses, and resolution of dactylitis and enthesitis.[8] New therapies are needed that enable patients with previous inadequate response or intolerance to TNFα inhibitors to reach high levels of response, similar to the response in patients who are naive to biologic disease-modifying antirheumatic drugs (DMARDs).

The IL-17 cytokine superfamily is strongly implicated in the pathogenesis of psoriatic disease. Two of the six IL-17 isoforms, IL-17A and IL-17F, share 50% sequence homology and can form both homodimers and heterodimers that promote tissue inflammation and bone remodelling.[9,10] Although IL-17A is the more potent isoform, IL-17F concentrations are on average 30-fold higher than those of IL-17A in psoriatic lesion tissues and serum,[9,11,12] suggesting that inhibition of both isoforms could provide a more effective treatment response than inhibition of IL-17A alone.

Bimekizumab is a humanised monoclonal IgG1 antibody that selectively inhibits IL-17A and IL-17F via a unique mode of action, binding to a similar site on both IL-17A and IL-17F. Bimekizumab was shown to more effectively suppress in vitro proinflammatory cytokine responses compared with inhibition of IL-17A or IL-17F alone.[9] The phase 2b BE ACTIVE study in patients with moderate-to-severe psoriatic arthritis showed that bimekizumab treatment resulted in rapid clinical improvements in joint and skin outcomes in patients with psoriatic arthritis.[13] Efficacy of bimekizumab was

sustained and treatment was well tolerated for up to 3 years in an open-label extension.[14]

We evaluated the efficacy and safety of bimekizumab in two phase 3 clinical trials, which were run in parallel in overlapping countries and sites, in patients with psoriatic arthritis who were naive to biologic DMARDs (BE OPTIMAL) or in patients with inadequate response or intolerance to TNFα inhibitors (BE COMPLETE). In this Article, we present the 16-week primary analysis results from BE COMPLETE, assessing the clinical efficacy and safety of subcutaneous bimekizumab 160 mg every 4 weeks, compared with placebo, in patients with active psoriatic arthritis and inadequate response or intolerance to TNFα inhibitors. Results from the BE OPTIMAL study are reported separately.[15]

Methods

Study design

BE COMPLETE was a 16-week, phase 3, multicentre, randomised, double-blind, placebo-controlled study. The study was done at 92 sites, including hospitals, clinics, doctors' offices, and research centres, across 11 countries (Australia, Canada, Czech Republic, Germany, Hungary, Italy, Japan, Poland, Russia, the UK, and the USA).

The study included a 2–5-week screening period and a 16-week placebo-controlled, double-blind treatment period. Patients completing week 16 and meeting eligibility criteria could be enrolled in an open-label extension study, receiving bimekizumab 160 mg every 4 weeks, regardless of previous treatment (appendix p 10).

See Online for appendix

The study was done in accordance with the Declaration of Helsinki and the International Conference on Harmonisation Guidance for Good Clinical Practice. Ethics approval was obtained from the relevant institutional review boards at participating sites.

Patients

Eligible patients were aged 18 years or older and had a documented diagnosis of adult-onset psoriatic arthritis that met the Classification Criteria for Psoriatic Arthritis for at least 6 months before screening.[16] Eligible patients had a baseline tender joint count (TJC) of three or more (of 68) and swollen joint count (SJC) of three or more (of 66), and at least one active psoriatic lesion or a documented history of psoriasis or both. Included patients had a history of inadequate response or intolerance to treatment with one or two TNFα inhibitors for either psoriatic arthritis or psoriasis, as assessed by the investigator.

Concomitant non-steroidal anti-inflammatory drugs, analgesics, oral corticosteroids, or conventional synthetic DMARDs at stable doses were allowed, subject to the restrictions outlined in the inclusion criteria (appendix pp 3–4). Patients with current or previous exposure to any biologics for the treatment of psoriatic arthritis or psoriasis, except TNFα inhibitors, were excluded. Full exclusion criteria are in the appendix (pp 4–6). All patients provided written informed consent in accordance with local requirements.

Randomisation and masking

Patients were randomly assigned 2:1 to receive either subcutaneous bimekizumab 160 mg or placebo every 4 weeks. Randomisation was stratified by region (North America, western Europe, eastern Europe, or Asia; appendix p 186) and previous exposure to TNFα inhibitors (inadequate response to one or two TNFα inhibitors, or intolerance to TNFα inhibitors). An interactive-voice and web-response system was used to assign patients eligible for enrolment to a treatment regimen on the basis of a predetermined randomisation schedule produced by an independent biostatistician.

To maintain double-blinding, placebo was administered in the same form and with the same dosing schedule as bimekizumab. Throughout the study, patients, investigators, and sponsors remained masked to treatment assignment, except for specially designated, unmasked site staff responsible for the preparation and administration of study treatments.

Procedures

Study visits occurred every 4 weeks from baseline to week 16. Bimekizumab and placebo injections were administered at baseline and subsequently every 4 weeks. Bimekizumab was administered via a 1 mL prefilled syringe containing 160 mg/mL bimekizumab. Placebo was provided as 0·9% sodium chloride aqueous solution in a 1 mL prefilled syringe. Both interventions were administered by subcutaneous injection on the lateral abdominal wall, thigh, and upper outer arm on a rotational basis.

Efficacy and safety outcomes were assessed at baseline and at each study visit, every 4 weeks, thereafter. All assessments were done by masked assessors.

Outcomes

The primary efficacy endpoint was the proportion of patients reaching 50% or greater response in the ACR criteria (ACR50) at week 16 for bimekizumab versus placebo. Calculation of ACR50 was done centrally by the statistics team.

Ranked secondary efficacy endpoints at week 16, in hierarchical order (appendix p 11), were the change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) total score, the proportion of patients achieving 90% or greater improvement in the Psoriasis Area and Severity Index (PASI90) response in patients with psoriasis affecting at least 3% body surface area (BSA) at baseline, change from baseline in Short-Form 36-item Health Survey (SF-36) Physical Component Summary (PCS) norm-based score, and the

proportion of patients achieving minimal disease activity (MDA) response (achievement of five or more of the following criteria: TJC of one or less, SJC of one or less, either PASI ≤1 or BSA ≤3%, patients' pain visual analogue scale [VAS 0–100] ≤15, Patient Global Assessment [PGA] for psoriatic arthritis ≤20 [VAS 0–100], HAQ-DI ≤0·5, and tender entheseal points ≤1 [measured with the Leeds Enthesitis Index]). Additional preplanned efficacy outcomes at week 16 included the proportion of patients reaching 20% or greater response in ACR criteria (ACR20) and the proportion of patients reaching 70% or greater response in ACR criteria (ACR70), the proportion of patients reaching 75% or greater response in PASI (PASI75) in the subset of patients with psoriasis affecting at least 3% BSA at baseline, the proportion of patients reaching 100% response in PASI (PASI100) in the subset of patients with psoriasis affecting at least 3% BSA at baseline, the proportion of patients reaching both ACR50 and PASI100 (ACR50+PASI100) in the subset of patients with psoriasis affecting at least 3% BSA at baseline, the proportion of patients reaching very low disease activity (VLDA; meeting all seven of the criteria outlined for MDA), the proportion of patients reaching an Investigator Global Assessment (IGA) score of 0 or 1 and at least a two-grade reduction from baseline in the subset of patients with a minimum IGA score of 2 and with psoriasis affecting at least 3% BSA at baseline, the proportion of patients reaching resolution of nail psoriasis measured using modified Nail Psoriasis Severity Index (mNAPSI), the proportion of patients with a minimum clinically important difference (MCID) in HAQ-DI (≥0·35) in the subset of patients with a HAQ-DI score of 0·35 or more at baseline, change from baseline in Psoriatic Arthritis Impact of Disease-12 (PsAID-12) total score, change from baseline in Patient's Assessment of Arthritis Pain (PtAAP) score, and change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) score. Unless stated otherwise, continuous outcomes are expressed as change from baseline relative to efficacy values at week 0 (first day of treatment).

Data for endpoints related to resolution of, and changes in score for, enthesitis or dactylitis were pooled with those from BE OPTIMAL, as prespecified in the BE OPTIMAL statistical testing hierarchy. Pooled data for these endpoints are reported in the associated full publication.[15]

Safety outcomes included the number of treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (SAEs), and TEAEs leading to withdrawal. Prespecified safety topics of interest included infections (serious, opportunistic [as defined in the appendix p 7], fungal [including *Candida*], and active tuberculosis), neutropenia, hypersensitivity (including anaphylaxis), suicidal ideation and behaviour, major adverse cardiovascular events, liver function test changes or enzyme elevations, malignancies, and inflammatory bowel diseases. Suicidal ideation and behaviour events, major adverse cardiovascular events, and inflammatory bowel disease events were adjudicated by external adjudication committees. Further details on safety topics are reported are listed in the appendix (pp 83–105). An independent data monitoring committee, including clinicians and statisticians, was responsible for evaluating safety data collected during the trial.

Statistical analysis

All sample size calculations were based on a significance level of 0·05 in a two-sided test, using the software nQuery Advisor 7.0. The sample size selected allowed for statistical powering of the comparison of bimekizumab with placebo for the primary endpoint ACR50 and ranked secondary endpoints at week 16. The assumed responder rates for ACR50 at week 16 were 26·0% in the bimekizumab group and 10·0% for placebo, based on data from a subgroup of patients with inadequate response or intolerance to TNFα inhibitors in the phase 2b BE ACTIVE trial and published data from other interventions.[13,17] Using these assumptions, a sample size of 260 patients in the bimekizumab group and 130 patients in the placebo group would have 96% power to show statistical superiority of bimekizumab 160 mg versus placebo for the primary endpoint, ACR50, and ensure adequate powering for all ranked secondary endpoints (as described in the statistical analysis plan [appendix pp 157–349]).

In this analysis, unless stated otherwise, we analysed demographics and baseline disease characteristics, in

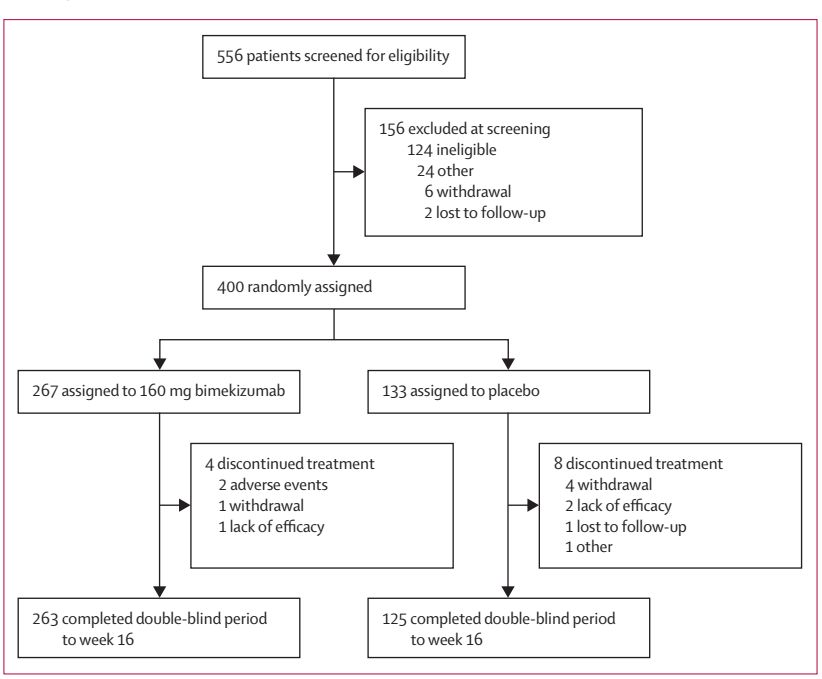

Figure 1: **Trial profile**
CONSORT diagram for BE COMPLETE to week 16.

addition to primary and ranked secondary efficacy endpoints, in the randomised set (intention-to-treat population) consisting of all randomly assigned study participants. Safety analyses are presented for patients who had one or more doses of bimekizumab or placebo during weeks 0–16 (safety set).

Multiplicity and type I error were controlled for in the evaluation of the primary and ranked secondary efficacy endpoints by using a sequential testing procedure; for each endpoint, we evaluated statistical significance only if the previous comparison reached statistical significance with a two-sided test using an α-level of 0·05. Preplanned sensitivity analyses were done to support the robustness of the main analysis of the primary endpoint, including on the full analysis set (all randomly assigned study participants who had one or more doses of bimekizumab or placebo and had a valid measurement of all ACR components at baseline) and per-protocol set (all randomly assigned study participants who had no important protocol deviations or prohibited medications affecting the primary efficacy variable). We also conducted a sensitivity analysis on a COVID-19-free set using identical methods as for the primary analysis but in patients deemed as not having an important protocol deviation related to COVID-19. Additional details of the supportive analyses conducted can be found in the appenidx (pp 222–226). Missing data for the primary and other binary endpoints at week 16 were imputed using non-responder imputation. We generated odds ratios (ORs), CIs, and p values for these endpoints using logistic regression adjusted for treatment, region (North America, western Europe, eastern Europe, or Asia), and previous TNFα inhibitor use (inadequate response to one or two previous TNFα inhibitors, or intolerance to TNFα inhibitors). For continuous outcomes, we imputed missing data using multiple imputation. We imputed missing data for ranked secondary continuous outcomes in the sequential testing procedure using reference-based multiple imputation. We generated least squares means, SEs, difference in least squares means, CIs, and p values for these endpoints using ANCOVA adjusted for treatment, region, previous TNFα inhibitor use, and the baseline value of the outcome as a covariate. All analyses were done with SAS (version 9.3 or higher).

This trial is registered with ClinicalTrials.gov, NCT03896581.

	Placebo (n=133)	Bimekizumab 160 mg every 4 weeks (n=267)	All patients (n=400)
Age, years	51·3 (12·9)	50·1 (12·4)	50·5 (12·5)
Gender			
Male	60 (45%)	130 (49%)	190 (48%)
Female	73 (55%)	137 (51%)	210 (53%)
BMI, kg/m²	29·0 (5·4)	30·1 (6·5)	29·8 (6·2)
Race, White*	128 (96%)	256 (96%)	384 (96%)
Time since psoriatic arthritis diagnosis, years†	9·2 (8·1)	9·6 (9·9)	9·5 (9·3)
Previous TNFα inhibitors			
Inadequate response to one TNFα inhibitor	103 (77%)	204 (76%)	307 (77%)
Inadequate response to two TNFα inhibitors	15 (11%)	29 (11%)	44 (11%)
Intolerance to TNFα inhibitors	15 (11%)	34 (13%)	49 (12%)
Any conventional synthetic DMARD at baseline	63 (47%)	139 (52%)	202 (51%)
Methotrexate at baseline	51 (38%)	119 (45%)	170 (43%)
TJC of 68 joints	19·3 (14·2)	18·4 (13·5)	18·7 (13·8)
SJC of 66 joints	10·3 (8·2)	9·7 (7·5)	9·9 (7·7)
High-sensitivity CRP ≥6 mg/L	59 (44%)	118 (44%)	177 (44%)
Affected BSA ≥3%	88 (66%)	176 (66%)	264 (66%)
PASI score‡	8·5 (6·6)	10·1 (9·1)	9·6 (8·4)
Nail psoriasis§	83 (62%)	159 (60%)	242 (61%)
mNAPSI score¶	4·5 (2·8)	4·3 (2·8)	4·4 (2·8)
HAQ-DI score	1·04 (0·69)	0·97 (0·59)	0·99 (0·62)
PtAAP score	61·7 (24·6)	58·3 (24·2)	59·5 (24·3)
PhGA score	57·7 (18·8)	59·3 (17·2)	58·7 (17·7)
PGA score	63·0 (22·0)	60·5 (22·5)	61·4 (22·3)
SF-36 PCS score	35·9 (10·2)	36·4 (9·0)	36·3 (9·4)
Presence of enthesitis (LEI >0)§	36 (27%)	106 (40%)	142 (36%)
LEI score‖	2·9 (1·6)	2·6 (1·5)	2·7 (1·5)
Presence of dactylitis (LDI >0)§	14 (11%)	34 (13%)	48 (12%)
Dactylitic sites**	1·9 (2·4)	2·0 (1·8)	1·9 (2·0)
LDI score**	66·4 (127·6)	72·7 (114·4)	70·9 (117·0)

Data are mean (SD) or n (%). BSA=body surface area. CRP=C-reactive protein. DMARD=disease-modifying antirheumatic drug. HAQ-DI=Health Assessment Questionnaire-Disability Index. LDI=Leeds Dactylitis Index. LEI=Leeds Enthesitis Index. mNAPSI=modified Nail Psoriasis Severity Index. PASI=Psoriasis Area and Severity Index. PGA=Patient Global Assessment. PhGA=Physician's Global Assessment. PtAAP=Patient's Assessment of Arthritis Pain. SF-36 PCS=Short-Form 36-item Health Survey Physical Component Summary. SJC=swollen joint count. TJC=tender joint count. TNFα=tumour necrosis factor-α. *As reported by the patient. †Data missing for one patient receiving placebo and one patient receiving bimekizumab. ‡In patients with psoriasis affecting at least 3% BSA at baseline (placebo n=88; bimekizumab n=176; all patients n=264). §Data missing for one patient receiving placebo. ¶In patients with nail psoriasis at baseline (placebo n=83; bimekizumab n=159; all patients n=242). ‖In patients with enthesitis at baseline (placebo n=36; bimekizumab n=106; all patients n=142). **In patients with dactylitis at baseline (placebo n=14; bimekizumab n=34; all patients n=48).

Table 1: **Baseline patient demographics and disease characteristics**

Role of the funding source

UCB Pharma contributed to study design, participated in data collection, completed the data analysis, and participated in data interpretation. UCB Pharma also participated in the writing, review, and approval of the manuscript. All authors had full access to the data, reviewed and approved of the final version, and were responsible for the decision to submit for publication. A medical writing agency, employed by UCB Pharma, assisted with manuscript preparation under the authors' direction.

Results

Between March 28, 2019, and Feb 14, 2022, 556 patients were screened and 400 patients were randomly assigned, 267 to subcutaneous bimekizumab 160 mg every 4 weeks and 133 to placebo every 4 weeks (figure 1). Discontinuation rates were low and similar between the treatment groups. In total, 388 (97%) patients completed the study to week 16 (figure 1) and 378 (95%) patients entered the open-label extension study. All patients who completed week 16 had a valid measurement of the

primary endpoint, ACR50. Important protocol deviations were reported in 35 (9%) patients (appendix p 8). COVID-19 had minimal effect on study procedures and results, despite the study being done during the COVID-19 pandemic; the treatment effect for ACR50, as measured by the OR, in the COVID-19-free set aligned with that for the overall population (appendix p 12).

Baseline patient demographics and disease characteristics were generally well balanced between the treatment groups and representative of a population with active moderate-to-severe psoriatic arthritis (table 1). The mean time since psoriatic arthritis diagnosis was 9·5 (SD 9·3) years. 264 (66%) of 400 patients had psoriasis affecting at least 3% BSA, and the mean PASI score for this subgroup was 9·6 (SD 8·4). 306 (77%) had inadequate response to one TNFα inhibitor, 45 (11%) had inadequate response to two TNFα inhibitors, and 49 (12%) had intolerance to TNFα inhibitors. Additionally, 202 (51%) patients reported use of one or more conventional synthetic DMARDs at baseline and 170 (43%) were receiving methotrexate. Additional baseline characteristics are presented in the appendix (p 9).

The study met the primary endpoint and all secondary endpoints in the statistical hierarchy. A greater proportion of patients receiving bimekizumab reached the primary endpoint of ACR50 at week 16 compared with those receiving placebo (116 [43%] of 267 *vs* nine [7%] of 133, p<0·0001; figure 2A; table 2). All prespecified sensitivity analyses were supportive of these results (appendix p 12). All ranked secondary endpoints in the prespecified statistical hierarchy reached statistical significance versus placebo at week 16 (p<0·0001; table 2).

Furthermore, a numerically greater proportion of patients receiving bimekizumab reached ACR20 and ACR70 at week 16 compared with those receiving placebo (ACR20: 179 [67%] of 267 *vs* 21 [16%] of 133; ACR70:

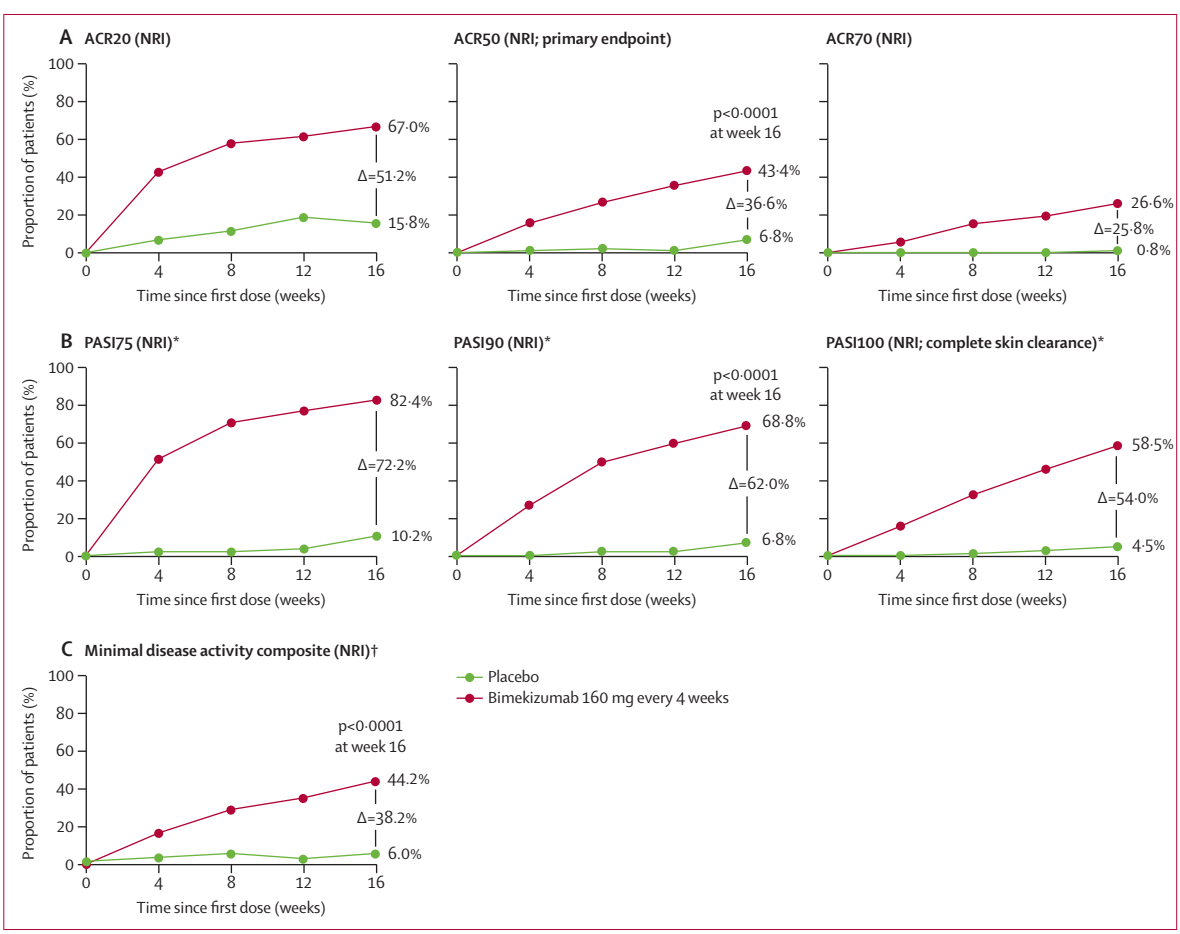

Figure 2: **ACR (A), PASI (B), and minimal disease activity composite (C) responders from week 0 to week 16**
The randomised set was used, unless otherwise stated. For panels A and C data are from 133 patients receiving placebo and 267 receiving bimekizumab. For panel B data are from 88 patients receiving placebo and 176 receiving bimekizumab. p values are reported for the primary and ranked secondary endpoints. p values were generated with adjusted odds ratios. ACR=American College of Rheumatology criteria. BSA=body surface area. HAQ-DI=Health Activity Questionnaire-Disease Index. NRI=non-responder imputation. PASI=Psoriasis Area and Severity Index. *PASI responders reported in patients with psoriasis affecting at least 3% BSA at baseline. †If a patient has five or more of the following criteria: tender joint count of one or less, swollen joint count one or less, PASI score of 1 or less or BSA 3% or less, patients' pain visual analogue scale 15 or less, Patient Global Assessment for psoriatic arthritis 20 or less, HAQ-DI score of 0·5 or less, and tender entheseal points 1 or less.

71 [27%] of 267 *vs* one [1%] of 133; figure 2A; table 2). ACR20, ACR50, and ACR70 responder rates were numerically higher in those receiving bimekizumab treatment than in those receiving placebo as early as week 4, after a single dose of bimekizumab (ACR20: 114 [43%] of 267 *vs* nine [7%] of 133; ACR50: 43 [16%] of 267 *vs* two [2%] of 133; ACR70: 15 [6%] of 267 *vs* 0 of 133; figure 2A).

In patients with psoriasis affecting at least 3% BSA at baseline, 103 (59%) of 176 patients receiving bimekizumab had complete skin clearance versus four (5%) of 88 receiving placebo at week 16, as measured by PASI100 (figure 2B; table 2). At week 16, PASI90 was reached by a statistically significantly greater proportion of patients receiving bimekizumab compared with placebo (121 [69%] of 176 *vs* six [7%] of 88, p<0·0001; figure 2B; table 2). PASI75, PASI90, and PASI100 responder rates were numerically higher on bimekizumab treatment compared with placebo at week 4 after a single dose of study drug (PASI75: 90 [51%] of 176 *vs* two [2%] of 88; PASI90: 47 [27%] of 176 *vs* 0 of 88; PASI100: 27 [15%] of 176 *vs* 0 of 88; figure 2B).

At week 16, MDA, a composite measure of multiple psoriatic arthritis disease domains, was reached by a statistically significantly greater proportion of patients receiving bimekizumab versus placebo (118 [44%] of 267 *vs* eight [6%] of 133; p<0·0001; figure 2C; table 2). Additionally, a greater proportion of patients receiving bimekizumab reached the VLDA and ACR50+PASI100 composite outcomes versus placebo at week 16 (VLDA: 36 [13%] of 267 *vs* three [2%] of 133; ACR50+PASI100: 59 [34%] of 176 *vs* one [1%] of 88; appendix p 13).

Improvements in clinical outcomes were accompanied by improvements in patient-reported physical function. At week 16, statistically significantly greater improvements in HAQ-DI and SF-36 PCS scores were reported by patients in the bimekizumab group compared with the placebo group (HAQ-DI change from baseline mean: –0·38 [SE 0·03] *vs* –0·07 [0·04]; SF-36 PCS change from baseline: 7·3 [SE 0·5] *vs* 1·4 [0·7]; both p<0·0001; table 2). Patients receiving bimekizumab also had greater improvements in pain and fatigue than those receiving placebo at week 16 (PtAAP change from baseline mean: –27·7 [SE 1·7] *vs* –4·5 [2·1]; FACIT-Fatigue change from baseline: 5·5 [SE 0·6] *vs* 0·1 [0·7]).

During the 16-week treatment period, 108 (40%) of 267 patients receiving bimekizumab and 44 (33%) of 132 patients receiving placebo had at least one TEAE (safety set). SAEs were reported in five (2%) of 267 patients in the bimekizumab group (one case each of intestinal obstruction, bronchitis, COVID-19 pneumonia, joint injury, and toxic encephalopathy) and in no patients in the placebo group (table 3). None of the serious or severe TEAEs led to discontinuation. The case of toxic encephalopathy was considered unrelated to bimekizumab treatment and due to polypharmacy, with concurrent baclofen treatment causing excessive sedation; there was no interruption to bimekizumab treatment, baclofen was discontinued, and the patient recovered. Discontinuation rates due to TEAEs were low, occurring in two (1%) of 267 patients in the bimekizumab group (one case each of stomatitis and oral candidiasis) and in no patients in the placebo group. There were no deaths throughout the study.

The most common TEAEs, reported in 2% or more patients in the bimekizumab group, were nasopharyngitis, oral candidiasis, and upper respiratory tract infection

	Placebo (n=133)	Bimekizumab 160 mg every 4 weeks (n=267)
Primary efficacy endpoint		
ACR50 response	9 (7%)	116 (43%)
OR *vs* placebo (95% CI); p value	..	11·1 (5·4 to 23·0); p<0·0001
Ranked secondary endpoints		
HAQ-DI score change from baseline, mean (SE)	–0·07 (0·04)	–0·38 (0·03)
Least squares mean difference *vs* placebo (95% CI); p value	..	–0·33 (–0·42 to –0·23); p<0·0001
PASI90 response*	6 (7%) of 88	121 (69%) of 176
OR *vs* placebo (95% CI); p value	..	30·2 (12·4 to 73·9); p<0·0001
SF-36 PCS score change from baseline, mean (SE)	1·4 (0·7)	7·3 (0·5)
Least squares mean difference *vs* placebo (95% CI); p value	..	6·0 (4·4 to 7·7); p<0·0001
MDA response	8 (6%)	118 (44%)
OR *vs* placebo (95% CI); p value	..	13·1 (6·1 to 28·0); p<0·0001
Additional efficacy outcomes		
ACR20†	21 (16%)	179 (67%)
ACR70†	1 (1%)	71 (27%)
PASI75*	9 (10%) of 88	145 (82%) of 176
PASI100*	4 (5%) of 88	103 (59%) of 176
ACR50+PASI100*	1 (1%) of 88	59 (34%) of 176
VLDA	3 (2%)	36 (13%)
IGA 0 or 1†‡§	3 (4%) of 82	99 (61%) of 163
mNAPSI 0¶	12 (14%) of 83	73 (46%) of 159
HAQ-DI MCID‖	24 (22%) of 110	130 (56%) of 231
PsAID-12 score change from baseline†, mean (SE)	–0·3 (0·2)	–2·2 (0·1)
PtAAP score change from baseline†, mean (SE)	–4·5 (2·1)	–27·7 (1·7)
FACIT-Fatigue score change from baseline, mean (SE)	0·1 (0·7)	5·5 (0·6)

Data are n (%), unless otherwise stated. The randomised set was used, unless otherwise stated. For binary variables, ORs, CIs, and p values were generated using logistic regression with treatment, previous exposure to TNFα inhibitors, and region as factors. For continuous variables, least squares mean, SEs, difference in least squares means, and p values were generated using ANCOVA with treatment, previous exposure to TNFα inhibitors, and region as fixed effects and the baseline value of the outcome as covariate. Binary variables were calculated with non-responder imputation, continuous outcomes with multiple imputation, and hierarchical continuous outcomes with reference-based multiple imputation. ACR=American College of Rheumatology. BSA=body surface area. FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy-Fatigue. HAQ-DI=Health Assessment Questionnaire—Disability Index. IGA=Investigator's Global Assessment. MCID=minimal clinically important difference. MDA=minimal disease activity. mNAPSI=modified Nail Psoriasis Severity Index. OR=odds ratio. PASI=Psoriasis Area and Severity Index. PsAID-12=Psoriatic Arthritis Impact of Disease-12. PtAAP=Patient Assessment of Arthritis Pain. SF-36 PCS=Short-Form 36-item Health Survey Physical Component Summary. TNFα=tumour necrosis factor-α. VLDA=very low disease activity. *In patients with psoriasis affecting at least 3% BSA at baseline. †Non-ranked secondary outcome. ‡Responders are patients with an IGA score of 0 or 1 and at least a two-grade reduction from baseline. §In patients with psoriatic skin lesions (IGA ≥2) and psoriasis affecting at least 3% BSA at baseline. ¶In patients with mNAPSI greater than 0 at baseline. ‖In patients with HAQ-DI score of 0·35 or greater at baseline.

Table 2: **Efficacy endpoints at week 16**

(table 3). There were two serious infections, occurring in two (1%) of 267 patients in the bimekizumab group (one case each of bronchitis and COVID-19 pneumonia). No opportunistic infections were reported, and there were no cases of active tuberculosis in the study. Fungal infections were reported in 12 (4%) of 267 patients receiving bimekizumab. Of those, seven (3%) patients were identified as having *Candida* infections. No fungal infections were reported in the placebo group. All *Candida* infections were oral candidiasis. All fungal infections were mild or moderate, none were systemic, and one moderate *Candida* infection led to study discontinuation. One patient had recurrent candidiasis (three infections reported to week 16), which did not lead to study discontinuation.

Of the safety topics of interest, there was one malignancy (basal cell carcinoma in the placebo group) and no reported cases of major adverse cardiovascular events, uveitis, inflammatory bowel disease, or suicidal ideation and behaviour (table 3). Incidence of injection site reactions was low, reported by three (1%) of 267 patients in the bimekizumab group and none in the placebo group. Four (1%) of 267 patients receiving bimekizumab reported neutropenia, all of which were non-serious and did not lead to study discontinuation. Hepatic events were reported in eight (3%) of 267 patients receiving bimekizumab and two (2%) of 132 patients receiving placebo; most of these were increased liver enzyme concentrations and none led to discontinuation (table 3).

Discussion

In this study, dual inhibition of IL-17A and IL-17F with bimekizumab had superior efficacy in the treatment of patients with active psoriatic arthritis with inadequate response or intolerance to TNFα inhibitors compared with placebo, as shown by the primary and all ranked secondary endpoints at week 16. The safety profile of bimekizumab was consistent with that observed in previous clinical studies of bimekizumab in psoriatic arthritis.[13,14]

Bimekizumab was superior to placebo in improving the signs and symptoms of psoriatic arthritis over 16 weeks across a range of outcomes assessing the multiple domains of psoriatic arthritis. At week 16, a significantly greater proportion of patients in the bimekizumab group reached ACR50 versus the placebo group. 59% of patients in the bimekizumab group with psoriasis affecting at least 3% BSA at baseline had complete skin clearance, as measured by PASI100, at week 16. The strong responses on bimekizumab and low responses on placebo led to large treatment effect sizes at week 16 for both joint outcomes and skin outcomes.

The superior composite MDA response reached by patients receiving bimekizumab at week 16 showed robust efficacy across the range of clinical psoriatic arthritis manifestations compared with placebo. A strong

	Placebo (n=132)*	Bimekizumab 160 mg every 4 weeks (n=267)
Any TEAE	44 (33%)	108 (40%)
Serious TEAEs†	0	5 (2%)
Discontinuation due to TEAEs‡	0	2 (1%)
Drug-related TEAEs	4 (3%)	35 (13%)
Severe TEAEs§	0	5 (2%)
Deaths	0	0
Most frequent TEAEs in the bimekizumab group¶		
Nasopharyngitis	1 (1%)	10 (4%)
Oral candidiasis	0	7 (3%)
Upper respiratory tract infection	2 (2%)	6 (2%)
Infections‖		
Serious**	0	2 (1%)
Opportunistic	0	0
Active tuberculosis	0	0
SARS-CoV-2 infections	6 (5%)	5 (2%)
Fungal infections	0	12 (4%)
Candida infections††	0	7 (3%)
Oral candidiasis††	0	7 (3%)
Fungal infections not elsewhere classified	0	4 (1%)
Fungal skin infection	0	1 (<1%)
Tongue fungal infection	0	1 (<1%)
Vulvovaginal mycotic infection	0	2 (1%)
Tinea infections	0	1 (<1%)
Tinea pedis	0	1 (<1%)
Serious fungal infections	0	0
Systemic fungal infections	0	0
Fungal infections leading to discontinuation	0	1 (<1%)
Candida infections leading to discontination	0	1 (<1%)
Neutropenia‡‡	0	4 (1%)
Serious hypersensitivity	0	0
Injection site reactions	0	3 (1%)
Adjudicated suicidal ideation and behaviour	0	0
Adjudicated major adverse cardiovascular event	0	0
Liver function test changes or increases in enzyme concentrations		
Alanine aminotransferase more than three times upper limit of normal	0	2 (1%)
Aspartate aminotransferase or alanine aminotransferase more than three times upper limit of normal	0	4 (1%)
Adjudicated inflammatory bowel disease	0	0
Malignancies	1 (1%)	0
Basal cell carcinoma	1 (1%)	0

Data are n (%). Data reported for the safety set. All TEAEs were coded according to the Medical Dictionary for Regulatory Activities (version 19.0). A safety follow-up was conducted 20 weeks after the last dose of bimekizumab for those not entering the open-label extension or who discontinued early. TEAE=treatment-emergent adverse event. *One patient was randomly assigned but did not receive any doses of placebo, so was not included in the safety set. †One case of intestinal obstruction, one of bronchitis, one of COVID-19 pneumonia, one of joint injury, and one of toxic encephalopathy. ‡One case of stomatitis and one of oral candidiasis. §Six events in five patients: one case of bronchitis, one of back pain, one of toxic encephalopathy, one of headache, one of pruritis, and one of renal pain; one patient reported both severe back pain and renal pain. ¶Most frequent adverse events are those occurring in 2% or more patients in the bimekizumab group. ‖Apart from one case of severe bronchitis, all infections were mild or moderate. **One case of bronchitis and one of COVID-19 pneumonia. ††One patient had recurrent candidiasis (three infections within the 16-week period). ‡‡Three cases of neutropenia and one case of decreased neutrophil count.

Table 3: **Safety outcomes to week 16**

MDA response is particularly relevant as international guidelines have identified remission and low or minimal disease activity as preferred targets for treatment,[2,18] and because achieving MDA is associated with improvements in quality of life.[19] The average MDA response in other studies of patients (who either had inadequate response or intolerance to TNFα inhibitors or were naive to TNFα inhibitors, or a mixed population of both) receiving other therapies for longer time periods has been reported as 36·3% (upper and lower limits 32·3–40·5%).[20] Improvements in clinical outcomes were supported by clinically meaningful improvements in patient-reported physical function as well as pain and fatigue, both of which have been identified by patients as important to address and as relevant to their disease burden.[21,22]

Bimekizumab treatment responses were rapid, with numerically higher responder rates compared with placebo observed as early as week 4 (after a single dose of bimekizumab), for outcomes across psoriatic arthritis manifestations, including joints, skin, and the MDA composite. This speed of response across the signs and symptoms of psoriatic arthritis is of value to patients, who have reported that symptom alleviation is a priority to reduce the impact of disease on daily life.[23]

Although BE OPTIMAL and BE COMPLETE are independent studies, the magnitude of efficacy measured in this study was similar to that measured in the population of patients who were naive to biologic DMARDs in the BE OPTIMAL study,[15] suggesting that bimekizumab treatment might lead to a similar magnitude of clinically meaningful improvements in psoriatic arthritis, irrespective of previous TNFα inhibitor treatment.

Efficacy in patients with psoriatic arthritis and previous inadequate response or intolerance to TNFα inhibitors is particularly relevant because the treatment of this patients population now comprises a common clinical scenario in routine practice, and efficacy in this population is frequently observed to be lower than in populations of patients who are naive to biologics in phase 3 studies of psoriatic arthritis treatments.[8,24,25] A similar pattern is seen in real-world studies, with patients with inadequate response or intolerance to TNFα inhibitors reporting lower effectiveness and greater rates of treatment discontinuation or switching compared with patients who are naive to TNFα inhibitors.[26,27] Given the lower effectiveness in this population, as well as the continued adoption of TNFα inhibitor treatments and TNFα inhibitor biosimilars as first-line therapies, efficacy in patients with inadequate response or intolerance to TNFα inhibitors with psoriatic arthritis becomes increasingly relevant. The efficacy of bimekizumab in this difficult-to-treat population of patients with inadequate response or intolerance to TNFα inhibitors could be due to an enrichment of patients with IL-17F-dependent signalling driving their disease, which cannot be inhibited by TNFα inhibitors or other treatments that only target IL-17A. This is a hypothesis worthy of additional exploration.

Radiographic outcomes were not evaluated in this trial; however, interim results from the BE OPTIMAL study report the inhibition of structural progression in patients with psoriatic arthritis who are naive to biologics treated with bimekizumab, compared with placebo, at week 16.[15]

The overall safety profile of bimekizumab in BE COMPLETE was similar to previous studies in psoriatic arthritis and consistent with its known safety profile.[13,14] Of note, more mild-to-moderate fungal infections occurred in the bimekizumab group than in the placebo group, which is consistent with the known role of IL-17A and IL-17F in mucosal host defences against fungal infections.[28] This safety profile is well understood and patients were managed with standard topical or oral antifungal therapies. There were no severe or systemic fungal infections, and recurrent infections were uncommon (one patient receiving bimekizumab with recurrent candidiasis reported three infections to week 16; these infections did not lead to study discontinuation). The fungal safety events reported in BE COMPLETE were also consistent with those in the trials of bimekizumab in patients with psoriasis,[29,30] for which bimekizumab has been approved for use by regulatory agencies.[31] There was a low rate of SAEs and discontinuations due to TEAEs throughout the study. No cases of inflammatory bowel disease or uveitis were reported. Administration of bimekizumab was well tolerated by patients, demonstrated by the low incidence of injection site reactions.

This study was 16 weeks in duration. Given that psoriatic arthritis is a chronic disease with the potential for lasting effects, such as irreversible joint damage, an increased risk of comorbidities, and impaired quality of life, it is important to establish the long-term efficacy and safety of treatments.[2,32] The open-label extension will provide data beyond week 16 and allow the efficacy and safety of long-term treatment with bimekizumab to be assessed.

A limitation of this study is that the patient population, although typical of phase 3 studies of psoriatic arthritis, did not include patients who have multiple active comorbidities, so the population might be less applicable to patients in real-world clinical practice. Another limitation is that this study does not allow the efficacy and safety of bimekizumab to be directly compared with other available psoriatic arthritis treatments. Future head-to-head studies will be advantageous for clinicians to formally compare treatment options for psoriatic arthritis.

In summary, this study showed rapid and clinically meaningful improvements consistent across a range of joint, skin, and patient-reported symptoms with bimekizumab treatment in patients with active psoriatic arthritis and inadequate response or intolerance to TNFα inhibitors. Data from the open-label extension are required to assess the long-term efficacy and safety of bimekizumab treatment for psoriatic arthritis.

Contributors

JFM, RL, IBM, PJM, CTR, YT, AA, FB, DDG, LG, ABG, DT, RBW, BI, DA, RB, VS, JC, and LCC made substantial contributions to study conception and design. JFM, RL, IBM, PJM, CTR, YT, AA, FB, DDG, LG, ABG, DT, RBW, BI, DA, RB, VS, JC, and LCC made substantial contributions to analysis and interpretation of the data. JFM, RL, IBM, PJM, CTR, YT, AA, FB, DDG, LG, ABG, DT, RBW, BI, DA, RB, VS, JC, and LCC drafted the article or revised it critically for important intellectual content. JFM, RL, IBM, PJM, CTR, YT, AA, FB, DDG, LG, ABG, DT, RBW, BI, DA, RB, VS, JC, and LCC approved the final version of the Article to be published. JFM, BI, DA, RB, VS, and JC accessed and verified the data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

JFM reports work as a consultant or investigator for AbbVie, Amgen, Biogen, BMS, Dermavant, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB Pharma. RL reports consultancy fees from Abbott, Ablynx, Amgen, AstraZeneca, BMS, Centocor, GSK, Merck, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, and Wyeth; research grants from Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, and Wyeth; and speaker's bureau fees from Abbott, Amgen, BMS, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, and Wyeth. IBM reports consulting fees and honoraria from AbbVie, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Novartis, and UCB Pharma; and research support from BMS, Boehringer Ingelheim, Celgene, Janssen, and UCB Pharma. PJM reports research grants from AbbVie, Amgen, BMS, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; consultancy fees from AbbVie, Acelyrin, Aclaris, Amgen, BMS, Boehringer Ingelheim, Eli Lilly, Galapagos, Gilead, GSK, Inmagene, Janssen, Moonlake Pharma, Novartis, Pfizer, Sun Pharma, and UCB Pharma; and speakers' bureau fees from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB Pharma. CTR reports research for AbbVie, Amgen, and UCB Pharma; and consultancy for Amgen, AbbVie, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma. YT reports speaking fees or honoraria from AbbVie, AstraZeneca, BMS, Boehringer Ingelheim, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, GSK, Mitsubishi-Tanabe, and Pfizer; and research grants from Asahi-Kasei, AbbVie, Boehringer Ingelheim, Chugai, Daiichi-Sankyo, Eisai, and Takeda. AA reports honoraria or research grants from AbbVie, Amgen, BMS, Boehringer Ingelheim, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi-Tanabe, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, and UCB Pharma. FB reports work as a consultant, speaker, or investigator for AbbVie, Affibody, Amgen, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, GSK, Janssen, MSD, MoonLake, Novartis, Pfizer, Roche, Sandoz, and Sanofi. DDG received grants from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma; and consulting fees from AbbVie, Amgen, BMS, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma. LG reports non-financial support from UCB Pharma during the conduct of the study; grants from Amgen, Eli Lilly, Galapagos, Pfizer, Sandoz, and UCB Pharma; personal fees from AbbVie, Amgen, BMS, Celltrion, Eli Lilly, Galapagos, Gilead, Janssen, MSD, Novartis, Pfizer, Sandoz, and UCB Pharma; and non-financial support from AbbVie, Janssen, Novartis, Pfizer, and UCB Pharma outside the submitted work. ABG reports honoraria as an advisory board member, non-promotional speaker, or consultant for Amgen, AnaptysBio, Avotres Therapeutics, Boehringer Ingelheim, BMS, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Xbiotech (stock options); and research or educational grants from AnaptysBio, BMS, Janssen, Novartis, Ortho Dermatologics, Sun Pharma, and UCB Pharma (all funds go to the Icahn School of Medicine at Mount Sinai). DT reports honoraria for participation on advisory boards as a speaker and for consultancy from AbbVie, Almirall, Amgen, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Galapagos, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung, Sanofi Genzyme, and UCB Pharma; and research grants from LEO Pharma and Novartis. RBW reports consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; and honoraria from Astellas, DiCE, GSK, and Union. BI is an employee of UCB Pharma, and stockholder of AbbVie, GSK, and UCB Pharma. DA, RB, VS, and JC are all employees and stockholders of UCB Pharma. LCC reports grants and research support from AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma; paid consultancy for AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Domain, Eli Lilly, Gilead, Galapagos, Janssen, Moonlake, Novartis, Pfizer, and UCB Pharma; and speaker fees from AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Medac, Novartis, Pfizer, and UCB Pharma.

Data sharing

Data from this manuscript can be requested by qualified researchers 6 months after product approval in the USA or Europe, or global development is discontinued, and 18 months after trial completion. Investigators can request access to anonymised individual patient data and redacted study documents, which can include: raw datasets, analysis-ready datasets, study protocol, blank case report form, annotated case report form, statistical analysis plan, dataset specifications, and clinical study report. Before use of the data, proposals need to be approved by an independent review panel at www.vivli.org and a signed data sharing agreement will need to be executed. All documents are available in English only, for a prespecified time, typically 12 months, on a password protected portal.

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