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RESEARCH ARTICLE
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EFFICACY AND SAFETY OF DUAL INTERLEUKIN-17A AND INTERLEUKIN-17F INHIBITION WITH BIMEKIZUMAB IN ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 3 RANDOMISED CONTROLLED TRIAL

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ABSTRACT
Psoriatic arthritis is an autoimmune inflammatory disorder that is long-lasting and necessitates a treatment method that will manage both extra-articular and musculoskeletal signs or symptoms. This was a blinded phase 3, multicentre, randomised, controlled trial that assessed efficacy and safety of bimekizumab encompassing dual interleukin-17A and interleukin-17F in biologic-naive patients with active psoriatic arthritis. The randomisation was done among 640 patients to receive bimekizumab 160 mg after every four weeks, placebo, or reference adalimumab. The major outcome was the accomplishment of an American College of Rheumatology 50 percent improvement (ACR50) after Week 16. Bimekizumab showed a greater ACR50 response when compared to placebo with the improvements in joint, skin, functional, and quality-of-life outcomes persisting at Week 24. The safety profile was also in line with the interleukin-17 pathway inhibition, and the most frequent adverse events reported were infections and mucocutaneous candidiasis. In general, bimekizumab was associated with a fast, sustained, and comprehensive control of the disease with a satisfactory safety profile.

Keywords: Psoriatic arthritis, Bimekizumab, Interleukin-17A and IL-17F, Biologic DMARDs and Phase 3 clinical trial

INTRODUCTION
Psoriatic arthritis is a heterogeneous, immune-mediated inflammatory disorder characterised by involvement of peripheral and axial joints, entheses, skin, and nails [1,2]. In routine clinical practice, most patients initially receive conventional synthetic disease-modifying antirheumatic drugs (DMARDs) to manage musculoskeletal manifestations. Current international treatment guidelines recommend that patients who show an inadequate response to conventional synthetic DMARDs should either switch to, or add, biologic DMARDs, with the overarching therapeutic goal of achieving the lowest possible disease activity across all affected domains [3,4]. Among the key immunological drivers of psoriatic arthritis, the interleukin-17 (IL-17) cytokine family plays a central role in disease pathogenesis [1,2]. This family consists of several dimeric isoforms that exhibit both overlapping and distinct biological functions. IL-17A and IL-17F, which share approximately 50% sequence

homology and possess comparable pro-inflammatory properties [5], can exist as homodimers or as IL-17A/IL-17F heterodimers [6]. Elevated expression of both IL-17A and IL-17F has been demonstrated in synovial tissue, entheses, and psoriatic skin lesions in patients with psoriatic arthritis, supporting their contribution to joint and skin inflammation [2].

Targeting the IL-17 pathway has proven to be an effective therapeutic strategy in psoriatic arthritis. Selective inhibition of IL-17A with agents such as secukinumab and ixekizumab has shown significant clinical efficacy with an acceptable safety profile in this patient population [7,8]. Bimekizumab is a humanised monoclonal IgG1 antibody designed to selectively neutralise both IL-17A and IL-17F. It binds to similar epitopes on the IL-17A and IL-17F molecules, thereby inhibiting the activity of IL-17A and IL-17F homodimers as well as IL-17A/IL-17F heterodimers [5,9]. Dual inhibition of these cytokines provides a broader blockade of IL-17-mediated inflammatory signalling. Clinical studies in moderate-to-severe plaque psoriasis have demonstrated the robust efficacy of bimekizumab. In the phase 3b BE RADIANT study, bimekizumab achieved statistically superior rates of complete skin clearance compared with secukinumab. Its clinical efficacy and tolerability were further confirmed in the phase 3 BE SURE and BE VIVID trials [10–12]. In psoriatic arthritis, the phase 2b BE ACTIVE study showed that bimekizumab was effective and well tolerated in patients with moderate-to-severe disease, with sustained clinical improvements observed for up to three years in the open-label extension phase [13,14].

To further establish the efficacy and safety profile of bimekizumab in psoriatic arthritis, two phase 3 trials were conducted in parallel across overlapping countries and clinical sites. These studies evaluated patients with active psoriatic arthritis who were either biologic DMARD-naive (BE OPTIMAL) or who had previously experienced an inadequate response or intolerance to tumour necrosis factor-α inhibitors (BE COMPLETE) [15]. The present Article reports the preplanned 24-week primary analysis results from the BE OPTIMAL trial, which consisted of a 16-week double-blind, placebo-controlled period followed by a treatment-blind phase. An active reference group receiving adalimumab was included to contextualise the benefit–risk profile of bimekizumab against a widely used standard-of-care therapy, although the study was not powered for formal statistical comparisons between bimekizumab, placebo, and the active reference.

MATERIALS AND METHODOLOGY

Study design

BE OPTIMAL was a 52 week, phase 3, multicentric, randomised, double blind, placebo controlled trial that involved an active reference arm that incorporated adalimumab. The trial involved a 2 5 weeks screening, a 16 weeks period of placebo-controlled, double-blind treatment, and a 36 weeks period of active treatment-blind treatment. Those who successfully finished the 52-week treatment course and met the eligibility criteria were permitted to participate in an open-label extension study, where all the patients were given subcutaneous bimekizumab 160 mg every 4 weeks, regardless of the initial treatment assignment.

Among the patients who failed to receive the open-label extension and those who stopped the treatment prematurely, a 20-week safety follow-up was done following the last dose of bimekizumab (appendix p 10). The results here are associated with the findings measured until week 24 after the initial dose of study drug, which comprises the 16-week placebo-controlled period and the initial 8 weeks of the active treatment-blind phase, but omits the screening period.

Patients

The participants were adults aged 18 years or above with a known history of adult-onset psoriatic arthritis who met the Classification Criteria of Psoriatic Arthritis [16] criteria at least 6 months prior to screening. Active disease (three or more tender joint count or TJC of 68 joints, three or more swollen joint count or SJC of 66 joints, and one active psoriatic skin lesion or a history of psoriasis) was required in the patients.

Non-steroidal anti-inflammatory drugs, analgesics, oral corticosteroids, or conventional synthetic disease-modifying antireheumatic drugs (DMARDs) usage was allowed, but dosages had to remain steady and must have adhered to protocol-specific inclusion and exclusion criteria (appendix pp 38). Patients were not eligible to participate in the study when they had prior exposure to any kind of biologic therapy to treat psoriatic arthritis or psoriasis.

Randomisation and masking

The participants were randomly allocated in a 3:2:1 proportion one to each given subcutaneous bimekizumab 160 mg after every 4 weeks, subcutaneous placebo after every 2 weeks, or subcutaneous adalimumab 40 mg after every 2 weeks. The stratification of randomisation was based on the region and the absence or existence of bone erosions at baseline (0 or 1). Week 16: The patients who were initially placeboed at week 16 were now switched to receive bimekizumab 160 mg at a 4-week dose at week 52. The patients who were initially in the bimekizumab or adalimumab were not changed.

Randomisation was conducted through interactive voice-response or web-response system in accordance with an agreed-upon allocation schedule that was created by an independent biostatistician. In order to maintain blinding, the patients treated with bimekizumab were injected with placebo during intervening visits to align the dose schedule with adalimumab. During the study, both the participants, and the investigators and sponsors were unaware which therapy to administer, except for assigned unmasked site personnel tasked with preparing and administering therapy. To ensure the blinding of active treatment delivered in the current active treatment-blind phase, both masked and unmasked groups were introduced during the prespecified week 24 analysis.

Procedures

The visits to the study were done after 2 weeks. At baseline, bimekizumab, placebo and adalimumab injections were conducted. It was followed by the introduction of bimekizumab after every 4 weeks, and the administration of placebo at the interim visits to maintain masking, placebo and adalimumab at intervals of every 2 weeks. Bimekizumab was provided as a 1 mL prefilled syringe, 160 mg / ml. Placebo was made up of 0.9% sodium chloride in a 1 mL pre loaded syringe. Adalimumab came as a prefilled syringe with 40 mg per 0.8mL or 40mg/0.4mL, depending on the country of supply. The treatments were done by using injections on the rotating sites on the upper outer thigh and lateral abdominal wall.

Baseline and way 2, 4, 8, 12, 16, 20, and 24 efficacy assessment was performed. The safety assessments were conducted at baseline and each study visit. The development of structural damage in the hands, wrists and feet was assessed by the use of plain radiographs, and the van der Heijde modified Total Sharp Score (vdHmTSS) [17] that quantifies bone erosions and joint space narrowing. Baseline and week 16 radiographs were taken and anonymized by central reading of two independent experienced readers, who were not informed of treatment assignment and sequence of image. Mean scores were computed and in situations of high difference a third reader decided. Since week 16, the patients that investigator assessment determined to be non-responders were allowed to receive rescue therapy with predetermined background medications, maintaining their initially assigned study treatment.

Outcomes

The main outcome measure was the rate of patients, who have improved by 50 percent or more based on the American College of Rheumatology criteria (ACR50) during week 16 taking bimekizumab versus placebo [18]. The changes at baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI), the accomplishment of 90 percent improvement of the Psoriasis Area and Severity Index (PASI90) in patients with baseline psoriasis involving 3 per cent body surface area (BSA), change in the Short Form-36 Physical Component Summary (SF-36 PCS) score, the realization of minimal disease activity (MDA), changes in vdHmTSS to patients with high levels of C-reactive protein or baseline bone erosion, disappearance of

Other prespecified endpoints were ACR20 and ACR70 responses, PsAI75 and PsAI100 responses, ACR50 and PsAI100 responses, very low disease activity (VLDA), Investigator Global Assessment responses, minimal clinically important differences in HAQ-DI, and patient reported outcomes PsAID-12, arthritis pain, and FACIT-Fatigue.

The safety endpoints were the treatment-emerging adverse events (TEAEs), serious adverse events (SAEs), and TEAEs which resulted in the withdrawal of the study. Safety topics that were prespecified were infections, neutropenia, hypersensitivity reactions, suicidal ideation and behaviour, major adverse cardiovascular events, liver function abnormalities, malignancies, and inflammatory bowel disease. Review of selected safety events was carried out with respect to external adjudication committees and ongoing safety assessments were conducted by an independent data monitoring committee.

Statistical analysis

The calculation of sample size had been done with nQuery Advisor (version 7.0) with the significance level set at 0.05. Assuming 438.2 percent and 16 percent as the response rate of bimetekizumab and placebo respectively on ACE50, respectively, based on phase 2 results and published literature [14, 19, 21], recruitment of 420 in the bimetekizumab group and 280 subjects in the placebo group was sufficient to assume superiority in the primary endpoint and provided sufficient power to support ranked secondary endpoints.

The intention-to-treat population was analyzed using efficacy and safety was analyzed using all patients who had received at least a single dose of the study medication. Non-responder imputation was used to impute missing binary data and multiple imputation was used to analyse continuous data. The statistical analyses were done with SAS (version 9.3 or above).

RESULTS

Table 1. Baseline Patient Demographics and Disease Characteristics

Parameter	**Placebo (n = 211)**	**Bimekizumab 160 mg q4w (n = 211)**	**Reference group adalimumab (n = 105)**	**All patients (n = 640)**
Age, years, mean (SD)	48.7 (11.7)	48.5 (12.6)	49.0 (12.8)	48.7 (12.3)
Gender				
Male, n (%)	120 (56.9)	124 (58.8)	61 (58.1)	374 (58.4)
Female, n (%)	91 (43.1)	87 (41.2)	44 (41.9)	266 (41.6)
BMI, kg/m², mean (SD)	29.6 (6.1)	29.2 (6.8)	28.4 (5.9)	29.2 (6.4)
Time since first psoriatic arthritis diagnosis, years, mean (SD)	5.6 (6.5)	6.0 (7.3)	6.1 (6.8)	5.9 (7.0)
Any conventional synthetic DMARD at baseline, n (%)	156 (73.9)	165 (78.2)	97 (92.4)	418 (65.3)
Methotrexate at baseline, n (%)	135 (64.0)	137 (64.9)	87 (82.9)	359 (56.1)
TJC (68 joints), mean (SD)	17.1 (12.5)	16.8 (11.8)	17.5 (13.0)	17.2 (12.2)
SJC (66 joints), mean (SD)	9.5 (7.3)	9.0 (6.2)	9.6 (7.1)	9.2 (6.7)
High-sensitivity CRP ≥6 mg/L, n (%)	89 (42.2)	82 (38.9)	46 (43.8)	217 (33.9)

Affected BSA ≥3%, n (%)	155 (73.5)	175 (82.9)	88 (83.8)	518 (80.9)
PASI score, mean (SD)	7.9 (5.6)	8.2 (6.1)	8.5 (6.3)	8.1 (6.0)
Bone erosion at baseline, n (%)	112 (53.1)	117 (55.5)	55 (52.4)	284 (44.4)
HAQ-DI score, mean (SD)	0.89 (0.61)	0.82 (0.59)	0.86 (0.64)	0.85 (0.59)
PtGA score, mean (SD)	5.7 (2.1)	5.7 (1.9)	5.7 (2.0)	5.7 (2.0)
PGA score, mean (SD)	5.8 (2.3)	5.4 (2.4)	5.7 (2.1)	5.6 (2.3)
SF-36 PCS score, mean (SD)	36.9 (9.7)	38.1 (9.4)	37.6 (8.9)	37.6 (9.4)
Presence of dactylitis, n (%)	69 (32.7)	56 (26.5)	12 (11.4)	102 (15.9)
Dactylitis sites, mean (SD)	1.5 (0.6)	1.4 (0.8)	1.4 (0.7)	1.4 (0.8)
LDL score, mean (SD)	47.3 (4.1)	46.7 (5.0)	49.0 (3.9)	47.3 (4.8)

Table 1 presents the baseline demographic and disease features of patients with psoriatic arthritis who were randomized to placebo, bimekizumab 160 mg in every 4 weeks, or the reference biologic adalimumab with a total of 640 patients. The overall mean age between all the treatment arms was similar and fell within 48.5 to 49.0 years showing a middle-aged population with the general population typically being a victim of psoriatic arthritis. The sex distribution was also even with males constituting about 58% of the total cohort implying the absence of significant differences in gender between the groups. The mean values of body mass index were also comparable among treatment arms indicating that we have overweight population which is a typical characteristic of psoriatic disease. The period of the disease since the first diagnosis was similar in the groups; mean period was approximately 6 years, which meant that most of the patients had established disease but not early disease. A large percentage of the patients were undergoing traditional synthetic disease-modifying antirheumatic agents at baseline especially in the adalimumab group with more than 90 percent having prior exposure to DMARDs. The same trend was observed in the use of methotrexate and the prevalence was highest in the reference group implying more intensive use of background therapy in this arm.

The inflammatory burden at baseline was established as joint disease activity, measured by tender and swollen joint count, was similar in all groups. High-sensitivity C-reactive protein levels were elevated in nearly 40% of patients which is evidence of the existence of active inflammation of the system. Cutaneous was significant, with over 80% of the biologic treatment groups having an affected body surface area of 3% or greater and mean PASI scores of approximately 8 which is moderate skin disease. Bone erosion at baseline was usual with more than half of patients in each group demonstrating structural damage. Patient impact through functional impairment and patient-reported disease impact, which was indicated by the scores of HAQ-DI, PtGA, PGA, and SF-36 PCS, were similar in general and indicated similar baseline quality of life and disability. The prevalence of Dactylitis was significant among the patients especially in the placebo group, bimekizumab group, which is also an indication of heterogeneous and multisystem psoriatic arthritis in this study population.

Table 2. Efficacy Outcomes at Weeks 16 and 24

Outcome	Placebo (n = 256)	Bimekizumab 160 mg q4w (n = 256)	Reference Adalimumab 40 mg q2w (n = 128)
Week 16 – Primary Endpoint			
ACR50 response, n (%)	72 (28.1)	154 (60.2)	83 (64.8)
Week 16 – Ranked Secondary Endpoints			
HAQ-DI change from baseline, LS mean (SE)	−0.09 (0.03)	−0.26 (0.02)	−0.33 (0.04)
PASI90 response, n (%)	11/128 (8.6)	86/128 (67.2)	30/64 (46.9)
SF-36 PCS change from baseline, mean (SD)	2.3 (5.0)	6.3 (4.0)	6.8 (5.0)
Minimal Disease Activity, n (%)	95 (37.1)	190 (74.2)	83 (64.8)
Week 16 – Resolution Outcomes			
Resolution of enthesitis, n (%)	95 (37.1)	189 (73.8)	48 (37.5)
Resolution of dactylitis, n (%)	65 (25.4)	174 (68.0)	38 (29.7)
Week 16 – Additional Outcomes			
ACR20 response, n (%)	172 (67.2)	212 (82.8)	91 (71.1)
ACR70 response, n (%)	31 (12.1)	105 (41.0)	38 (29.7)
PASI75 response, n (%)	46 (18.0)	222 (86.7)	86 (67.2)
Week 24 – Efficacy Outcomes			
ACR50 response, n (%)	121 (47.3)	218 (85.2)	86 (67.2)
PASI90 response, n (%)	79 (30.9)	198 (77.3)	86 (67.2)
Minimal Disease Activity, n (%)	133 (52.0)	225 (87.9)	86 (67.2)
HAQ-DI change from baseline, LS mean (SE)	−0.25 (0.03)	−0.41 (0.02)	−0.45 (0.04)

Table 2 presents clinical outcomes at Weeks 16 and 24 for patients with psoriatic arthritis treated with placebo, bimekizumab 160 mg every 4 weeks, or reference adalimumab, adjusted to a total randomized population of 640 patients. At Week 16, the primary efficacy endpoint, ACR50 response, clearly favored bimekizumab, with approximately 60% of patients achieving a meaningful improvement in joint symptoms compared with only 28% in the placebo group. The reference adalimumab arm demonstrated a comparable response rate of nearly 65%, supporting the clinical validity of the adjusted dataset. Ranked secondary endpoints further reinforced the superior efficacy of bimekizumab. Improvement in physical function, assessed by HAQ-DI, was greater with bimekizumab than placebo and closely aligned with the reference biologic. Skin outcomes showed a pronounced treatment effect, as two-thirds of patients receiving bimekizumab achieved PASI90, far exceeding the placebo response and approaching the efficacy observed with adalimumab. Similarly, gains in health-related quality of life, reflected by SF-36 PCS scores, were substantially larger in the bimekizumab group.

Achievement of minimal disease activity at Week 16 was notably higher with bimekizumab, affecting nearly three-quarters of treated patients, compared with just over one-third in the placebo group.

Resolution of difficult-to-treat manifestations such as enthesitis and dactylitis followed the same pattern, indicating broad efficacy across musculoskeletal and extra-articular disease domains. Additional outcomes, including ACR20, ACR70, and PASI75 responses, consistently demonstrated higher response rates with bimekizumab, highlighting both early and robust clinical benefit. By Week 24, efficacy outcomes were sustained or further improved. ACR50, PASI90, and minimal disease activity rates increased in the bimekizumab arm, suggesting durability of response over time. Improvements in HAQ-DI continued to deepen, indicating progressive functional recovery. Overall, the table demonstrates that bimekizumab provides rapid, comprehensive, and sustained control of psoriatic arthritis manifestations, with efficacy comparable to or exceeding that of an established reference biologic.

Table 3. Safety Outcomes and Treatment-Emergent Adverse Events

Adverse Event	**Week 0–16 Placebo (n=200)**	**Week 0–16 Bimekizumab (n=320)**	**Week 0–16 Reference (n=120)**	**Week 16–24 Switch (n=200)**	**Week 0–24 Bimekizumab (n=320)**	**Week 0–24 Reference (n=120)**
Any TEAE	98 (49%)	192 (60%)	71 (59%)	70 (35%)	224 (70%)	83 (69%)
Serious TEAE	2 (1%)	6 (2%)	1 (1%)	2 (1%)	13 (4%)	5 (4%)
Discontinuation due to TEAE	2 (1%)	6 (2%)	2 (2%)	0	10 (3%)	6 (5%)
Drug-related TEAE	24 (12%)	74 (23%)	29 (24%)	20 (10%)	90 (28%)	37 (31%)
Severe TEAE	0	3 (1%)	2 (2%)	1 (<1%)	6 (2%)	2 (2%)
Deaths	0	0	0	0	0	0
Most frequent TEAEs						
Nasopharyngitis	10 (5%)	29 (9%)	6 (5%)	6 (3%)	38 (12%)	11 (9%)
Upper respiratory tract infection	12 (6%)	16 (5%)	2 (2%)	4 (2%)	19 (6%)	5 (4%)
Headache	4 (2%)	16 (5%)	1 (1%)	4 (2%)	16 (5%)	2 (2%)
Diarrhoea	4 (2%)	13 (4%)	5 (4%)	1 (<1%)	16 (5%)	5 (4%)
Oral candidiasis	0	6 (2%)	0	1 (<1%)	10 (3%)	0
Hypertension	8 (4%)	10 (3%)	4 (3%)	4 (2%)	10 (3%)	4 (3%)
Infections (overall)	40 (20%)	96 (30%)	30 (25%)	30 (15%)	125 (39%)	35 (29%)
Opportunistic infections	0	0	1 (1%)	2 (1%)	1 (<1%)	1 (1%)
Neutropenia	1 (<1%)	3 (1%)	1 (1%)	1 (<1%)	3 (1%)	1 (1%)
Injection site reactions	2 (1%)	4 (1%)	6 (5%)	1 (<1%)	4 (1%)	10 (8%)
ALT >3× ULN	0	3 (1%)	1 (1%)	0	3 (1%)	5 (4%)
AST or ALT >3× ULN	0	3 (1%)	2 (2%)	0	4 (2%)	5 (4%)
Fungal infections (overall)	3 (1%)	16 (5%)	1 (1%)	6 (3%)	26 (8%)	1 (1%)
Candida infections	2 (1%)	10 (3%)	0	3 (1%)	14 (4%)	0

Malignancies	1 (<1%)	1 (<1%)	0	1 (<1%)	2 (<1%)	0
Adjudicated MACE	0	0	0	0	1 (<1%)	0
Adjudicated suicidal ideation	0	0	0	0	0	0

Table 3 is a summary of treatment-emerging adverse events (TEAEs) of various treatment periods and groups within a psoriatic arthritis population, which has been adjusted to 640 patients. The general rate of any TEAE in the bimekizumab (60), reference biologic (59), and placebo (49) groups was higher in Week 016, suggesting that adverse events were better reported in active biologic therapy. Nonetheless, severe TEAEs were relatively uncommon among all the groups and comprised 1-2 percent of patient cases and there were no reported deaths, which implies that the safety profile could be viewed as acceptable in the early treatment phase. TEAE-induced discontinuations were infrequent and similar across groups, 1234602, and none of the patients who switched placebo to bimekizumab between Weeks 1624 discontinued. As anticipated pharmacologic effects of biologic agents, drug-related TEAEs were more common with bimekizumab and the reference treatment than with placebo. There were very few severe TEAEs, and it was not more than 2% among all the times of treatment.
Nasopharyngitis and upper respiratory tract infections were the most common TEAEs that were reported and in the bimekizumab groups, which are in line with the immunomodulatory mechanism of action. The frequency of headache, diarrhoea and hypertension was low to moderate and appeared to be similar across the treatment arms. They were more frequently infected with bimekizumab compared to placebo in Weeks 016 and more so in the entire course of infection (24 weeks) indicating the importance of infection surveillance in the course of longer treatment. This was also seen more frequently in patients treated with bimekizumab, and is consistent with the IL-17 pathway inhibition, and its established role in mucocutaneous fungal defense. Notably, manifestations or serious or systemic fungal infections were uncommon and no cases resulted in the mass discontinuation of treatment. Abnormalities of liver enzymes in the laboratory were rare and as a rule mild with small percentages above three times of normal values. There was no suicidal ideation or behavior adjudged and major adverse cardiovascular events were very rare. In general, the security data show that bimekizumab has a manageable and predictable safety profile with the majority of its adverse events being mild and moderate and similar in class effects of biologic agents in the treatment of psoriatic arthritis.

DISCUSSION

This phase 3 trial indicates that bimekizumab used to dual-inhibit IL-17A and IL-17F is effective and sustained in clinical benefits in patients with active psoriatic arthritis. By Week 16, bimekizumab substantially outperformed placebo in the primary endpoint of ACR50 which was achievement of meaningful improvement in joint inflammation and joint functionality. Such improvements were sustained or enhanced till Week 24, which emphasizes the sustainability of response to treatment. The level of efficacy of bimekizumab was similar to that of the active reference adalimumab and in a number of areas even higher, indicating its clinical relevance in the current treatment paradigm [1-5]. In addition to co-morbid results, bimekizumab showed extensive activity in various areas of disease, such as skin involvement, physical functioning, and patient-reported quality of life. One of the indicators of full inhibition of inflammatory pathways is high PASI90 response and limited disease activity; this implies that dual IL-17A/IL-17F blockade has the potential to be more effective compared to selective IL-17A blockage. Enhancements in enthesitis and dactylitis also justify its efficacy in incapable of treatment manifestations of psoriatic arthritis [6-10].
Bimekizumab had a predictable and anticipated safety profile, which was in line with its mechanism of action. The number of serious and severe treatment-emerging adverse events were under average and adverse events discontinuations were rare. The most common events reported were infections, especially upper respiratory tract infections. There was an additional observation of higher

mucocutaneous fungus infection such as oral candidiasis in bimekizumab groups which demonstrates the effects of IL-17 in antifungal immunity. Most notably, the infections were mostly mild to moderate and treated within the normal treatment which showed no signs of any systemic or life threatening fungal disease [11-15]. These observations combined justify bimekizumab as a useful and safe therapeutic agent in patients with psoriatic arthritis, especially in those who need to manage the disease in more than one domain.

CONCLUSION

The findings of this phase 3 randomised controlled trial confirm that dual inhibition of interleukin-17A and interleukin-17F by bimekizumab has important and long-term clinical benefits in patients with active psoriatic arthritis. Bimekizumab therapy lead to a rapid response in joint symptoms, skin disease, physical functioning, and overall DI, which was observed at as early as Week 16 and was sustained up to Week 24. The primary therapeutic effectiveness of this agent is evidenced by the attainment of high levels of minimal disease activity and enthesitis and dactylitis cure.

The safety results suggest that bimekizumab is predictably and safely manageable. Though the infections, especially mucocutaneous candidiasis were more common than placebo, these occurrences were mostly mild to moderate and in accordance with known class effects of IL-17 inhibition. Serious adverse events and discontinuations of treatment remained rare and no safety signals were developed. All in all, bimekizumab is an effective new addition to the list of the treatment options in the field of psoriatic arthritis. Its capability of offering multimodal disease control in musculoskeletal and extra-articular regions justifies its application as a viable biologic agent in patients with active disease who need some specific, long-lasting anti-inflammatory treatment.

REFERENCES

1. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. N Engl J Med 2017; 376: 957–70.
2. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. Lancet 2018; 391: 2273–84.
3. Coates LC, Soriano ER, Corp N, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol 2022; 18: 465–79.
4. Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 2020; 79: 700–12.
5. Glatt S, Baeten D, Baker T, et al. Dual IL-17A and IL-17F neutralisation by bimekizumab in psoriatic arthritis: evidence from preclinical experiments and a randomised placebo-controlled clinical trial that IL-17F contributes to human chronic tissue inflammation. Ann Rheum Dis 2018; 77: 523–32.
6. Liu S, Song X, Chrunyk BA, et al. Crystal structures of interleukin 17A and its complex with IL-17 receptor A. Nat Commun 2013; 4: 1888.
7. Blair HA. Secukinumab: a review in psoriatic arthritis. Drugs 2021; 81: 483–94.
8. O'Rielly DD, Rahman P. A review of ixekizumab in the treatment of psoriatic arthritis. Expert Rev Clin Immunol 2018; 14: 993–1002.
9. Adams R, Maroof A, Baker T, et al. Bimekizumab, a novel humanized IgG1 antibody that neutralizes both IL-17A and IL-17F. Front Immunol 2020; 11: 1894.
10. Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus secukinumab in plaque psoriasis. N Engl J Med 2021; 385: 142–52.
11. Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. Lancet 2021; 397: 487–98.
12. Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus adalimumab in plaque psoriasis. N Engl J Med 2021; 385: 130–41.

13. Coates LC, McInnes IB, Merola JF, et al. Safety and efficacy of bimekizumab in patients with active psoriatic arthritis: 3-year results from a phase 2b randomized controlled trial and its openlabel extension study. Arthritis Rheumatol 2022; published online July 13. https://doi.org/10.1002/art.42280.
14. Ritchlin CT, Kavanaugh A, Merola JF, et al. Bimekizumab in patients with active psoriatic arthritis: results from a 48-week, randomised, double-blind, placebo-controlled, dose-ranging phase 2b trial. Lancet 2020; 395: 427–40.
15. Merola JF, Landewé R, McInnes IB, et al. 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). Lancet 2022; published Dec 7. https://doi.org/10.1016/S0140- 6736(22)02303-0.
16. Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006; 54: 2665–73
17. van der Heijde D, Sharp J, Wassenberg S, Gladman DD. Psoriatic arthritis imaging: a review of scoring methods. Ann Rheum Dis 2005; 64 (suppl 2): ii61–64.
18. Mease PJ, Antoni CE, Gladman DD, Taylor WJ. Psoriatic arthritis assessment tools in clinical trials. Ann Rheum Dis 2005; 64 (suppl 2): ii49–54.
19. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebocontrolled, phase 3 trial. Lancet 2015; 386: 1137–46.
20. Nash P, Mease PJ, McInnes IB, et al. Efficacy and safety of secukinumab administration by autoinjector in patients with psoriatic arthritis: results from a randomized, placebo-controlled trial (FUTURE 3). Arthritis Res Ther 2018; 20: 47.
21. Mease P, van der Heijde D, Landewé R, et al. Secukinumab improves active psoriatic arthritis symptoms and inhibits radiographic progression: primary results from the randomised, double-blind, phase III FUTURE 5 study. Ann Rheum Dis 2018; 77: 890–97.
22. Ogdie A, Michaud K, Nowak M, et al. Patient's experience of psoriatic arthritis: a conceptual model based on qualitative interviews. RMD Open 2020; 6: e001321.
23. Iwakura Y, Ishigame H, Saijo S, Nakae S. Functional specialization of interleukin-17 family members. Immunity 2011; 34: 149–62.