Psoriasis: Targets and Therapy

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REVIEW

Bimekizumab for the Treatment of Psoriasis: A Review of the Current Knowledge

Angelo Ruggiero, Luca Potestio, Elisa Camela, Gabriella Fabbrocini, Matteo Megna

Section of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, 80131, Italy

Correspondence: Angelo Ruggiero, Section of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Via Pansini 5, Napoli, 80131, Italy, Tel +39-0817462457, Fax +39-081-7462442, Email angeloruggiero1993@libero.it

Abstract: Bimekizumab, a novel humanized monoclonal IgG1 antibody that neutralizes both IL-17A and IL-17F, was recently approved the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Bimekizumab represents the latest anti IL-17 treatment available for the management of moderate to severe psoriasis. Bimekizumab safety and efficacy profiles were evaluated in four Phase III clinical trials, which evaluated bimekizumab versus placebo and ustekinumab (BE VIVID), versus placebo (BE READY), versus adalimumab (BE SURE), and versus secukinumab (BE RADIANT). Overall, bimekizumab displayed promising results in terms of both efficacy and safety, allowing reach PASI90 and PASI100 in short time (as early as week 4) and maintain it in the long term (52 weeks), with acceptable safety profile. Also, bimekizumab showed a rapid onset of response and a higher efficacy when compared to adalimumab, ustekinumab and secukinumab, with comparable safety profile. Herein, we carried out a comprehensive literature review of the available literature data about bimekizumab in the treatment of moderate to severe psoriasis.

Keywords: psoriasis, bimekizumab, IL-17, anti-IL-17, review, biologic, IL-23, IL-17A

Introduction

Psoriasis is a chronic, inflammatory skin disease, affecting up to 3% of the worldwide population.[1] Even if the exact etiology is still not fully elucidated, it appears to be multifactorial given the interaction between several exogenous and endogenous factors that justify the extremely variable clinical expression and severity.[1] Luckily, the growing advancements in understanding psoriasis pathogenesis have led to the development of target therapies that, by selectively halting pro-inflammatory cytokines [tumor necrosis factor (TNF), interleukin (IL)-17, and IL-23], have revolutionized psoriasis treatment scenario.[2] Hence, this wide therapeutic armamentarium allows achieving the goal of offering the right drug at the right moment and for the right patient.[2] Overall, the IL-17/23 immunologic pathway has shown a pivotal role in psoriasis pathogenesis.[2–6] Indeed, T-helper 17 cells, under the stimulus of IL-23, induce the release of a great amount of cytokines of the IL-17 family, resulting in psoriatic inflammation.[7] To date, research has mostly focused on the isoform A and its receptor (IL-17RA): indeed, the first is targeted by secukinumab and ixekizumab, while the latter by brodalumab.[8] Recent studies have pointed out a great structural homology (around 50%) between IL-17A and IL-17F, thus hypothesizing an overlapping mechanism of action.[8] Moreover, the two isoforms appear to cooperate with other pro-inflammatory cytokines such as IL-6, IL-8 and TNF-α, boosting inflammation.[9–11] Although IL-17F is biologically less active that the isoform A, its levels in the psoriatic plaque and serum are higher.[12–15] Hence, it has been postulated and further confirmed in preclinical models that the dual neutralization of the isoforms A and F could have a synergistic effect in the treatment of psoriasis.[8,10,11,14,15] Indeed, they share the same receptor complex (IL17RA and ILRC) through which inducing analogous inflammatory gene expression in keratinocytes.[7–15] In this context, bimekizumab, a novel humanized monoclonal IgG1antibody that neutralizes both IL-17A and IL-17F, has been recently approved the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy, at the scheduled dose of 320 mg (2 subcutaneous injections of 160 mg each) at week 0, 4, 8, 12, 16 and every 8 weeks thereafter.[16] It has received the marketing authorization in several European and non-European countries (Great Britain, Japan, Canada and Australia).[16] Moreover, bimekizumab is under investigation in clinical trials for psoriatic arthritis, ankylosing spondylitis, nonradiographic axial spondyloarthritis, and hidradenitis suppurativa.[7] The aim of the

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present narrative review is to sum up and discuss the current evidence regarding efficacy and safety profiles of bimekizumab for the treatment of moderate to severe psoriasis, as to provide an updated view and future perspectives of this new drug.

Materials and Methods

A narrative review of the English-language medical literature was performed using PubMed, Scopus, clinicaltrials.gov, Embase, and Cochrane Library databases from their inception to 31 March 2022, using Medical Subject Headings (mesh) terms (if applicable) and medical terms for the concepts of the use of bimekizumab efficacy and safety in the treatment of psoriasis. Search strategy to identify articles was performed using the following research terms: "Bimekizumab", AND "psoriasis", AND "real life", AND "real world evidence", AND "trial", AND "clinical trial", and combinations thereof. Search involved all fields including title, abstract, keywords, and full text. Clinical and epidemiological studies, review and systematic review regarding the use of bimekizumab in the treatment of psoriasis were included. Papers published from the start of time through April 2022 and from all origins were considered. Therapies and management strategies that could be categorized as traditional Chinese medicine, herbal medicine or Ayurveda/Ayurvedic medicine have been excluded. The article is based on previously conducted studies. PRISMA guidelines 2020 were used as basis for this narrative review.

Results

A total of 9 articles were retrieved. Data regarding the effectiveness and safety of bimekizumab for the treatment of psoriasis are reported in Table 1.[8,9,12,13,17–21]

Efficacy and Safety of Bimekizumab per se

The first-in human study assessing the efficacy, safety, and tolerability of bimekizumab was performed by Glatt et al on 39 subjects affected by mild and moderate psoriasis (NCT02529956).[9] Enrolled patients were randomized to a single intravenous infusion of bimekizumab at different dosage (8 mg [n = 4], 40 mg [n = 4], 160 mg [n = 6], 480 mg [n = 6] and 640 mg [n = 6]), or placebo (n = 13). Concerning efficacy, bimekizumab displayed a dose-dependent clinical improvement as shown by drastic score reduction in all the psoriasis severity indexes (lesion severity score [LSS], Psoriasis Area and Severity Index [PASI] and Physician's Global Assessment [PGA]).[9] In detail, by week 2, the highest dosage of bimekizumab (480 mg and 640 mg) provided a >80% reduction in the baseline LSS.[9] Likewise, baseline PASI and PGA reduced by >65% and >50%. A maximal magnitude of response was observed as early as 4 weeks (75–100% reduction in disease activity scores) that was maintained up to weeks 12–20, in all clinical features of plaque psoriasis.[9] As for safety, bimekizumab showed to be well tolerated across the evaluated dose range (≤640 mg).[9] Treatment-emergent adverse events (TEAEs) were common in those receiving bimekizumab and placebo (84.6% and 76.9%, respectively), and were mainly mild in severity.[9] In the first group, TEAEs included headache (n = 6, 23.1%), oropharyngeal pain (n = 5, 19.2%), nasopharyngitis (n = 4, 15.4%) and medical device (ECG) site reaction (n = 3, 11.5%).[9] No serious TEAEs were reported, apart from a case of moderately intense vomit in a patient receiving bimekizumab 40 mg that was not related to the ongoing treatment, and no one discontinued treatment for AEs.[9] Also, none of the enrolled subjects experienced meaningful changes in neutrophil count nor infusion-site reactions during the study period.[9]

The maintenance dose interval of bimekizumab was evaluated in a multicentric, prospective, randomized, phase IIa study ran by Oliver et al (NCT03025542).[17] A total of 49 patients were 2:1 randomized to receive subcutaneous bimekizumab 320 mg at week 0, 4 and placebo at week 16 [the bimekizumab plus placebo (BKZ+PBO) group (n = 32)] or bimekizumab 320 mg at week 0, 4 and 16 (the BKZ group, n = 17).[17] As regards efficacy, PASI 90 was achieved by 79.6% of all patients by week 16 (84.4% of the combination group and 70.6% of the BKZ one); anyway, such response was maintained at week 28 only in patients receiving an additional dose of bimekizumab as compared to placebo (64.7% vs 31.3%, respectively).[17] Similarly, IGA 0/1 was reached by 81.3% of the BKZ+ PBO and 64.7% of the BKZ groups at week 16, and by week 28, the first displayed a stable response, while the latter underwent a dramatic decrease to 18.8%.[17] Concerning safety, TEAEs were reported in 28 (88%) and 15 (88%) of patients in the BKZ + PBO and BKZ group, respectively, leading to treatment discontinuation only in 2 (12%) patients receiving bimekizumab at week 16.[17] Most commonly reported TEAEs were upper respiratory tract infections (18%) and nasopharyngitis (12%) in all the study population.[17] These data contributed to the identification of the appropriate interval dosage of bimekizumab, discouraging 12 weeks in favor of 8 weeks (Q8W).[17]

Table 1 Clinical Trials Reporting the Effectiveness and Safety of Bimekizumab in Moderate to Severe Psoriasis

Study	Drug and Dosage	Patients	Period	Outcomes	AE n(%)/Dis	Main AEs n (%)
NCT02529956 (phase I)	Group A: placebo sd Group B: BKZ 8mg sd Group C: BKZ 40mg sd Group D: BKZ 160mg sd Group E: BKZ 480mg sd Group F: BKZ 640mg sd	Group A: 13 Group B: 4 Group C: 4 Group D: 6 Group E: 6 Group F: 6	20 W	PASI reduction of >65% from baseline in the top two treatment groups at W 2. PASI reduction of >85% from baseline reached at week 6 in group D. PASI reduction of >94% from baseline reached at week 12 in group E and F.	Group A: 10 (76.9)/0 (0) Group B: 1 (25.0)/0 (0) Group C: 4 (100.0)/0 (0) Group D: 5 (83.3)/0 (0) Group E: 6 (100.0)/0 (0) Group F: 6 (100.0)/0 (0)	Group B-F: headache: 6 (23.1); oropharyngeal pain: 5 (19.2); nasopharyngitis: 4 (15.4), medical device (ECG) site reaction (n = 3, 11.5%).
NCT03025542 (phase IIa)	Group A: BKZ 320 mg W0, 4 and placebo at W16 Group B: BKZ 320 mg W0, 4 and 16	Group A: 32 Group B: 17	36 W	PASI 90 (W16) Group A: 84.4% Group B: 70.6% PASI 90 (W28) Group A: 31.3% Group B: 64.7% IGA 0/1 (W16) Group A: 81.3% Group B: 64.7% IGA 0/1 (W28) Group A: 64.7% Group B: 18.8%	Group A: 28 (88)/0 (0) Group B: 15 (88)/2 (12)	Group A: upper respiratory tract infection: 6 (19); urinary tract infection - hyperkalemia: 4 (13); headache: 3 (9). Group B: nasopharyngitis: 4 (24); upper respiratory tract infection –alanine aminotransferase increased - γ glutamyl transferase increased – with blood cell count decreased – neutrophil count decreased: 3 (18); viral upper respiratory tract infection – aspartate aminotransferase increased – blood cholesterol increased: 2 (12).

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Table 1 (Continued).

Study	Drug and Dosage	Patients	Period	Outcomes	AE n(%)/Dis	Main AEs n (%)
BE ABLE 1 (phase IIb)	Group A: placebo Q4W Group B: BKZ 64 mg Q4W Group C: BKZ 160mg Q4W Group D: BKZ 160mg Q4W (320 mg loading dose) Group E: BKZ 320 mg Q4W Group F: BKZ 480mg Q4W	Group A: 42 Group B: 39 Group C: 43 Group D: 40 Group E: 43 Group F: 43	12 W	PASI 90 (W12) Group A: 0 Group B: 46.2% Group C: 67.4% Group D: 75.0% Group E: 79.1% Group F: 72.1% PASI 100 (W12) Group A: 0 Group B: 28.2% Group C: 27.9% Group D: 60.0% Group E: 55.8% Group F: 48.8%	Group A: 15 (35.7)/1 (2.4) Group B: 27 (69.2)/1 (2.6) Group C: 24 (55.8)/3 (7.0) Group D: 24 (60.0)/3 (7.5) Group E: 26 (60.5)/1 (2.3) Group F: 25 (58.1)/2 (4.7)	Group A: hypertension: 3 (7.1); nasopharyngitis: 2 (4.8); upper respiratory tract infection – γ glutamyl transferase increase - respiratory tract infection – rhinitis: 1 (2.4). Group B: nasopharyngitis - upper respiratory tract infection: 5 (12.8); arthralgia - respiratory tract infection – neutropenia – rhinitis – tonsillitis – headache – leukopenia – vomiting: 2 (5.1); hypertension 1 (2.6). Group C: nasopharyngitis - γ glutamyl transferase increase: 3 (7.0); upper respiratory tract infection – rhinitis: 2 (4.7); hypertension – respiratory tract infection, rhinitis: 1 (2.3). Group D: nasopharyngitis - upper respiratory tract infection: 3 (7.5); γ glutamyl transferase increase: 2 (5.0); arthralgia – hypertension – respiratory tract infection – neutropenia – oral candidiasis: 1 (2.5). Group E: nasopharyngitis: 6 (14.0); oral candidiasis: 3 (7.0); upper respiratory tract infection – neutropenia: 2 (4.7). Group F: nasopharyngitis: 4 (9.3); arthralgia: 3 (7.0); hypertension – rhinitis – headache – leukopenia: 1 (2.3).

BE ABLE 2 (phase IIb)	Group A: BKZ 64 mg Q4W Group B: BKZ 160mg Q4W Group C: BKZ 320 mg Q4W	Group A: 15 Group B: 111 Group C: 91	From W 12 to W 60	PASI90 response was maintained in 80.0–100% of patients at W60. PASI 90 no responders in BE ABLE 1 who were treated with a higher bimekizumab dose in BE ABLE 2 showed a rapid increase in PASI 90 response rate (68.4–91.9%). IGA 0/1 from 78.2% to 100.0% in responders to bimekizumab at W60. IGA 0/1 from 62.5% to 89.2% of non-responders to bimekizumab at W60.	Group A: 10 (66.7)/0 (0) Group B: 98 (88.3)/7 (6.3) Group C: 76 (83.5)/7 (7.7)	Group A: hypertension – psoriasis – nasopharyngitis: 2 (13.3); oral candidiasis – upper respiratory tract infection: 1 (6.7). Group B: nasopharyngitis: 15 (13.5); oral candidiasis: 13 (11.7); upper respiratory tract infection: 10 (9.0). Group C: oral candidiasis: 15 (16.5) – nasopharyngitis: 11 (12.1) – upper respiratory tract infection: 9 (9.9)
BE READY (phase III)	Group A: BKZ 320 mg Q4W Group B: placebo Q4W	Group A: 349 Group B: 86	16 W	PASI 75 (W4) Group A: 265 (76%) Group B: 1 (1%) PASI 90 (W16); Group A: 317 (91%) Group B: 1 (1%) PASI 90 (W16); Group A: 238 (68%) Group B: 1 (1%)	Group A: 213 (61)/3 (1) Group B: 35 (41)/0 (0)	Group A: nasopharyngitis: 23 (7); oral candidiasis: 21 (6); upper respiratory tract infections: 14 (4). Group B: upper respiratory tract infections: 7 (8); nasopharyngitis: 4 (5).
BE READY (phase III)	Group A: BKZ 320 mg Q4W Group B: BKZ 320 mg Q8W Group C: placebo Q4W	Group A: 106 Group B: 100 Group C: 105	From W 16 to W 56	PASI 90 (W16) Group A-B:183 (89%) Group C: 17 (16%)	Group A: 78 (74)/0 () Group B: 77 (77)/2 (2) Group C: 72 (69)/3 (3)	Group A: nasopharyngitis: 11 (10); oral candidiasis: 12 (11); upper respiratory tract infections: 12 (11). Group B: nasopharyngitis: 23 (23); oral candidiasis: 9 (9); upper respiratory tract infections: 8 (8). Group C: nasopharyngitis: 20 (19); oral candidiasis: 6 (6); upper respiratory tract infections: 5 (5).

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Table 1 (Continued).

Study	Drug and Dosage	Patients	Period	Outcomes	AE n(%)/Dis	Main AEs n (%)
BE SURE (phase III)	Group A: BKZ 320 mg Q4W Group B: BKZ 320 mg Q4W up to week 16 then Q8W Group C: ADA 40 mg Q2W up to 24 weeks then BKZ 320 mg Q4W	Group A: 158 Group B: 161 Group C: 159	56 W	PASI 90 (W16) Group A – B: 86.2% Group C: 47.2%	Week 24 Group A: 112 (70.9)/3 (1.9) Group B: 116 (72.0)/6 (3.7) Group C: 111 (69.8)/5 (3.1)	Week 24 Group A: upper respiratory tract infection: 48 (30.4); oral candidiasis: 15 (9.5); diarrhea: 8 (5.1). Group B: upper respiratory tract infection: 45 (28.0); oral candidiasis: 19 (11.8); hypertension: 9 (5.6). Group C: upper respiratory tract infection: 55 (34.6); hypertension: 13 (8.2); diarrhea: 4 (2.5).
BE VIVID (phase III)	Group A: placebo Group B: BKZ 320 mg Q4W Group C: UST 45/90 mg 0.4 and Q12W	Group A: 83 Group B: 321 (395 from week 16) Group C: 163	52 W	PASI 90 (W16) Group A: 5% Group B: 85% Group C: 50% PASI 90 (W52) Group A: NA Group B: 78% Group C: 61%	Group A: NA Group B: 323 (82)/21 (5) Group C: 130 (80)/7 (4)	Group A: NA Group B: nasopharyngitis: 86 (22); oral candidiasis: 60 (15); upper respiratory tract infection 36 (9). Group C: nasopharyngitis: 36 (22); upper respiratory tract infection 18 (11); oral candidiasis: 1 (1).
BE RADIANT (phase III)	Group A: BKZ 320 mg Q4W up to week 16, then Q4W (A1) or Q8W (A2) Group B: SEC 300 mg Q1W up to week 4, then Q4W	Group A: 373 (A1:147, A2:215) Group B: 370	48 W	PASI 90 (W16) Group A: 85.5% Group B: 74.3% PASI 90 (W48) Group A: 83.6% Group B: 70.5%	Group A: 321 (86.1)/13 (3.5) Group B: 301 (81.4)/10 (2.7)	Group A: upper respiratory tract infection: 145 (38.9); oral candidiasis: 72 (19.3); urinary tract infection: 25 (6.7). Group B: upper respiratory tract infection: 154 (41.6); urinary tract infection: 22 (5.9); oral candidiasis: 11 (3.0).

Abbreviations: ADA, adalimumab; AE, Adverse Event; BKZ, bimekizumab; Dis, discontinuation; PASI, Psoriasis Area Severity Index; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; SEC, secukinumab; Sd, single dose; UST, ustekinumab; W, week.

The BE ABLE 1 was a 12-weeks, randomized, placebo-controlled, phase IIb study performed on a larger population of adult psoriasis patients in order to assess the effectiveness and safety of bimekizumab (64–480 mg) in comparison with placebo.[8] A total of 250 patients were randomized (1:1:1:1:1:1) to receive bimekizumab 64 mg, 160 mg, 160 mg (with 320 mg loading dose at baseline), 320 mg, 480 mg every 4 weeks (Q4W) or placebo.[8] Patients who previously failed an anti-IL17 were excluded. PASI90 response was reported in all bimekizumab-treatment groups compared to placebo at week 12 (46.2%–79.1%, $p < 0.0001$).[8] As regards safety, AEs were collected in 126 (61%) bimekizumab-treated patients and 15 (36%) placebo-treated subjects, leading to treatment discontinuation in 10 (4.8%) and 1 (2.4%) case, respectively.[8]

An extension of the previous study from week 12 up to week 60 was performed in the BE ABLE 2 study (48 weeks of duration).[18] The same treatment was administered to patients receiving placebo, bimekizumab 64 mg, 160 mg (with or without a 320 mg loading dose) who reached PASI 90 at week 12 in BE ABLE 1.[18] Subjects receiving bimekizumab 320 mg or 480 mg Q4W who achieved PASI 90 at week 12 in BE ABLE 1 were switched to bimekizumab 320 mg Q4W.[18] Finally, patients not achieving PASI 90 were switched to bimekizumab 160 mg or 320 mg Q4W.[18] A total of 217 patients were recruited and received bimekizumab 64 mg ($n = 15$), bimekizumab 160 mg ($n = 111$), or bimekizumab 320 mg ($n = 91$).[18] PASI90 response was maintained in 80.0–100.0% of patients at week 60 in those receiving bimekizumab.[18] Week 12 PASI 90 non-responders in BE ABLE 1 who were switched to higher bimekizumab dose in BE ABLE 2 showed a rapid increase in PASI 90 response rate (68.4–91.9%) by week 60.[18] In PASI 90 responders, IGA 0/1 responses were higher than in non-responders and also maintained through week 60, with 78.2% to 100.0% of patients across dose groups achieving "clear" or "almost clear" skin at week 60.[18] Moreover, the PASI 90 non-responders experienced a rapid increase in IGA 0/1 response rate, which was maintained up to week 60 (62.5–89.2%), and a high proportion also achieved "clear" skin by week 60 (33.3–75.7%).[18] AEs incidence was similar between patients receiving bimekizumab 160 mg (98; 88.3%) and 320 mg (76; 83.5%), and lower in patients treated with bimekizumab 64 mg (10; 66.7%).[18] The most common TEAEs, which overall were mild to moderate in severity, included were oral candidiasis (13.4%) and nasopharyngitis (12.9%).[18] In general, 6.9% ($n = 15$) of subjects reported a serious AE, of which only one was related to bimekizumab treatment (increased hepatic enzyme).[18] Treatment discontinuation was reported in 7 (6.3%) and 7 (7.7%) patients treated with bimekizumab 160 mg and 320 mg, respectively.[18]

A Phase III, multicenter, randomized, placebo-controlled trial (BE READY) evaluated the effectiveness and safety of bimekizumab in a greater number of adults with moderate to severe plaque psoriasis for at least 6 months.[19] Patients who previously failed at least one anti-IL17 were excluded from the study.[19] A total of 435 subjects were enrolled and randomized to receive bimekizumab 320 mg Q4W ($n = 349$) or placebo Q4W.[19] At week 16, those treated with bimekizumab reaching PASI90 response were re-allocated to receive bimekizumab 320 mg Q4W, bimekizumab 320 mg every 8 weeks (Q8W), or placebo up to week 56.[19] Conversely, subjects receiving placebo who achieved PASI90 response at week 16 continued to receive placebo Q4W up to week 56 and patients who did not achieve PASI90 at week 16 were included in a 12-week open-label escape group and treated with bimekizumab 320 mg Q4W ($n = 86$).[19] The effectiveness was assessed at weeks 1, 2, 4, 8, 12, 16, and Q4W up to week 52.[19] At week 16, PASI90 and PASI100 were reached by 317 (91%) and 238 (68%) patients in the bimekizumab group, respectively, while only 1 (1%) patient in the placebo group achieved PASI90 and PASI100 ($p < 0.0001$).[19] Similarly, 323 (93%) patients receiving bimekizumab achieved an IGA score of 0/1 compared with one (1%) of placebo group ($p < 0.0001$).[19] Moreover, a statistically significant improvement in Dermatology Life Quality Index (DLQI) and core psoriasis symptoms measured by psoriasis symptoms and impacts measure (P-SIM) items was reported in bimekizumab group compared with placebo ($p < 0.0001$).[19] Patients who reached PASI90 at week 16 were randomized to receive bimekizumab 320 mg Q4W, Q8W or placebo Q4W up to week 56.[19] A PASI 90 response at week 56 was reported in most of the patients re-allocated to bimekizumab 320 mg Q4W or Q8W compared with placebo ($p < 0.0001$).[19] As regards safety, AEs were reported in 213 (61%) patients receiving bimekizumab during the initial 16-week treatment period, leading to treatment discontinuation in 3 cases (1%).[19]

During the randomized withdrawal period, AEs were collected in 78 (74%) and 77 (77%) of patients treated with bimekizumab 320 mg Q4W and Q8W, respectively.[19] Of note, 10 hepatic events (mostly elevated liver enzyme) and 2 serious infections were reported in the bimekizumab treated group up to week 16.[19]

The long-term efficacy and safety of bimekizumab up to 160 weeks is under investigation in an ongoing trial, ie, the BE BRIGHT, as an extension of BE READY study.[20] Recruiting status is active and results are not available.[20]

The Efficacy and Safety of Bimekizumab in Comparison with Other Biologicals

The effectiveness and safety of bimekizumab was reported in comparison to adalimumab, ustekinumab and secukinumab.[12,13,21]

Bimekizumab was compared to adalimumab in a 56-week, Phase 3, multicenter, double-blind trial (BE SURE).[21] A total of 478 patients were enrolled and randomized to receive bimekizumab 320 mg Q4W (n = 158), bimekizumab 320 mg Q4W up to week 16 and Q8W thereafter (n = 161) or adalimumab 40 mg Q2W up to week 24 and bimekizumab 320 mg Q4W thereafter (n = 159).[21] At week 4, a statistically significant psoriasis improvement was observed in the bimekizumab cohort compared to adalimumab group, with 244 (76.5%) and 50 (31.4%) patients reaching PASI 75 ($p < 0.001$).[21] At week 16, 275 (86.2%) subjects treated with bimekizumab achieved a PASI 90 response compared with 75 (47.2%) patients of adalimumab cohort ($p < 0.001$).[21] Finally, a PASI 90 response was observed in 134 (84.8%) patients treated bimekizumab Q4W, 133 (82.6%) subjects receiving bimekizumab Q4W then Q8W and 82 (81.8%) patients switched from adalimumab to bimekizumab at week 56.[21] Regarding safety, until week 24, AEs were collected in 112 (70.9%), 116 (72.0%) and 111 (69.8%) of patients assigned to bimekizumab Q4W, Q4W and then Q8W and adalimumab, respectively.[21] Oral candidiasis and diarrhea occurred more frequently in bimekizumab patients compared with adalimumab cohort.[21]

BE RADIANT compared the efficacy and safety of bimekizumab with secukinumab in a 48-weeks, phase 3b trial.[12] A total of 743 patients were included and randomized to receive bimekizumab 320 mg Q4W (n = 373) or secukinumab 300 mg Q1W up to week 4 and Q4W thereafter (n = 370).[12] Moreover, patients in bimekizumab group were divided in 2 groups from week 16 to receive maintenance dosing Q4W or Q8W (147 and 215, respectively).[12] At week 16, a PASI 90 response was observed in 319 (85.5%) patients treated with bimekizumab compared to 275 (74.3%) receiving secukinumab.[12] At week 48, 83.6% and 70.5% of patients in bimekizumab and secukinumab cohort achieved a PASI90 response.[12] The safety was similar for both groups.[12]

Finally, a 52-week multicenter, placebo-controlled study (BE VIVID) compared the effectiveness and safety of bimekizumab 320 mg Q4W (n = 321) to ustekinumab 45 mg for patients ≤100 kg and 90 mg for patients >100 kg at week 0, 4 and Q12W thereafter (n = 163) and placebo (n = 83).[13] At week 16, patients receiving placebo were switched to bimekizumab 320 mg Q4W.[13] At week 16, the proportion of patients achieving PASI90 response in bimekizumab treated group was significantly higher than ustekinumab and placebo group (85% vs 50% vs 5%, respectively, $p < 0.0001$).[13] Similar results were reported for PASI100 and IGA response.[13] Moreover, patients receiving bimekizumab showed a rapid response compared to ustekinumab and placebo at week 4 ($p < 0.0001$).[13]

Clinical efficacy was maintained up to week 52 in bimekizumab group.[13] Moreover, PASI100 was observed in 207 (65%) of patients receiving bimekizumab at week 52, compared to 62 (38%) in ustekinumab cohort ($p < 0.0001$).[13] Finally, patients switched to bimekizumab at week 16 reported similar responses in all efficacy outcomes at week 52 to patients receiving bimekizumab since baseline.[13] As regards safety, AEs were reported in 181 (56%), 83 (51%) and 39 (47%) patients treated with bimekizumab, ustekinumab and placebo, respectively.[13] Nasopharyngitis, upper respiratory tract infection and oral candidiasis were the most common AEs reported in the bimekizumab cohort throughout the study.[13]

The Efficacy and Safety of Bimekizumab for Psoriatic Arthritis

As regards psoriatic arthritis (PsA), the first clinical trial on bimekizumab was a phase Ib randomized, double-blind, placebo-controlled clinical trial performed on 53 patients with active psoriatic arthritis who had failed conventional disease-modifying antirheumatic drugs (DMARDs) and/or one biologic DMARD.[22] Thirty-nine subjects were treated with bimekizumab while 14 with placebo.[22] Those under bimekizumab were randomized to four different treatment regimens of varying loading doses (ranging from 80 to 560 mg) and maintenance doses (from 40 to 320 mg) at weeks 0, 3 and 6 up to 20 weeks.[22] A faster and higher response was detected with bimekizumab as compared to placebo, as early as week 2 and was maintained up to the end of the study.[22] ACR20, 50 and 70 responses were the highest at week 8 (80%), week 12 (57%) and week 16 (37%).[22] Concerning safety, 90% of AEs were mild or moderate and two fungal infection easily managed with oral medications were reported.[22]

The BE ACTIVE study, a 48-week multicenter phase IIb dose-ranging trial, was conducted on adult patients with active psoriatic arthritis. Two hundred and six patients were enrolled and randomly (1:1:1:1) assigned to placebo, 16 mg

bimekizumab, 160 mg bimekizumab, 160 mg bimekizumab with a one-off 320 mg loading dose, or 320 mg bimekizumab, every 4 weeks for 12 weeks.[22] Then, at week 12, all patients under placebo and 16 mg bimekizumab groups were reassigned (1:1) to either 160 mg or 320 mg bimekizumab up to 48 weeks.[22] The primary outcome was a 50% improvement in American College of Rheumatology (ACR) response at week 12.[22] At week 12, the groups of patients under bimekizumab 16 mg, 160 mg, 160 mg (loading dose) achieved ACR50 and ACR20 with a higher percentage as compared to placebo.[22] Moreover, at the same timepoint, a statistically significant association between increasing dose (up to 160 mg) and ACR50 response was observed ($p = 0.0314$).[22] Finally, patients under bimekizumab (160 mg, 160 mg [loading dose], and 320 mg) achieved ACR20, ACR50, and ACR70 responses and PASI75 and PASI90 responses as soon as week 24 up to 48.[22] As regards safety, up to week 12 no statistically significant difference between placebo and active treatment was observed.[22] Thereafter, those under bimekizumab, regardless of its dose, reported mainly mild or moderate AEs such as nasopharyngitis and upper respiratory tract infections.[22]

An extension of the BE ACTIVE study (the BE ACTIVE2) up to week 108 was performed where all enrolled patients were administered bimekizumab 160 mg.[22] No loss of response was showed and few AEs were reported.[22]

Conclusions

Bimekizumab showed to be a safe and effective treatment option in the management of moderate to severe psoriasis and psoriatic arthritis. Indeed, the available results of clinical trials reported bimekizumab as a high effective treatment, being able to reach both PASI90 and PASI100 responses and ACR50 in a relatively short time. Furthermore, comparative studies showed the higher efficacy and a comparable safety profile of bimekizumab than other biologic classes, including anti-TNF (adalimumab), anti-IL-17 (secukinumab), and anti-IL12/23 (ustekinumab). Although the promising results showed by clinical trials, more studies are needed to confirm bimekizumab efficacy and safety also in a real-world setting. Indeed, clinical trials typically present strict inclusion and exclusion criteria which may not reflect the cohort of patients of daily clinical practice.[23] Particularly, it will be important to evaluate the efficacy of bimekizumab also in elderly patients, who frequently presents multiple comorbidities and related polypharmacotherapy,[24] in other forms than plaque psoriasis, such as erythrodermic psoriasis,[25] as well as in multifailure patients, including patients previously treated with other anti-IL-17 (which were excluded from bimekizumab registration trials).[26] Furthermore, another aspect which should be evaluated is related to eventual concerns raised in particular situations,[27,28] such as patients presenting latent tuberculosis infection (LTBI), or patients with SARS-Cov-2 infection, in which the role of biologic was highly discussed during the ongoing pandemic period.[29,30]

Hence, even if bimekizumab showed promising safety and efficacy profiles, more studies are needed to confirm its role in the management of moderate to severe psoriasis, as well as its long-term safety and effectiveness.

Abbreviations

IL, interleukin; AE, Adverse Event; PASI, Psoriasis Area Severity Index; DLQI, Dermatology Life Quality Index; P-SIM, Psoriasis symptoms and impacts measure; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks.

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Disclosure

G. Fabbrocini acted as a speaker or consultant for Abbvie, Amgen, Eli Lilly, Janssen, Leo-Pharma, Almyrall, Novartis, and UCB. M. Megna acted as a speaker or consultant for Abbvie, Eli Lilly, Janssen, Leo-Pharma, and Novartis. None of the other contributing authors have any conflict of interest, including specific financial interests of relationships and affiliation relevant to the subject matter or discussed materials in the manuscript.

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