Bimekizumab Efficacy and Safety versus Adalimumab in Patients with Moderate to Severe Plaque Psoriasis: Results from a Multicenter, Randomized, Double-Blinded Active Comparator-Controlled Phase 3 Trial (BE SURE)

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Objectives

To compare the efficacy and safety of bimekizumab versus adalimumab in patients with moderate to severe plaque psoriasis.

To assess the maintenance of efficacy of bimekizumab dosed every four weeks versus every eight weeks.

Background

- Psoriasis is the archetypal Th17-driven disease for which both interleukin (IL)-17A and IL-17F have emerged as pivotal drivers of inflammation.[1,2]
- Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A.[3,4]
- Bimekizumab led to substantial clinical improvements in patients with moderate to severe plaque psoriasis in the phase 3 studies BE VIVID and BE READY with no unexpected safety findings.[5,6]
- Here, efficacy and safety of bimekizumab were evaluated versus adalimumab in patients with moderate to severe plaque psoriasis.

Methods

- Patients in BE SURE (NCT03412747) were randomized 1:1:1 to bimekizumab 320 mg every four weeks (Q4W), bimekizumab 320 mg Q4W through Week 16 followed by bimekizumab 320 mg every eight weeks (Q8W), or adalimumab (dosed 80 mg at Week 0 and 40 mg at Week 1, then 40 mg Q2W until Week 23) followed by bimekizumab 320 mg Q4W from Week 24–56 **(Figure 1)**.
- Co-primary endpoints were 90% improvement from baseline in Psoriasis Area and Severity Index (PASI 90) and an Investigator's Global Assessment score of 0 or 1 (IGA 0/1) versus adalimumab at Week 16.
- Secondary endpoints included PASI 75 at Week 4, PASI 90 at Weeks 24 and 56, and complete skin clearance (PASI 100) at Weeks 16 and 24.
- Treatment-emergent adverse events (TEAEs) were assessed and coded according to MedDRA v19.0.
- Missing data were imputed using non-response imputation (NRI).

Results

Patient Population

- 478 patients were randomized to bimekizumab 320 mg Q4W (n=158), bimekizumab 320 mg Q4W/Q8W (n=161), and adalimumab 40 mg Q2W/bimekizumab 320 mg Q4W (n=159).
- Baseline characteristics for all randomized patients are shown in **Table 1**.

Response Rates at Weeks 4 and 16

- At Week 4, a larger proportion of patients treated with bimekizumab reached PASI 75 than those receiving adalimumab (p<0.001; **Figure 2A**).
- Both co-primary endpoints were achieved at Week 16:
  - Significantly more bimekizumab-treated patients achieved PASI 90 and IGA 0/1 than those who received adalimumab (p<0.001; **Figure 2B–C**).
- PASI 100 was achieved by significantly more patients receiving bimekizumab versus adalimumab at Week 16 (p<0.001; **Figure 2D**).

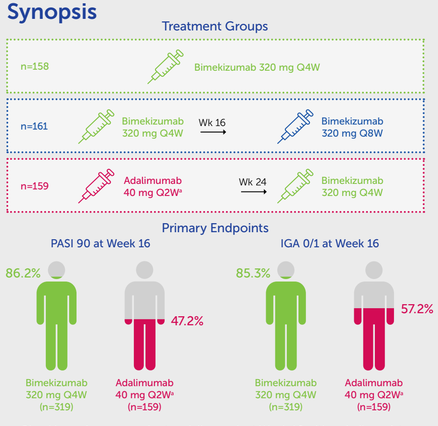
Response Rates Through Week 56

- At Week 24, PASI 90 and PASI 100 response rates remained greater in bimekizumab-treated patients compared with those receiving adalimumab, regardless of bimekizumab dosing regimen (all comparisons: p<0.001; **Figure 3**).
- After switching from adalimumab to bimekizumab at Week 24, response rates rapidly increased. By Week 56, response rates for those who switched were similar to patients initially treated with bimekizumab **(Figure 3)**.

Safety

- Proportions of TEAEs, severe TEAEs, and discontinuations due to TEAEs were similar between treatment groups **(Table 2)**.
- There were no unexpected safety findings in patients who switched from adalimumab to bimekizumab in comparison with patients who received continuous bimekizumab treatment **(Table 2)**.
- In patients receiving bimekizumab, the most common TEAEs through both Weeks 0–24 and Weeks 24–56 were nasopharyngitis, oral candidiasis, and upper respiratory tract infection **(Table 2)**.
  - The vast majority of oral candidiasis cases were localized, mild or moderate, superficial infections. There were no discontinuations due to candidiasis infection.
- One death occurred during adalimumab treatment **(Table 2)**.

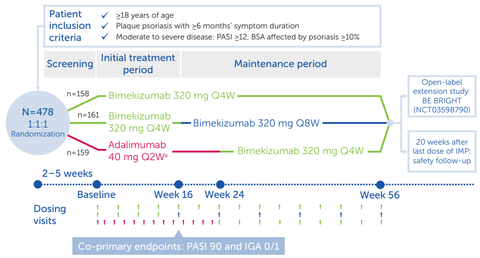
Synopsis



Bimekizumab was superior to adalimumab at Week 16 with a similar safety profile to previous studies.

[a]Adalimumab was dosed 80 mg at Week 0 and 40 mg at Week 1, then 40 mg every 2 weeks until Week 23. The first dose of bimekizumab in this group was administered at Week 24.

Figure 1 Study design



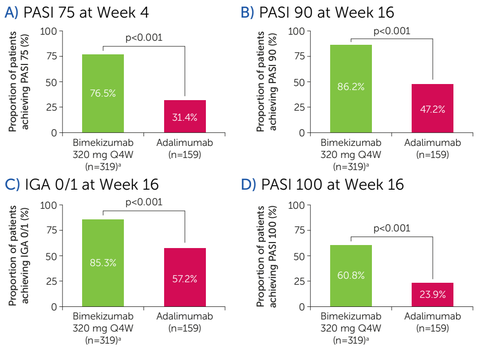
[a]Adalimumab was dosed 80 mg at Week 0 and 40 mg at Week 1, then 40 mg every 2 weeks until Week 23. The first dose of bimekizumab in this group was administered at Week 24.

Table 1 Baseline characteristics

	Bimekizumab 320 mg Q4W n=158	Bimekizumab 320 mg Q4W/Q8W n=161	Adalimumab/Bimekizumab 320 mg Q4W n=159
Age (years), mean ± SD	45.3 ± 13.2	44.0 ± 13.5	45.5 ± 14.3
Male, n (%)	102 (64.6)	112 (69.6)	114 (71.7)
Caucasian, n (%)	140 (88.6)	140 (87.0)	141 (88.7)
Weight (kg), mean ± SD	89.6 ± 21.4	93.2 ± 24.4	90.5 ± 22.1
Duration of psoriasis (years), mean ± SD	20.4 ± 13.2	17.3 ± 10.9	16.2 ± 11.9
PASI, mean ± SD	20.5 ± 6.9	19.9 ± 6.1	19.1 ± 5.9
BSA (%), mean ± SD	26.5 ± 15.9	25.2 ± 12.4	25.0 ± 14.4
IGA, n (%)			
3: moderate	102 (64.6)	111 (68.9)	114 (71.7)
4: severe	56 (35.4)	50 (31.1)	45 (28.3)
DLQI total, mean ± SD	11.1 ± 6.5	10.8 ± 6.2	10.5 ± 7.4
Any prior systemic therapy, n (%)	112 (70.9)	116 (72.0)	110 (69.2)
Prior biologic therapy, n (%)[a]	50 (31.6)	50 (31.1)	53 (33.3)
anti-TNF	14 (8.9)	10 (6.2)	14 (8.8)
anti-IL-17	33 (20.9)	37 (23.0)	35 (22.0)
anti-IL-12/23	11 (7.0)	9 (5.6)	15 (9.4)
anti-IL-23	3 (1.9)	2 (1.2)	2 (1.3)

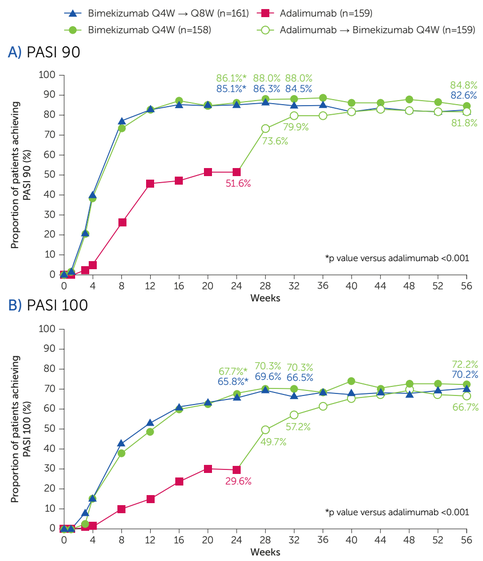
[a]Patients with multiple prior biologics use included in n (%).

Figure 2 Response rates at Weeks 4 and 16 (ITT, NRI)



[a]Data were pooled from both bimekizumab arms as all patients received the same dose regimen through Week 16 (pre-specified). p values for the comparison of treatment groups are based on the Cochran-Mantel-Haenszel test from the general association.

Figure 3 Response rates through Week 56 (ITT, NRI)



p values for the comparison of treatment groups are based on the Cochran-Mantel-Haenszel test from the general association. Data shown include all randomized patients.

Table 2 TEAEs and safety topics of interest

	Weeks 0–24[a]		Weeks 24–56[b]		
	Bimekizumab Total (n=319) n (%)[c]	Adalimumab (n=159) n (%)	Bimekizumab 320 mg Q4W (n=152) n (%)	Bimekizumab 320 mg Q8W (n=149) n (%)	Adalimumab/Bimekizumab 320 mg Q4W (n=149) n (%)
Incidence of TEAEs					
Any TEAE	228 (71.5)	111 (69.8)	101 (66.4)	104 (69.8)	111 (74.5)
Serious TEAEs	5 (1.6)	5 (3.1)	2 (1.3)	8 (5.4)	9 (6.0)
Discontinuation due to TEAEs	9 (2.8)	5 (3.1)	3 (2.0)	2 (1.3)	5 (3.4)
Drug-related TEAEs	87 (27.3)	38 (23.9)	40 (26.3)	35 (23.5)	45 (30.2)
Severe TEAEs	5 (1.6)	5 (3.1)	5 (3.3)	8 (5.4)	7 (4.7)
Deaths	0 (0.0)	1 (0.6)[d]	0 (0.0)	0 (0.0)	0 (0.0)
Common TEAEs (>5% patients[e])					
Nasopharyngitis	59 (18.5)	38 (23.9)	18 (11.8)	15 (10.1)	20 (13.4)
Oral candidiasis	34 (10.7)	0 (0.0)	20 (13.2)	13 (8.7)	26 (17.4)
Upper respiratory tract infection	19 (6.0)	15 (9.4)	8 (5.3)	11 (7.4)	9 (6.0)
Hypertension	15 (4.7)	13 (8.2)	2 (1.3)	3 (2.0)	3 (2.0)
Diarrhea	13 (4.1)	4 (2.5)	2 (1.3)	3 (2.0)	2 (1.3)
Pharyngitis	9 (2.8)	1 (0.6)	3 (2.0)	8 (5.4)	3 (2.0)
Safety topics of interest					
Inflammatory bowel disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Adjudicated SIB	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Serious hypersensitivity reaction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Adjudicated MACE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
All malignancies (inc. NMSC)	4 (1.3)	1 (0.6)	0 (0.0)	2 (1.3)	1 (0.7)
Neutropenia	2 (0.6)	4 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic events	7 (2.2)	11 (6.9)	1 (0.7)	3 (2.0)	6 (4.0)
Liver function analyses[f]	7 (2.2)	11 (6.9)	1 (0.7)	2 (1.3)	6 (4.0)
Fungal infections[g]	50 (15.7)	11 (6.9)	30 (19.7)	22 (14.8)	35 (23.5)
Candida infections	38 (11.9)	0 (0.0)	22 (14.5)	14 (9.4)	27 (18.1)
Tinea infections	11 (3.4)	1 (0.6)	2 (1.3)	6 (4.0)	1 (0.7)
Serious infections	1 (0.3)	1 (0.6)	1 (0.7)	2 (1.3)	4 (2.7)

[a]Data for Weeks 0–24 are from the full safety set; [b]Data for Weeks 24–56 include only bimekizumab-treated patients; [c]Includes all patients who received bimekizumab from Weeks 0–24, regardless of dosing regimen; [d]50 year-old male diagnosed with squamous cell carcinoma of the tongue 6 weeks after the start of adalimumab treatment, which led to a fatal outcome 5 months later; [e]Occurred in >5% of patients in any treatment group through Weeks 0–24 or 24–56; [f]The majority of liver function test elevations were transient and resolved by end of study; [g]All fungal infections not classified as *Candida* or Tinea were classified as fungal infections NEC (not elsewhere classified).

BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: score of 0 (clear) or 1 (almost clear) with ≥2-category improvement relative to baseline Investigator's Global Assessment; IL: interleukin; IMP: investigational medicinal product; ITT: intent-to-treat; MACE: major adverse cardiovascular event; NMSC: non-melanoma skin cancer; NRI: non-responder imputation; PASI 75/90/100: ≥75/90/100% improvement from baseline Psoriasis Area and Severity Index; Q2W: every 2 weeks; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; SIB: suicidal ideation and behavior; TEAE: treatment-emergent adverse event; TNF: tumor necrosis factor.

Conclusions

Results demonstrated that bimekizumab was superior to adalimumab over 16 weeks of treatment in terms of the speed, depth and durability of skin clearance in patients with moderate to severe plaque psoriasis.

Switching from adalimumab to bimekizumab resulted in rapid increases in response rates, comparable to rates in bimekizumab-randomized patients at Week 56.

No unexpected safety findings were reported in patients who switched from adalimumab to bimekizumab compared with patients who received continuous bimekizumab.

Bimekizumab 320 mg Q8W maintenance dose efficacy was comparable to bimekizumab Q4W.

The most common TEAEs were nasopharyngitis, oral candidiasis and upper respiratory tract infections. Cases of oral candidiasis were mostly mild or moderate and localized; none led to discontinuation.

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