Efficacy and Safety of Bimekizumab in Patients with Moderate to Severe Plaque Psoriasis: Results from BE VIVID, a 52-Week Phase 3, Randomized, Double-Blinded, Ustekinumab- and Placebo-Controlled Study

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Objectives

To compare the efficacy and safety of bimekizumab with ustekinumab and placebo in patients with moderate to severe plaque psoriasis treated for one year.

Background

Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. Both of these interleukins are implicated in the immunopathogenesis of psoriasis (PSO).[1–3]

Bimekizumab led to substantial clinical improvements in patients with moderate to severe plaque PSO in the phase 2 BE ABLE study, with no unexpected safety findings.[4,5]

Methods

Adult patients with moderate to severe PSO were enrolled in the pivotal phase 3 BE VIVID study (NCT03370133), a randomized, double-blinded superiority study in which patients were treated with bimekizumab, ustekinumab, or placebo **(Figure 1)**.

- The co-primary endpoints were superiority of bimekizumab versus placebo in PASI 90 and IGA 0/1 at Week 16.
- Secondary endpoints: PASI 100 at Week 16, PASI 75 at Week 4, and safety.
- Missing data were imputed with non-responder imputation (NRI).
- Treatment emergent adverse events (TEAEs) were classified using MedDRA version 19.0.

Results

Patient Population

- Baseline characteristics are shown in **Table 1**.

Efficacy

- At Week 16, the proportions of patients receiving bimekizumab who achieved PASI 90 and IGA 0/1 were significantly greater than for ustekinumab or placebo **(Figure 2)**.
- Response was rapid, with 76.9% of bimekizumab-treated patients achieving PASI 75 at Week 4, compared to 15.3% for ustekinumab and 2.4% for placebo (p<0.001 vs ustekinumab and placebo).

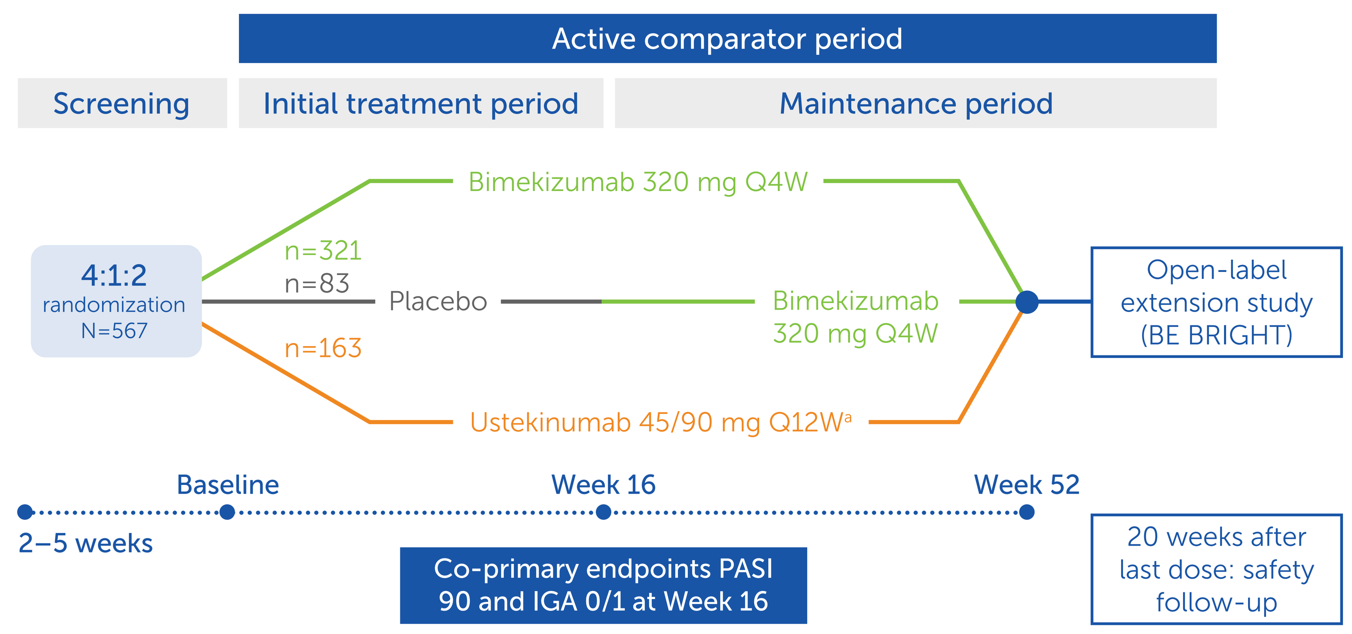
Safety

- Overall, bimekizumab was well-tolerated and discontinuation due to TEAEs was low **(Table 2)**.
- The vast majority of the oral candidiasis cases were localized, mild or moderate superficial infections, and did not lead to discontinuation **(Table 2)**.
- All incidences of major adverse cardiac events (MACE) occurred in patients with ≥2 pre-existing cardiovascular risk factors **(Table 2)**.
- Overall incidence of MACE across the bimekizumab in PSO clinical program (phase 2/phase 3/open-label extension to 01 Nov 2019) was 0.66/100 patient-years and consistent with the background risk within the PSO population and incidence for other anti-IL biologics.[6–8]

Conclusions

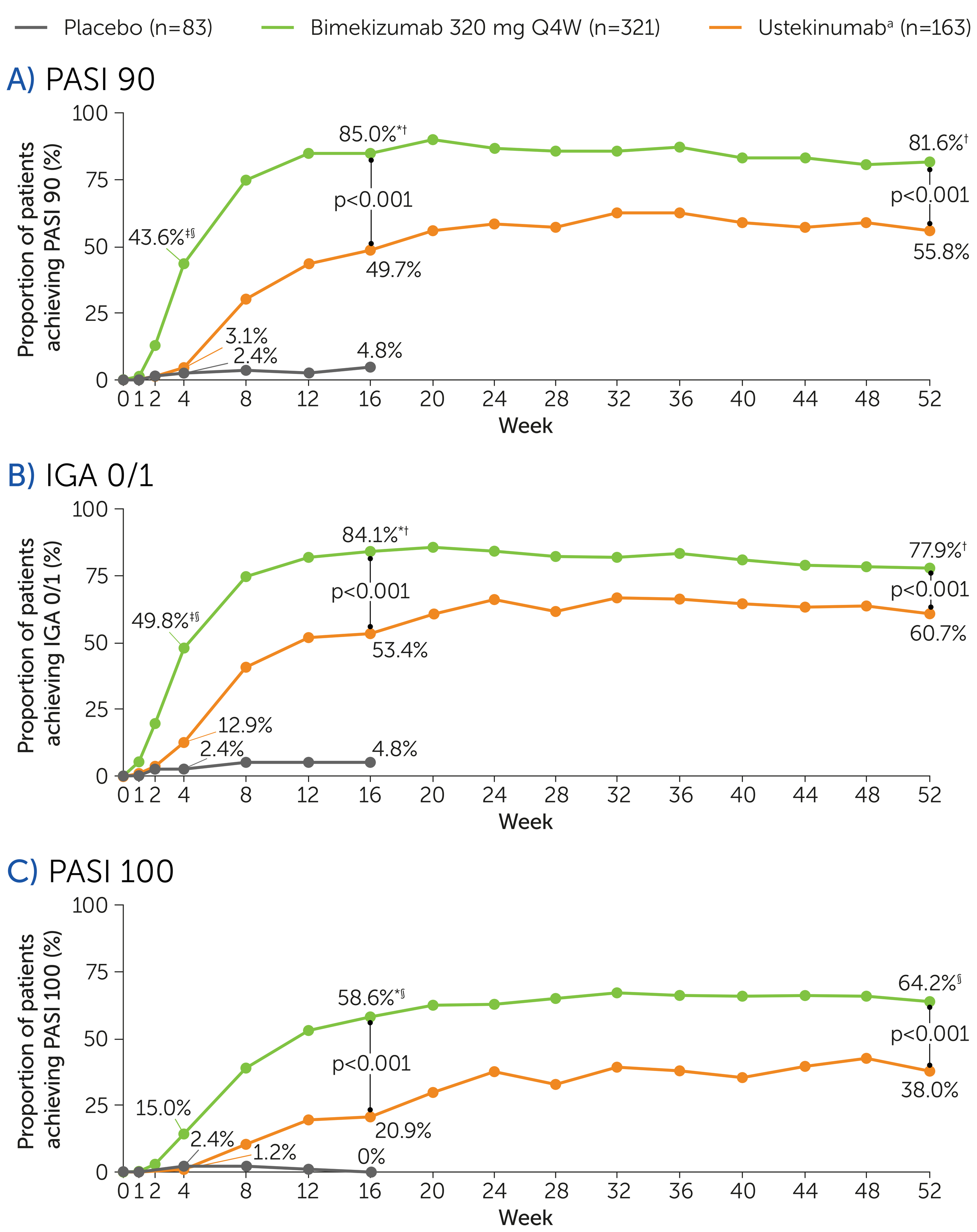
Superior PASI 90 and IGA 0/1 responses were observed with bimekizumab compared with ustekinumab at Week 16. After one dose, faster onset of response was observed with bimekizumab compared with ustekinumab. Clinical responses with bimekizumab were durable through Week 52. Bimekizumab was well-tolerated and the safety profile was consistent with previous studies.[9–12]

Figure 1 Study design



[a]Ustekinumab dosing was based on weight: patients ≤100 kg at baseline received one ustekinumab 45 mg injection and one placebo injection, patients >100 kg at baseline received two ustekinumab 45 mg injections.

Figure 2 Responder rates over 52 weeks (ITT, NRI)



[a]Ustekinumab (Q12W) dosing was based on weight: patients ≤100 kg at baseline received one ustekinumab 45 mg injection and one placebo injection, patients >100 kg at baseline received two ustekinumab 45 mg injections; *p<0.001 vs placebo; †p<0.001 vs ustekinumab; ‡nominal p<0.001 vs placebo; §nominal p<0.001 vs ustekinumab. p values for the comparison of treatment groups were based on the Cochran–Mantel–Haenszel test from the general association; nominal p values for the general association were based on a stratified Cochran–Mantel–Haenszel test where region and prior biologic exposure were used as stratification variables and were not controlled for multiplicity. At Week 16, patients receiving placebo were switched to bimekizumab 320 mg Q4W.

Table 1 Baseline characteristics

	PBO/bimekizumab 320 mg Q4W (n=83)	Bimekizumab 320 mg Q4W (n=321)	Ustekinumab[a] (n=163)
Age (years), mean ± SD	49.7 ± 13.6	45.2 ± 14.0	46.0 ± 13.6
Male, n (%)	60 (72.3)	229 (71.3)	117 (71.8)
Caucasian, n (%)	63 (75.9)	237 (73.8)	120 (73.6)
Weight (kg), mean ± SD	89.1 ± 26.4	88.7 ± 23.1	87.2 ± 21.1
Duration of PSO (years), mean ± SD	19.7 ± 13.8	16.0 ± 11.6	17.8 ± 11.6
PASI, mean ± SD	20.1 ± 6.8	22.0 ± 8.6	21.3 ± 8.3
BSA (%), mean ± SD	27.0 ± 16.3	29.0 ± 17.1	27.3 ± 16.7
IGA, n (%)[b]			
3: moderate	54 (65.1)	201 (62.6)	96 (58.9)
4: severe	28 (33.7)	119 (37.1)	66 (40.5)
DLQI total, mean ± SD	10.0 ± 6.8	9.9 ± 6.3	11.0 ± 6.9
Any prior systemic therapy, n (%)	64 (77.1)	267 (83.2)	132 (81.0)
Prior biologic therapy, n (%)	33 (39.8)	125 (38.9)	63 (38.7)
anti-TNF	16 (19.3)	51 (15.9)	24 (14.7)
anti-IL-17	18 (21.7)	76 (23.7)	38 (23.3)
anti-IL-23	5 (6.0)	16 (5.0)	6 (3.7)

[a]Ustekinumab (Q12W) dosing was based on weight: patients ≤100 kg at baseline received one ustekinumab 45 mg injection and one placebo injection, patients >100 kg at baseline received two ustekinumab 45 mg injections; [b]In each treatment group, one patient with mild IGA score was mistakenly enrolled.

Table 2 Safety

	Initial Period (Weeks 0–16)			Initial and Maintenance Periods (Weeks 0–52)	
	Placebo (n=83) n (%)	Bimekizumab 320 mg Q4W (n=321) n (%)	Ustekinumab[a] (n=163) n (%)	Bimekizumab 320 mg Q4W[b] (n=395) n (%)	Ustekinumab[a] (n=163) n (%)
Incidence of TEAEs					
Any TEAE	39 (47.0)	181 (56.4)	83 (50.9)	323 (81.8)	130 (79.8)
Serious TEAEs	2 (2.4)	5 (1.6)	5 (3.1)	24 (6.1)	12 (7.4)
Discontinuation due to TEAEs	6 (7.2)	6 (1.9)	3 (1.8)	21 (5.3)	7 (4.3)
Drug-related TEAEs	8 (9.6)	79 (24.6)	19 (11.7)	147 (37.2)	33 (20.2)
Severe TEAEs	3 (3.6)	5 (1.6)	3 (1.8)	20 (5.1)	8 (4.9)
Deaths	1 (1.2)	1 (0.3)	1 (0.6)	2 (0.5)	1 (0.6)
Common TEAEs (>5% of Patients)					
Nasopharyngitis	7 (8.4)	30 (9.3)	14 (8.6)	86 (21.8)	36 (22.1)
Oral candidiasis	0	28 (8.7)	0	60 (15.2)	1 (0.6)
Upper respiratory tract infection	2 (2.4)	9 (2.8)	5 (3.1)	36 (9.1)	18 (11.0)
Urinary tract infection	5 (6.0)	6 (1.9)	2 (1.2)	12 (3.0)	7 (4.3)
Back pain	2 (2.4)	3 (0.9)	4 (2.5)	10 (2.5)	9 (5.5)
Headache	0	11 (3.4)	7 (4.3)	16 (4.1)	9 (5.5)
Hypertension	1 (1.2)	7 (2.2)	5 (3.1)	14 (3.5)	10 (6.1)
Safety Topics of Interest					
Inflammatory bowel disease	0	1 (0.3)	0	1 (0.3)	0
Adjudicated SIB	0	0	0	1 (0.3)	1 (0.6)
Malignancies	1 (1.2)[c]	0	0	1 (0.3)[d]	1 (0.6)[e]
Neutropenia	0	2 (0.6)	0	4 (1.0)	1 (0.6)
Hypersensitivity reactions[f]	0	16 (5.0)	10 (6.1)	47 (11.9)	15 (9.2)
Adjudicated MACE	0	1 (0.3)	0	5 (1.3)	0
Acute myocardial infarction	0	0	0	1 (0.3)	0
Cardiac arrest	0	1 (0.3)	0	1 (0.3)	0
Myocardial infarction	0	0	0	2 (0.5)	0
Cerebral infarction	0	0	0	1 (0.3)	0
Hepatic events	1 (1.2)	4 (1.2)	0	10 (2.5)	4 (2.5)
Liver function analyses[g]	1 (1.2)	4 (1.2)	0	8 (2.0)	4 (2.5)
Fungal infections[h,i]	0	45 (14.0)	1 (0.6)	92 (23.3)	4 (2.5)
Candida infections	0	33 (10.3)	0	72 (18.2)	1 (0.6)
Tinea infections	0	5 (1.6)	0	11 (2.8)	1 (0.6)

[a]Ustekinumab (Q12W) dosing was based on weight: patients ≤100 kg at baseline received one ustekinumab 45 mg injection and one placebo injection, patients >100 kg at baseline received two ustekinumab 45 mg injections; [b]Includes patients switching from placebo to bimekizumab 320 mg Q4W at Week 16; only events occurring after switching are included in this column; [c]One esophageal adenocarcinoma; [d]One gastric cancer; [e]One basal cell carcinoma; [f]Hypersensitivity reactions were predominantly cutaneous and subcutaneous, with no cases of anaphylaxis in any treatment group; [g]Incidence of LFT elevations among bimekizumab-treated patients was generally low and comparable to placebo and ustekinumab; [h]All fungal infections not classified as *Candida* or *Tinea* were classified as fungal infections NEC; [i]In addition, all opportunistic infections were localized mucocutaneous fungal infections defined as opportunistic by convention; there were no systemic opportunistic infections or cases of active tuberculosis reported.

BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA 0/1: score of 0 (clear) or 1 (almost clear) with ≥2-category improvement relative to Baseline in Investigator's Global Assessment, scored on a 5-point scale; IL: interleukin; ITT: intent-to-treat; LFT: liver function test; MACE: major adverse cardiac events; NEC: not elsewhere classified; NRI: non-responder imputation; PASI: Psoriasis Area Severity Index; PSO: psoriasis; Q4W: every 4 weeks; Q12W: every 12 weeks; SD: standard deviation; SIB: suicide-ideation behaviours; TEAEs: treatment emergent adverse events; TNF: tumor necrosis factor.

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