Efficacy and Safety of Bimekizumab in Patients with Moderate to Severe Plaque Psoriasis: Results from BE READY, a 56-Week Phase 3, Randomized, Double-Blinded, Placebo-Controlled Study with Randomized Withdrawal

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Objectives

To compare the efficacy and safety of bimekizumab with placebo over 16 weeks in patients with plaque psoriasis, and evaluate the effect of randomized treatment withdrawal, compared with continued treatment, in Week 16 responders.

Background

Bimekizumab is a monoclonal IgG1 antibody that has been rationally designed to selectively inhibit IL-17F in addition to IL-17A.[1,2] Both of these interleukins are implicated in the immunopathogenesis of plaque psoriasis (PSO).[3]

Bimekizumab led to substantial clinical improvements in patients with moderate to severe PSO in the phase 2 BE ABLE study (NCT02905006, NCT03010527), with no unexpected safety findings.[4,5]

Methods

Adult patients with moderate to severe PSO were enrolled in the pivotal phase 3 BE READY study (NCT03410992), which incorporated a 16-week randomized, double-blinded, placebo-controlled period followed by a 40-week randomized withdrawal period **(Figure 1)**.

- The co-primary endpoints were a 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) at Week 16. Secondary endpoints included PASI 100 at Week 16 and PASI 75 at Week 4. Other endpoints included PASI 75, PASI 90, and PASI 100 at other timepoints.
- 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

- Co-primary endpoints of PASI 90 and IGA 0/1 at Week 16 were achieved by 90.8% and 92.6% of bimekizumab-treated patients, respectively, compared with 1.2% and 1.2% in the placebo group, respectively (p<0.001 for both).
- Response was rapid, with over 75% of bimekizumab-treated patients achieving PASI 75 at Week 4, after just one dose **(Figure 2)**.
- PASI 90 response was well-maintained in patients re-randomized to bimekizumab, regardless of dosing schedule **(Figure 3)**.
- Among patients re-randomized to placebo, loss of response was slow; median time to relapse (loss of PASI 75 response following re-randomization was ~28 weeks (~32 weeks from last bimekizumab dose).

Safety

- Overall, bimekizumab was well-tolerated; discontinuation due to TEAEs was low, and there were no deaths in the study **(Table 2)**.
- All cases of oral candidiasis were localized, mild, or moderate superficial infections, and no cases led to discontinuation **(Table 2)**. The most common TEAEs with bimekizumab were nasopharyngitis, oral candidiasis, and upper respiratory tract infection.

Synopsis

Objective

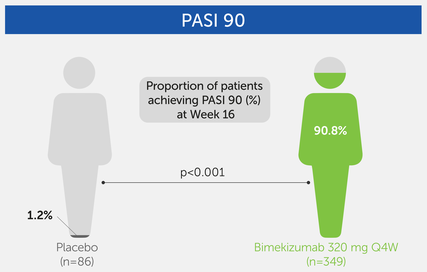
To compare the efficacy and safety of bimekizumab with placebo in patients with moderate to severe plaque psoriasis

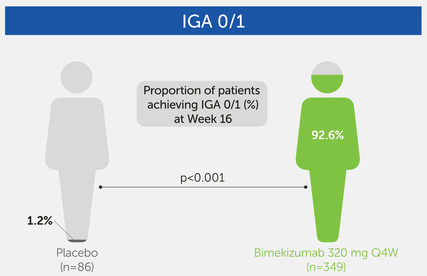
Methods

Patients were randomized 4:1 to receive bimekizumab every four weeks or placebo for an initial 16 weeks of treatment

Results

BE READY met both of its co-primary endpoints at Week 16, with significantly higher PASI 90 and IGA 0/1 responder rates vs placebo



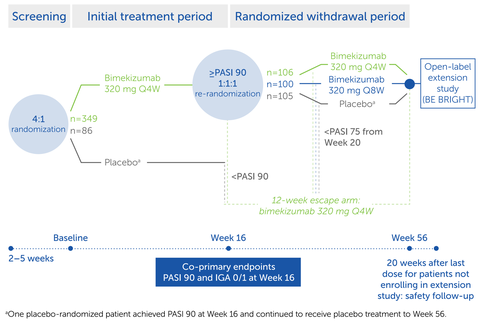


Conclusion

High levels of skin clearance were observed with bimekizumab at Week 16

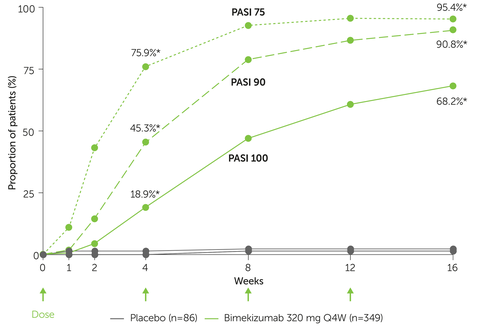
Bimekizumab was well-tolerated and the safety profile was consistent with previous studies

Figure 1 Study design



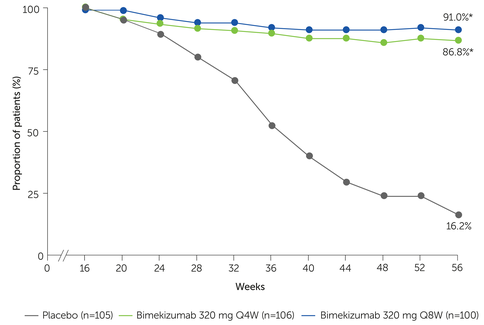
[a]One placebo-randomized patient achieved PASI 90 at Week 16 and continued to receive placebo treatment to Week 56.

Figure 2 PASI 75, PASI 90, and PASI 100 over 16 weeks (ITT, NRI)



*p<0.001 versus placebo. For PASI 75 at Week 4, and PASI 90/PASI 100 at Week 16, p values for the comparison of treatment groups were based on the Cochran–Mantel–Haenszel test from the general association; for other comparisons, p values for a general association were based on a stratified Cochran–Mantel–Haenszel test, where region and prior biologic exposure were used as stratification variables, are considered nominal, and were not controlled for multiplicity. Placebo responder rates at Week 4: PASI 75=1.2%, PASI 90=0%, PASI 100=0%; Placebo responder rates at Week 16: PASI 75=2.3%, PASI 90=1.2%, PASI 100=1.2%.

Figure 3 PASI 90 in maintenance and withdrawal arms (Week 16 PASI 90 responders, NRI)



*nominal p<0.001 versus placebo. p values for the comparison of treatment groups were based on stratified Cochran–Mantel–Haenszel test, where region and prior biologic exposure were used as stratification variables. Patients randomized to bimekizumab 320 mg Q4W who achieved PASI 90 at Week 16 were re-randomized for maintenance treatment; for patients re-randomized to placebo, the last dose of bimekizumab was at Week 12.

Table 1 Baseline characteristics

	Placebo n=86	Bimekizumab 320 mg Q4W n=349	All patients N=435
Age (years), mean ± SD	43.5 ± 13.1	44.5 ± 12.9	44.3 ± 12.9
Male, n (%)	58 (67.4)	255 (73.1)	313 (72.0)
Caucasian, n (%)	79 (91.9)	324 (92.8)	403 (92.6)
Weight (kg), mean ± SD	91.7 ± 22.2	88.7 ± 20.6	89.3 ± 20.9
Duration of PSO (years), mean ± SD	19.1 ± 12.8	19.6 ± 13.3	19.5 ± 13.2
PASI, mean ± SD	20.1 ± 7.6	20.4 ± 7.6	20.3 ± 7.6
BSA (%), mean ± SD	24.4 ± 16.0	24.6 ± 15.2	24.5 ± 15.4
IGA, n (%)			
3: moderate	62 (72.1)	242 (69.3)	304 (69.9)
4: severe	24 (27.9)	107 (30.7)	131 (30.1)
DLQI total, mean ± SD	11.3 ± 6.9	10.4 ± 6.3	10.6 ± 6.4
Any prior systemic therapy, n (%)	71 (82.6)	276 (79.1)	347 (79.8)
Prior biologic therapy, n (%)	37 (43.0)	154 (44.1)	191 (43.9)
anti-TNF	12 (14.0)	62 (17.8)	74 (17.0)
anti-IL-17	18 (20.9)	85 (24.4)	103 (23.7)
anti-IL-23	5 (5.8)	28 (8.0)	33 (7.6)
anti-IL-12/23	11 (12.8)	40 (11.5)	51 (11.7)

Table 2 Safety

	Initial period (Weeks 0–16)		Randomized withdrawal period (Weeks 16–56)		
			Bimekizumab 320 mg Q4W		
	Placebo (n=86) n (%)	Bimekizumab 320 mg Q4W (n=349) n (%)	Placebo (n=105) n (%)	Bimekizumab 320 mg Q8W (n=100) n (%)	Bimekizumab 320 mg Q4W (n=106) n (%)
Incidence of TEAEs					
Any TEAE	35 (40.7)	213 (61.0)	72 (68.6)	77 (77.0)	78 (73.6)
Serious TEAEs	2 (2.3)	6 (1.7)	4 (3.8)	3 (3.0)	5 (4.7)
Discontinuation due to TEAEs	1 (1.2)	4 (1.1)	3 (2.9)	2 (2.0)	0
Drug-related TEAEs	7 (8.1)	65 (18.6)	23 (21.9)	23 (23.0)	28 (26.4)
Severe TEAEs	1 (1.2)	3 (0.9)	4 (3.8)	1 (1.0)	4 (3.8)
Deaths	0	0	0	0	0
Common TEAEs (>5% of Patients)					
Nasopharyngitis	4 (4.7)	23 (6.6)	20 (19.0)	23 (23.0)	11 (10.4)
Oral candidiasis	0	21 (6.0)	6 (5.7)	9 (9.0)	12 (11.3)
Upper respiratory tract infection	7 (8.1)	14 (4.0)	5 (4.8)	8 (8.0)	12 (11.3)
TEAEs of Interest					
Inflammatory bowel disease	0	0	0	0	0
Adjudicated SIB	0	0	0	0	0
Malignancies	0	1 (0.3)[a]	1 (1.0)[b]	0	0
Neutropenia	0	3 (0.9)	0	1 (1.0)	0
Hypersensitivity reactions[c]	1 (1.2)	12 (3.4)	3 (2.9)	2 (2.0)	3 (2.8)
Adjudicated MACE	0	0	0	1 (1.0)[d]	0
Hepatic events	1 (1.2)	10 (2.9)	0	3 (3.0)	8 (7.5)
Liver function analyses[e]	1 (1.2)	9 (2.6)	0	2 (2.0)	8 (7.5)
Fungal infections[f,g]	2 (2.3)	40 (11.5)	7 (6.7)	14 (14.0)	22 (20.8)
Candida infections	0	27 (7.7)	6 (5.7)	10 (10.0)	16 (15.1)
Tinea infections	0	9 (2.6)	0	1 (1.0)	4 (3.8)

[a]One case of basal cell carcinoma; [b]One case of prostate cancer; [c]Hypersensitivity reactions were predominantly cutaneous, with no cases of acute anaphylaxis in any treatment group; [d]A non-fatal myocardial infarction in a 53-year old male with 6 pre-existing cardiovascular risk factors, which was not attributed to the study drug; [e]In the initial treatment period, incidence of LFT elevations with bimekizumab was generally low and comparable to placebo, majority of LFT elevations were transient and resolved by end of study; [f]All fungal infections not classified as Candida or Tinea were classified as fungal infections NEC; [g]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.

Conclusions

High levels of skin clearance were observed with bimekizumab after one dose and at Week 16, compared with placebo. Clinical responses were durable through 56 weeks, regardless of bimekizumab dosing schedule. Bimekizumab was well-tolerated and the safety profile was consistent with previous studies.[4–7]

BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator's Global Assessment; IL: interleukin; ITT: intent-to-treat; LFT: liver function test; MACE: major adverse cardiovascular event; NEC: not elsewhere classified; NRI: non-responder imputation; PASI 75/90/100: ≥75/90/100% improvement from baseline in Psoriasis Area and Severity Index; PSO: psoriasis; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; SIB: suicidal-ideation behavior ; TEAE: treatment emergent adverse event; TNF: tumor necrosis factor.

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