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

K. Gordon,[1] P. Foley,[2] J.G. Krueger,[3] A. Pinter,[4] K. Reich,[5] R. Vender,[6] V. Vanvoorden,[7] C. Madden,[8] L. Peterson,[8] A. Blauvelt[9]

SDDS Virtual Experience 2020 | September 11–13, 2020

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 psoriasis (PSO).[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 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 PASI 90 and IGA 0/1 at Week 16.
- Secondary endpoints included PASI 100 at Week 16, 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).

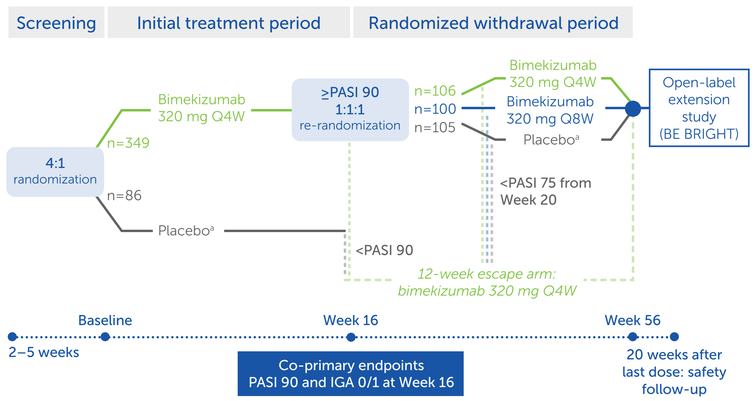
Safety

- 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.

Conclusions

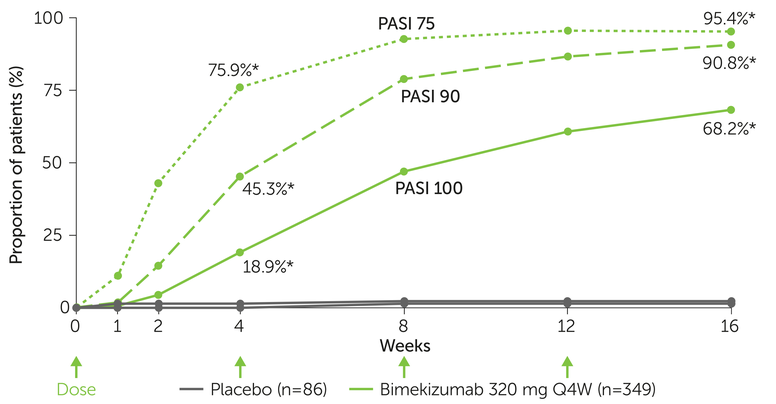
High levels of skin clearance were observed with bimekizumab after one dose and at Week 16 compared with placebo. Clinical responses were durable through 56 weeks, regardless of bimekizumab dosing schedule. Bimekizumab was well-tolerated and the safety profile was consistent with previous studies.[6–9]

Figure 1 Study design



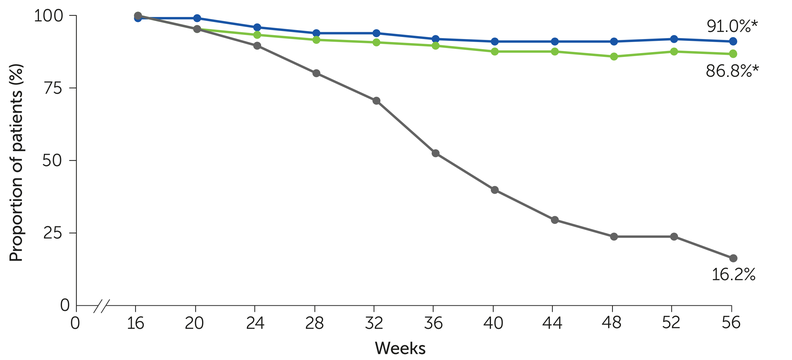
[a]One placebo-randomized patient achieved PASI 90 at Week 16 and continued to receive placebo treatment to Week 56.

Figure 2 PASI 75, PASI 90, and PASI 100 over 16 weeks



*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 BKZ 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.

BKZ: bimekizumab; BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator's Global Assessment; IL: interleukin; 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; PBO: placebo; 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.

Institutions: [1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]Skin Health Institute, Carlton, Victoria, Australia; [3]The Rockefeller University, New York, NY, USA; [4]University Hospital Frankfurt am Main, Department of Dermatology, Frankfurt am Main, Germany; [5]Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf and *Skin*flammation® Center, Hamburg, Germany; [6]Division of Dermatology, McMaster University, Hamilton, Ontario, Canada; [7]UCB Pharma, Brussels, Belgium; [8]UCB Pharma, Raleigh, NC, USA; [9]Oregon Medical Research Center, Portland, OR, USA.

References: [1]Durham L. Curr Rheumatol Reports 2015;17:55; [2]Fujishima S. Arch Dermatol Res 2010;302:499–505; [3]Johnston A. *et al.* J Immunol 2013;190:2252–62; [4]Papp K. *et al.* JAAD 2018;79:277–86, NCT02905006; [5]Blauvelt A. *et al.* AAD 2019 (OP11180), NCT03010527; [6]Glatt S. *et al.* Br J Clin Pharm 2017;83(5):991i1001; [7]Glatt S. *et al.* Ann Rheum Dis 2018;77:523–32; [8]Papp K. *et al.* J Am Acad Dermatol 2018;79(2)277–2864; [9]Blauvelt A. *et al.* AAD 2019 (OP11180). **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **KG**, **PF**, **JGK**, **AP**, **KR**, **RV**, **VV**, **CM**, **LP**, **AB**; Drafting of the publication, or revising it critically for important intellectual content: **KG**, **PF**, **JGK**, **AP**, **KR**, **RV**, **VV**, **CM**, **LP**, **AB**; Final approval of the publication: **KG**, **PF**, **JGK**, **AP**, **KR**, **RV**, **VV**, **CM**, **LP**, **AB**. **Author Disclosures: KG:** Honoraria and/or research support from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira Inc., Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma. **PF:** Received grant support from AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sun Pharma, and Sanofi; served as an Investigator for AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira Inc., Eli Lilly, Galderma, Genentech, Geneseq, GSK, Hexima, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma, and Valeant; served on the advisory board of AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galderma, Janssen, LEO Pharma, Mayne Pharma, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Valeant; served as a consultant for Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma, and Wintermute; received travel grants from AbbVie, Eli Lilly, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, and Sanofi; served as a speaker for or received honoraria from AbbVie, Celgene, Eli Lilly, Galderma, Janssen, LEO Pharma, Merck, Novartis, Pfizer, and Roche. **JGK:** Grants paid to institution from AbbVie, Akros, Allergan, Amgen, Avillion, Biogen MA, Boehringer Ingelheim, Botanix, Bristol-Myers Squibb, Celgene, Eli Lilly, Exicure, Incyte, Innovaderm, Janssen, LEO Pharma, Novan, Novartis, Paraxel, Pfizer, Regeneron, Sienna, UCB Pharma, and Vitae; personal fees from AbbVie, Allergan, Almirall, Amgen, Arena, Aristea, Asana, Aurigne, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Escalier, LEO Pharma, Nimbus, Novartis, Menlo, Sanofi, Sienna, Sun Pharma, Pfizer, UCB Pharma, and Valeant. **AP:** Worked as an investigator and/or speaker and/or advisor for AbbVie, Almirall Hermal, Amgen, Biogen, Boehringer Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Hexal, Janssen, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Schering-Plough, and UCB Pharma. **KR:** Served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Affibody, Almirall, Amgen, Avillion, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Covagen, Dermira Inc., Eli Lilly, Forward Pharma, Fresenius Medical Care, Galapagos, GSK, Janssen-Cilag, Kyowa Kirin, LEO Pharma, Medac, Merck Sharp & Dohme, Miltenyi Biotec, Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Sun Pharma, Takeda, UCB Pharma, Valeant, and Xenoport. **RV:** Consultant, and/or scientific advisor, and/or investigator, and/or speaker for Amgen, AbbVie, Astellas, Bausch Health/Valeant, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Dermira Inc., Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck, Sharp & Dohme, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, and UCB Pharma. **VV, CM, LP:** Employees of UCB Pharma. **AB:** Served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira Inc., Eli Lilly, Forte, Galderma, Janssen, LEO Pharma, Novartis, Ortho, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma; paid speaker for AbbVie. **Acknowledgements:** This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Susanne Wiegratz and Eva Cullen for publication coordination and critical review and Joe Dixon, PhD, Costello Medical, Cambridge, UK, for medical writing and editorial assistance. All costs associated with development of this poster were funded by UCB Pharma.

Previously presented at AAD 2020