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

K. Reich,[1] K.A. Papp,[2] A. Blauvelt,[3] R. Langley,[4] A. Armstrong,[5] R.B. Warren,[6] K. Gordon,[7] J.F. Merola,[8] C. Madden,[9] M. Wang,[9] V. Vanvoorden,[10] M. Lebwohl[11]

Presented at Fall Clinical Dermatology Conference 2020 | October 29–November 1 | Las Vegas, NV

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.[1–3]

Bimekizumab led to substantial clinical improvements in patients with moderate to severe plaque psoriasis (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 90% improvements from baseline in Psoriasis Area and Severity Index (PASI 90) and an Investigator's Global Assessment score of 0 or 1 (IGA 0/1).
- 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 Nov 1, 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]

Synopsis

Objective

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

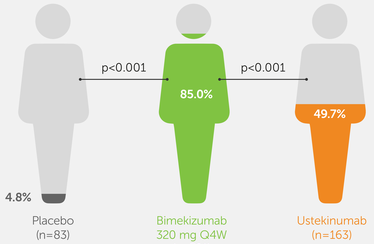
Methods

Patients were randomized 4:1:2 to receive bimekizumab every four weeks, placebo or ustekinumab

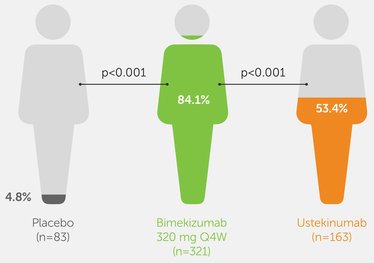
Results

BE VIVID met both of its co-primary endpoints at Week 16, with significantly higher PASI 90 and IGA 0/1 responder rates vs placebo; superiority vs ustekinumab was also demonstrated

Week 16 PASI 90 Proportion of patients achieving PASI 90 (%)



Week 16 IGA 0/1 Proportion of patients achieving IGA 0/1 (%)

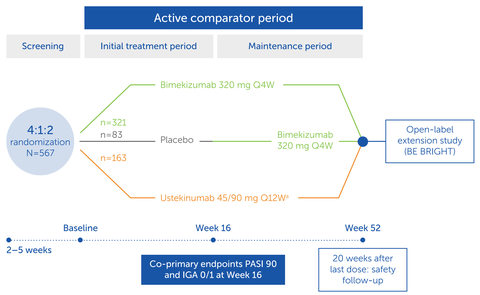


A rapid response was observed, with over 75% of bimekizumab-treated patients achieving PASI 75 at Week 4, after only one dose

Conclusion

Bimekizumab was superior to ustekinumab and placebo in PASI 90 and IGA 0/1 at Week 16, and was generally well tolerated with a safety profile consistent with phase 2 studies

Figure 1 Study design



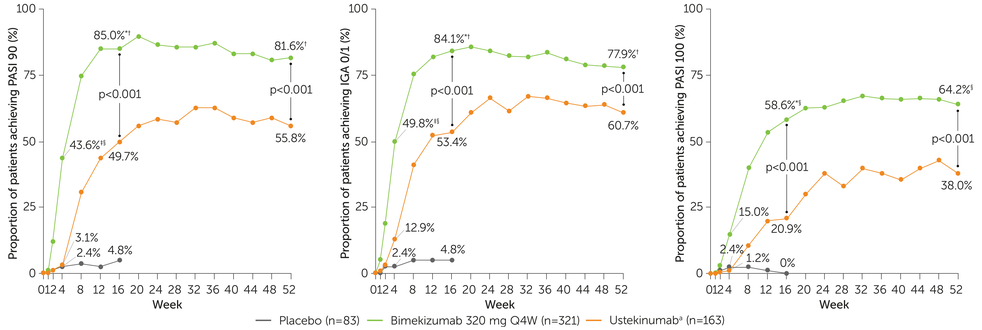
[a]Ustekinumab dosing was based on weight: patients ≤100 kg at baseline received one ustekinumab 45 mg injection and one placebo injection, patients >100 kg at baseline received two ustekinumab 45 mg injections.

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.

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 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.

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 behaviors; TEAEs: treatmentemergent adverse events; TNF: tumor necrosis factor.

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]	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.

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.[4,5,9,10]

Author Affiliations: [1]Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf and Skinflammation® Center, Hamburg, Germany; [2]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [3]Oregon Medical Research Center, Portland, OR, USA; [4]Dalhousie University, Halifax, NS, Canada; [5]Keck School of Medicine of USC, Dermatology, Los Angeles, CA, USA; [6]The Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, University of Manchester, Manchester, UK; [7]Medical College of Wisconsin, Milwaukee, WI, USA; [8]Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; [9]UCB Pharma, Raleigh, NC, USA; [10]UCB Pharma, Brussels, Belgium; [11]Icahn School of Medicine, New York, NY, USA.

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NCT03010527; [6]FDA Briefing Document, Dermatologic and Opthalmic Drugs Advisory Committee, July 19 2016; [7]Kerkhof PC. *et al.* JAAD 2016; 75:83–98; [8]Australian Public Report for Ixekizumab, May 2017; [9]Glatt S. *et al.* Br J Clin Pharm 2017;83(5):991–1001; [10]Glatt S. *et al.* Ann Rheum Dis 2018;77:523–32. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **KR, KAP, AB, RL, AA, RBW, KG, JFM, CM, MW, VV, ML.** Drafting of the publication, or revising it critically for important intellectual content: **KR, KAP, AB, RL, AA, RBW, KG, JFM, CM, MW, VV, ML.** Final approval of the publication: **KR, KAP, AB, RL, AA, RBW, KG, JFM, CM, MW, VV, ML.** **Author Disclosures: 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, GlaxoSmithKline, 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. **KAP:** Honoraria and/or grants from AbbVie, Akros, Amgen, Arcutis, Astellas, Baxalta,Boehringer Ingelheim, Bristol-Myers Squibb, Canfite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Gilead, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, LEO Pharma, MedImmune, Merck Sharp & Dohme, Merck-Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi Aventis/Genzyme, Sun Pharma, Takeda, UCB Pharma, and Valeant/Bausch Health; Consultant (no compensation) for AstraZeneca and Meiji Seika 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, and as a paid speaker for AbbVie. **RL:** Honoraria from AbbVie, Amgen, Centocor, Pfizer, Janssen Pharmaceuticals, LEO Pharma, Boehringer Ingelheim, Eli Lilly, and Valeant Pharmaceuticals for serving as an advisory board member, principal investigator, and speaker. **AA:** Research investigator and/or consultant for AbbVie, Bristol-Myers-Squibb, Dermavant, Dermira Inc., Eli Lilly, Janssen, LEO Pharma, KHK, Modernizing Medicine, Novartis, Ortho Dermatologics, Regeneron, Sanofi, Sun Pharma, and UCB Pharma. **RBW:** Research grants and/or consulting fees from AbbVie, Almirall, Amgen, Arena, Avillion, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma. **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. **JFM:** Consultant and/or investigator for AbbVie, Aclaris, Almirall, Amgen, Biogen, Celgene, Dermavant, Eli Lilly, GlaxoSmithKline, Incyte, Kiniksa, Janssen, Mallinckrodt, Merck, Momenta, Novartis, Pfizer, Samumed, Sanofi Regeneron, Science 37, Sun Pharma, and UCB Pharma; Speaker's bureau for AbbVie. **CM, MW, VV:** Employees of UCB Pharma. **ML:** Employee of Mount Sinai which receives research funds from: AbbVie, Amgen, Arcutis, AstraZeneca, Boehringer Ingelheim, Celgene, Clinuvel, Eli Lilly, Incyte, Janssen Research & Development, LLC, Kadmon Corp., LLC, LEO Pharma, MedImmune, Novartis, Ortho Dermatologics, Pfizer, Sciderm, UCB Pharma, Inc., and VIDac. Consultant for Allergan, Almirall, Arcutis, Inc., Avotres Therapeutics, BirchBioMed Inc., Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Evelo, Foundation for Research and Education in Dermatology, Inozyme Pharma, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi, Neuroderm, Pfizer, Promius/Dr. Reddy's Laboratories, Theravance, and Verrica. **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, MSc, UCB Pharma, Monheim am Rhein, Germany and Eva Cullen, PhD, UCB Pharma, Brussels, Belgium for publication coordination and critical review, Daniel Smith, BA (Hons), Costello Medical, Cambridge, UK, for medical writing and editorial assistance, and the Costello Medical Design Team for design support. All costs associated with development of this poster were funded by UCB Pharma in accordance with the Good Publication Practice (GPP3) guidelines.

Previously presented at AAD 2020