Bimekizumab versus secukinumab continuous maintenance of response at every visit through one year in patients with moderate to severe plaque psoriasis: Post-hoc results from the BE RADIANT phase 3b trial

R.B. Warren,[1] C. Conrad,[2] P. Foley,[3] L. Iversen,[4] R.G. Langley,[5] G. Kokolakis,[6] L. Davis,[7] V. Vanvoorden,[8] S. Wiegratz,[9] J.F. Merola[10]

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Objective

To assess the continual maintenance of Week 16 responses with bimekizumab (BKZ) versus secukinumab (SEC) treatment at every visit to Week 48 in patients with moderate to severe plaque psoriasis.

Introduction

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, whilst SEC is a widely used monoclonal IgG1 antibody that targets IL-17A.[1]
- BE RADIANT (NCT03536884) was the first phase 3 study to compare inhibition of IL-17A and IL-17F with inhibition of IL-17A alone.
- Patient surveys have confirmed that maintaining a long-lasting response is a key treatment goal for patients who have already achieved skin clearance.[2,3]

Materials and Methods

- BE RADIANT is a phase 3b, randomized trial, consisting of a 48-week double-blinded, active comparator-controlled period followed by an ongoing open-label extension (**Figure 1**).[4] Patients who did not enter the open-label extension entered a safety follow-up period.
- This analysis includes patients who achieved a Psoriasis Area and Severity Index (PASI) of ≤2 (a key treat-to-target objective)[5] or 0 (complete skin clearance) at Week 16 and continued to receive study medication at Week 16 or later, reported with BKZ dose groups pooled.
- We report the proportion of responders who continued to achieve their response at every study visit up to and including Week 48, as well as PASI=0 responders who maintained PASI ≤1 or PASI ≤2.
- Missing data are primarily accounted for using modified non-responder imputation (mNRI), whereby patients with missing data at a given week following discontinuation due to lack of efficacy or due to an adverse event were considered non-responders at subsequent visits; all other missing data were imputed using multiple imputation methodology.
- Supporting analyses are also reported:
  - Observed case (OC): missing data is discounted in the consideration of continuous maintenance of response.
  - NRI: patients with missing data at a given week are considered non-responders from that timepoint onwards.

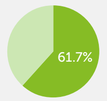
Results

- At baseline, 373 patients were randomized to BKZ, and 370 were randomized to SEC.
- At Week 16, 230/373 (61.7%) BKZ-randomized and 181/370 (48.9%) SEC-randomized patients achieved PASI=0, whilst 318/373 (85.3%) BKZ-randomized and 283/370 (76.5%) SEC-randomized patients achieved PASI ≤2.
- Baseline demographics and characteristics were largely consistent across both randomization arms for PASI=0 and PASI ≤2 responders, although the overall population of BKZ-randomized patients, as well as Week 16 PASI=0 and PASI ≤2 responders, had higher baseline disease severity as measured via the Investigators Global Assessment (IGA) compared with SEC-randomized patients (**Table 1**).
- PASI=0 was continuously maintained through Week 48 by 63.7% BKZ-treated and 54.3% SEC-treated Week 16 responders (**Table 2**).
  - Among Week 16 PASI=0 responders, PASI ≤2 was continuously maintained at each study visit through Weeks 16–48 by 93.0% of BKZ-treated and 87.4% of SEC-treated patients.
- PASI ≤2 was continuously maintained at each study visit through Weeks 16–48 by 88.0% BKZ-treated and 79.1% SEC-treated Week 16 responders (**Table 2**).
- Rates for both PASI=0 and PASI ≤2 response maintenance were consistent when using NRI and OC imputation (**Table 2**).

Summary

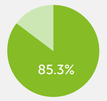
We report the proportions of patients who **continuously maintained their response** from Week 16 through Week 48

Response at every single study visit



61.7% (230/373) of BKZ-randomized patients achieved PASI=0 at Week 16 (NRI)

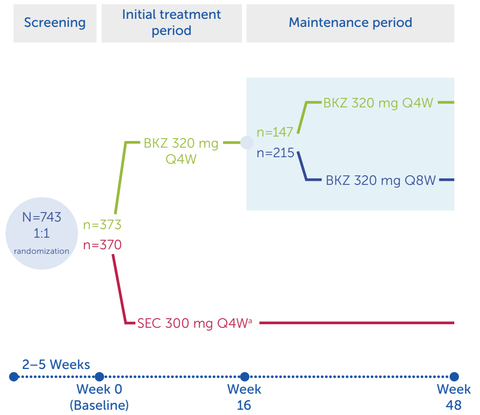
63.7% of BKZ Week 16 PASI=0 responders continually maintained PASI=0 response to Week 48 (mNRI)



85.3% (318/373) of BKZ-randomized patients achieved PASI ≤2 at Week 16 (NRI)

88.0% of BKZ Week 16 PASI ≤2 responders continually maintained PASI ≤2 response to Week 48 (mNRI)

Figure 1 Study design



[a]SEC 300 mg was administered at baseline. Weeks 1, 2, 3 and 4, then Q4W for the remainder of the double-blinded treatment period. At Week 48, patients entered the open-label extension, or entered the safety follow-up period.

Table 1 Baseline characteristics

	BKZ-randomized patients			SEC-randomized patients		
	All patients (N=373)	PASI=0 responders (N=230)	PASI ≤2 responders (N=318)	All patients (N=370)	PASI=0 responders (N=180)	PASI ≤2 responders (N=281)
Age (years), mean ± SD	45.9 ± 14.2	45.8 ± 13.8	45.3 ± 13.9	44.0 ± 14.7	42.8 ± 14.5	43.0 ± 14.4
Male, n (%)	251 (67.3)	156 (67.8)	212 (66.7)	235 (63.5)	110 (61.1)	177 (63.0)
Caucasian, n (%)	347 (93.0)	215 (93.5)	298 (93.7)	348 (94.1)	169 (93.9)	266 (94.7)
Weight (kg), mean ± SD	90.1 ± 21.3	88.0 ± 20.9	89.0 ± 21.4	88.8 ± 20.0	86.4 ± 19.7	87.3 ± 19.6
Duration of psoriasis (years), mean ± SD	18.4 ± 13.1	18.8 ± 13.1	18.0 ± 12.7	17.2 ± 12.3	16.9 ± 12.0	17.0 ± 12.0
PASI, mean ± SD	20.2 ± 7.5	19.8 ± 7.3	20.0 ± 7.5	19.7 ± 6.7	19.7 ± 6.6	19.4 ± 6.2
BSA (%), mean ± SD	24.8 ± 15.5	23.7 ± 14.7	24.4 ± 15.4	23.8 ± 14.3	23.8 ± 14.3	23.1 ±13.3
IGA, n (%)						
3: moderate	240 (64.3)	154 (67.0)	211 (66.4)	268 (72.4)	136 (75.6)	214 (76.2)
4: severe	131 (35.1)	76 (33.0)	105 (33.0)	102 (27.6)	44 (24.4)	67 (23.8)
DLQI, mean ± SD	10.8 ± 6.6	11.0 ± 6.7	11.0 ± 6.6	11.3 ± 7.2	10.8 ± 6.8	11.3 ± 7.1
Any prior systemic therapy, n (%)	267 (71.6)	164 (71.3)	225 (70.8)	272 (73.5)	134 (74.4)	206 (73.3)
Any prior biologic therapy, n (%)	125 (33.5)	76 (33.0)	109 (34.3)	119 (32.2)	57 (31.7)	87 (31.0)

Table 2 Proportion of Week 16 responders maintaining responses at every single visit through Week 48

	BKZ-randomized patients			SEC-randomized patients		
	mNRI, % (95% CI)	NRI, % (n/N)	OC, % (n/Nsub)	mNRI, % (95% CI)	NRI, % (n/N)	OC, % (n/Nsub)
Week 16 PASI=0 responders maintaining:						
PASI=0	63.7 (57.3, 70.0)	60.4 (139/230)	65.0 (139/214)	54.3 (46.9, 61.7)	51.7 (93/180)	55.7 (93/167)
PASI ≤1	83.6 (78.7, 88.4)	74.3 (171/230)	79.9 (171/214)	74.9 (68.4, 81.4)	65.6 (118/180)	70.7 (118/167)
PASI ≤2	93.0 (89.7, 96.3)	82.6 (190/230)	88.8 (190/214)	87.4 (82.5, 92.3)	72.8 (131/180)	78.4 (131/167)
Week 16 PASI ≤2 responders maintaining:						
PASI ≤2	88.0 (84.4, 91.5)	76.7 (244/318)	82.4 (244/296)	79.1 (74.3, 83.9)	64.4 (181/281)	70.7 (181/256)

BKZ: bimekizumab; **BSA:** body surface area; **CI:** confidence interval; **DLQI:** Dermatology Life Quality Index; **IGA:** Investigator's Global Assessment; **IL:** interleukin; **mNRI:** modified non-responder imputation; **NRI:** non-responder imputation; **Nsub:** number of patients with a non-missing measurement; **OC:** observed case; **PASI:** Psoriasis Area and Severity Index; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SEC:** secukinumab; **SD:** Standard Deviation.

Institutions: [1]Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, The University of Manchester, Manchester, UK; [2]Department of Dermatology, University Hospital Lausanne, Lausanne, Switzerland; [3]The University of Melbourne, St. Vincent's Hospital Melbourne, Fitzroy and Probity Medical Research Inc. Skin Health Institute, Carlton, Victoria, Australia; [4]Department of Dermatology, Aarhus University Hospital, Aarhus, Denmark; [5]Dalhousie University, Halifax, Nova Scotia, Canada; [6]Psoriasis Research and Treatment Center, Charité – Universitätsmedizin Berlin, Berlin, Germany; [7]UCB Pharma, Raleigh, NC, USA; [8]UCB Pharma, Brussels, Belgium; [9]UCB Pharma, Monheim, Germany; [10]Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts, USA.

References: [1]Papp KA *et al.* J Am Acad Dermatol 2018;79:2; [2]Tada Y *et al.* J Dermatol 2021;48:1665–74; [3]Rasmussen MK *et al.* Acta Derm Venereol 2019;99:158–63; [4]Reich K *et al.* N Engl J Med 2021;385:142–52; [5]Mahil SK *et al.* Br J Dermatol 2020;182:1158–66. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **RBW, CC, PF, LI, RGL, GK, LD, VV, SW, JFM**; Drafting of the publication, or revising it critically for important intellectual content: **RBW, CC, PF, LI, RGL, GK, LD, VV, SW, JFM**; Final approval of the publication: **RBW, CC, PF, LI, RGL, GK, LD, VV, SW, JFM**. **Author Disclosures: RBW:** Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis and UCB Pharma; honoraria from Astellas, DiCE, GSK and Union. **CC:** Consultant and/or principal investigator in clinical trials for: AbbVie, Actelion, Amgen, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galderma, Incyte, Janssen-Cilag, LEO Pharma, MSD, Novartis, Pfizer, Samsung, Sanofi Genzyme and UCB Pharma. **PF:** Institution received grant support from AbbVie, Amgen, Celgene, Eli Lilly, Galderma, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Sanofi and Sun Pharma; investigator for AbbVie, Akaal, Amgen, Arcutis, Argenx, Aslan, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira Inc., Eli Lilly, Galderma, Genentech, Geneseq, GSK, Hexima, Janssen, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma and Valeant; served on the advisory board for AbbVie, Amgen, Aslan, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, GSK, Hexima, Janssen, LEO Pharma, Mayne Pharma, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma and Valeant; consultant for Aslan, Bristol Myers Squibb, Eli Lilly, Galderma, Hexima, Janssen, LEO Pharma, Mayne Pharma, MedImmune, Novartis, Pfizer, Roche, UCB Pharma and Wintermute; received travel grants from AbbVie, Eli Lilly, Galderma, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sanofi, and Sun Pharma; speaker for or received honoraria from AbbVie, Amgen, Celgene, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sanofi, Sun Pharma, UCB Pharma, and Valeant. **LI:** Consultant and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, LEO Pharma, MSD, Novartis, Pfizer, Regranion, Samsung-Bioepis, UCB Pharma and Union Therapeutics. **RGL:** Principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer and UCB Pharma; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer and UCB Pharma; provided lectures for AbbVie, Amgen, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis and Pfizer. **GK:** Received travel grants or honoraria, or has been a consultant member of advisory boards and speakers bureaus or has served as investigator for AbbVie, Actelion, Basilea, Biogen, Boehringer Ingelheim, Celgene, Hexal-Sandoz, Janssen-Cilag, LEO Pharma, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma. **LD, VV, SW:** Employee and shareholder of UCB Pharma. **JFM:** JFM has been a consultant for AbbVie, Amgen, Bayer, Biogen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi-Regenero and UCB Pharma; principal investigator for Dermavant, LEO Pharma and UCB Pharma. **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, Germany, for publication coordination, Natalie Nunez Gomez, MD, UCB Pharma, Monheim, Germany, for critical review, Emma Francis-Gregory, BA, Costello Medical, Cambridge, UK, for medical writing and editorial assistance and the Design team, Costello Medical, UK, for graphic design assistance.

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Conclusions

A higher proportion of BKZ-randomized patients achieved PASI=0 and PASI ≤2 at Week 16, compared with SEC-randomized patients.

Of the BKZ-randomized PASI=0 Week 16 responders, 93.0% continuously maintained disease control.

A higher proportion of BKZ-randomized patients compared with SEC-randomized patients also maintained PASI ≤2 response at every single visit.