PO704

Sustained efficacy and safety of bimekizumab in patients with active psoriatic arthritis and prior inadequate response to tumour necrosis factor inhibitors: Results from the phase 3 BE COMPLETE Study and its open-label extension up to 1 year

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Objective

To assess the long-term efficacy and safety of bimekizumab (BKZ) treatment up to 52 weeks in patients with active psoriatic arthritis (PsA) and prior inadequate response or intolerance to tumour necrosis factor-α inhibitors (TNFi-IR).

Introduction

- BKZ is a humanised monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- BKZ has shown superior efficacy to 16 weeks versus placebo (PBO) and tolerability in patients with active PsA in two phase 3 studies, BE OPTIMAL (naïve to biologic disease-modifying antirheumatic drugs [bDMARDs]) and BE COMPLETE (TNFi-IR).[1,2]
- The efficacy and tolerability of BKZ to 52 weeks has also been demonstrated in BE OPTIMAL.[3]
- Patients with PsA and TNFi-IR typically exhibit reduced treatment responses compared with biologic-naïve patients,[4,5] so identifying treatments that effectively manage the long-term clinical needs of these patients is important.

Methods

- BE COMPLETE included a 16-week double-blinded, PBO-controlled period.[2]
- Patients were randomised 2:1 to subcutaneous BKZ 160 mg or PBO every 4 weeks (Q4W).
- Patients who completed Week 16 were eligible for entry into an open-label extension, BE VITAL **Figure 1**).[6] Upon entry, PBO-randomised patients switched to receive BKZ (PBO/BKZ).
- BE VITAL included patients from BE OPTIMAL and BE COMPLETE; data here are only for patients randomised at baseline (Week 0) of BE COMPLETE, up to 1 year.
- Efficacy data reported are observed case or have imputed missing data using non-responder imputation (binary) or multiple imputation (continuous).
- The number of treatment-emergent adverse events (TEAEs) to Week 52 are reported for patients who received ≥1 dose of BKZ, including patients who switched from PBO to BKZ at Week 16.

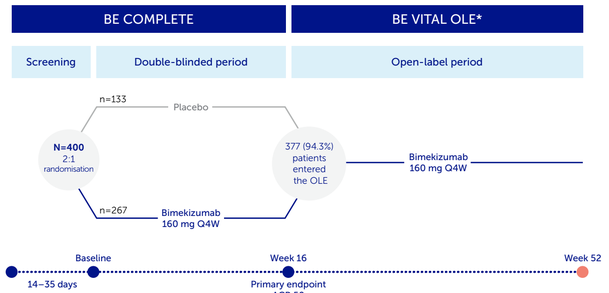
Results

- 388/400 (97.0%) patients completed Week 16; 377 (94.3%) entered BE VITAL and 347 (86.8%) completed Week 52.
- Baseline characteristics were comparable between groups (**Table 1**).
- Improvements in joint and skin responses with BKZ treatment at Week 16 were sustained to Week 52 (**Figure 2** and **Table 2**).
- Patients who switched to BKZ at Week 16 demonstrated improvements in efficacy responses to Week 52 (**Figure 2** and **Table 2**).
- To Week 52, 243/388 (62.6%) patients had ≥1 TEAE whilst receiving BKZ (exposure-adjusted incident rate [EAIR]: 126.0 per 100 patient-years; **Table 3**).
- The most frequent TEAEs were coronavirus infection, oral candidiasis, nasopharyngitis and urinary tract infection (**Table 3**).
- All *Candida* infections were mild or moderate and none were systemic.
- Two cases of oral candidiasis led to study discontinuation.
- There was one death, considered unrelated to study treatment by the investigator (BKZ-treated patient with a history of cardiac events).

Conclusions

In patients with PsA and prior TNFi-IR, BKZ treatment demonstrated sustained improvements across joints and skin from Week 16 to Week 52. Patients who switched to BKZ at Week 16 also displayed meaningful improvements in efficacy responses at Week 52. The safety profile was consistent with previous reports.[1–3]

Figure 1 BE COMPLETE and BE VITAL study design



*BE VITAL includes patients from the BE OPTIMAL and BE COMPLETE studies; results are only presented for patients from BE COMPLETE. BKZ-treated patients were eligible to receive rescue therapy from Week 16 at the discretion of the investigator, while continuing to receive BKZ.

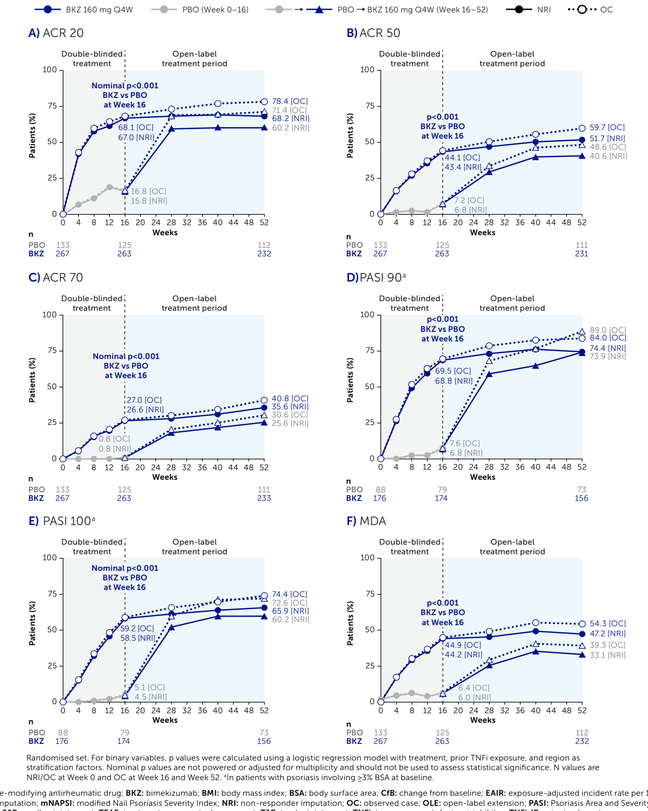
Table 1 Baseline characteristics

	PBO n=133	BKZ 160 mg Q4W n=267
Age, years, mean (SD)	51.3 (12.9)	50.1 (12.4)
Male, n (%)	60 (45.1)	130 (48.7)
BMI, kg/m², mean (SD)	29.0 (5.4)	30.1 (6.5)
Time since first diagnosis of PsA,[a] years, mean (SD)	9.2 (8.1)	9.6 (9.9)
TJC (of 68 joints), mean (SD)	19.3 (14.2)	18.4 (13.5)
SJC (of 66 joints), mean (SD)	10.3 (8.2)	9.7 (7.5)
hs-CRP ≥6 mg/L, n (%)	59 (44.4)	118 (44.2)
Patients with psoriasis involving ≥3% BSA, n (%) / **PASI score**,[b] mean (SD)	88 (66.2) / 8.5 (6.6)	176 (65.9) / 10.1 (9.1)
HAQ-DI score, mean (SD)	1.04 (0.69)	0.97 (0.59)
SF-36 PCS score, mean (SD)	35.9 (10.2)	36.4 (9.0)
Dactylitis (LDI >0),[c,d] n (%) / **LDI score**,[e] mean (SD)	14 (10.5) / 66.4 (127.6)	34 (12.7) / 72.7 (114.4)
Enthesitis (LEI >0),[d,f] n (%) / **LEI score**,[g] mean (SD)	36 (27.1) / 2.9 (1.6)	106 (39.7) / 2.6 (1.5)
Nail psoriasis (mNAPSI >0),[d] n (%) / **mNAPSI score**,[h] mean (SD)	83 (62.4) / 4.5 (2.8)	159 (59.6) / 4.3 (2.8)

Randomised set. [a]Data missing for 1 PBO patient; 1 BKZ patient; [b]Patients with psoriasis involving ≥3% BSA at baseline; [c]The presence of dactylitis was defined by a score greater than 0 on the Leeds Dactylitis Index (higher scores indicate a greater number of affected sites); [d]Data missing for 1 PBO patient; [e]In patients with dactylitis at baseline; [f]The presence of enthesitis was defined by a score greater than 0 on the Leeds Enthesitis Index (range 0 to 6, with higher scores indicating a greater number of affected sites); [g]In patients with enthesitis at baseline; [h]In patients with nail psoriasis at baseline.

ACR: American College of Rheumatology; **ACR 20/50/70**: ≥20/50/70% improvement from baseline in ACR criteria; **AE**: adverse event; **bDMARD**: biologic disease-modifying antirheumatic drug; **BKZ**: bimekizumab; **BMI**: body mass index; **BSA**: body surface area; **CfB**: change from baseline; **EAIR**: exposure-adjusted incident rate per 100 patient-years; **HAQ-DI**: Health Assessment Questionnaire-Disability Index; **hs-CRP**: high-sensitivity C-reactive protein; **IBD**: inflammatory bowel disease; **IL**: interleukin; **LDI**: Leeds Dactylitis Index; **LEI**: Leeds Enthesitis Index; **MACE**: major adverse cardiovascular event; **MDA**: minimal disease activity; **MI**: multiple imputation; **mNAPSI**: modified Nail Psoriasis Severity Index; **NRI**: non-responder imputation; **OC**: observed case; **OLE**: open-label extension; **PASI**: Psoriasis Area and Severity Index; **PASI 75/90/100**: ≥75/90/100% improvement from baseline in Psoriasis Area and Severity Index; **PBO**: placebo; **PsA**: psoriatic arthritis; **PYAR**: patient years at risk; **Q4W**: every four weeks; **SD**: standard deviation; **SE**: standard error; **SF-36 PCS**: Short-Form 36-item Health Survey Physical Component Summary; **SJC**: swollen joint count; **TEAE**: treatment-emergent adverse event; **TJC**: tender joint count; **TNFi**: tumour necrosis factor-α inhibitor; **TNFi-IR**: prior inadequate response or intolerance to tumour necrosis factor-α inhibitors.

Figure 2 ACR, PASI and MDA response rates over time to Week 52 (NRI, OC)



Randomised set. For binary variables, p values were calculated using a logistic regression model with treatment, prior TNFi exposure, and region as stratification factors. Nominal p values are not powered or adjusted for multiplicity and should not be used to assess statistical significance. N values are NRI/OC at Week 0 and OC at Week 16 and Week 52. [a]In patients with psoriasis involving ≥3% BSA at baseline.

Table 2 Additional efficacy endpoints at Week 16 and Week 52 (NRI)

NRI, n/N (%), unless otherwise specified	PBO (Weeks 0–16) n=133 → BKZ 160 mg Q4W (Weeks 16–52) n=133		BKZ 160 mg Q4W n=267	
	Week 16	Week 52	Week 16	Week 52
PASI 75 response[a]	9/88 (10.2)	71/88 (80.7)	145/176 (82.4)	148/176 (84.1)
Enthesitis resolution[b]	8/36 (22.2)	21/36 (58.3)	52/106 (49.1)	60/106 (56.6)
Dactylitis resolution[c]	6/14 (42.9)	12/14 (85.7)	24/34 (70.6)	29/34 (85.3)
Nail psoriasis resolution[d]	12/83 (14.5)	51/83 (61.4)	73/159 (45.9)	107/159 (67.3)
HAQ-DI CfB, **MI**, mean (SE)	−0.07 (0.04)	−0.35 (0.05)	−0.38 (0.03)	−0.39 (0.03)
	Week 16	**Week 40***	**Week 16**	**Week 40***
SF-36 PCS CfB, **MI**, mean (SE)	1.4 (0.7)	7.3 (0.9)	7.3 (0.5)	8.4 (0.6)

Randomised set. Previously reported data through Week 16 included for reference.[2] *Data not collected at Week 52 for SF-36 PCS. [a]In patients with psoriasis involving ≥3% BSA at baseline; [b]Patients with enthesitis at baseline (LEI >0); [c]Patients with dactylitis at baseline (LDI >0); [d]Patients with nail psoriasis at baseline (mNAPSI >0).

Table 3 Safety to Week 16 and Week 52

n (%) [EAIR]	Weeks 0–16[a] (Double-blinded period)		Weeks 16–52 (Open-label period)	Weeks 0–52 (Overall study period)	
	PBO n=132 (PYAR: 42.5)	BKZ 160 mg Q4W n=267 (PYAR: 87.1)	PBO/BKZ 160 mg Q4W[b] n=121 (PYAR: 80.3)	BKZ 160 mg Q4W n=267 (PYAR: 259.5)	BKZ 160 mg Q4W Total[b] n=388 (PYAR: 339.8)
Any TEAE	44 (33.3)	108 (40.4)	68 (56.2) [127.7]	175 (65.5) [125.4]	243 (62.6) [126.0]
Severe TEAEs	0.0	5 (1.9)	3 (2.5)[c]	14 (5.2)[c]	17 (4.4)[c]
Study discontinuation due to TEAEs	0.0	2 (0.7)	6 (5.0) [7.6]	10 (3.7) [3.9]	16 (4.1) [4.8]
Drug-related TEAEs	4 (3.0)	35 (13.1)	21 (17.4)[c]	66 (24.7)[c]	87 (22.4)[c]
Serious TEAEs	0.0	5 (1.9)	8 (6.6) [10.2]	15 (5.6) [6.0]	23 (5.9) [7.0]
Deaths	0.0	0.0	1 (0.8)[c,d]	0.0	1 (0.3)[c,d]
Most frequent TEAEs[e]					
Coronavirus infection	6 (4.5)	5 (1.9)	7 (5.8) [8.9]	21 (7.9) [8.4]	28 (7.2) [8.5]
Oral candidiasis	0.0	7 (2.6)	7 (5.8) [9.0]	17 (6.4) [6.8]	24 (6.2) [7.3]
Nasopharyngitis	1 (0.8)	10 (3.7)	4 (3.3) [5.0]	19 (7.1) [7.7]	23 (5.9) [7.0]
Urinary tract infection	3 (2.3)	5 (1.9)	4 (3.3) [5.1]	19 (7.1) [7.7]	23 (5.9) [7.0]
Serious infections	0.0	2 (0.7)	3 (2.5) [3.8]	4 (1.5) [1.6]	7 (1.8) [2.1]
Opportunistic infections	0.0	0.0	1 (0.8) [1.3][f]	0.0	1 (0.3) [0.3][f]
Neutropenia	0.0	4 (1.5)[g]	0.0	5 (1.9) [2.0][h]	5 (1.3) [1.5][h]
Hypersensitivity	1 (0.8)	7 (2.6)	4 (3.3) [5.1]	15 (5.6) [6.0]	19 (4.9) [5.8]
Injection site reactions	0.0	3 (1.1)	0.0	6 (2.2) [2.4]	6 (1.5) [1.8]
Adjudicated MACE	0.0	0.0	2 (1.7) [2.5][i]	0.0	2 (0.5) [0.6][i]
Malignancies excluding non-melanoma skin cancer	0.0	0.0	1 (0.8) [1.3][j]	2 (0.7) [0.8][k]	3 (0.8) [0.9][k]
Non-melanoma skin cancer	1 (0.8)[j]	0.0	0.0	0.0	0.0

Safety set. No cases of active tuberculosis, definite or probable adjudicated IBD or uveitis were reported. [a]EAIRs not available for double-blinded period; [b]Includes patients who switched from PBO to BKZ and only includes TEAEs occurring whilst receiving BKZ; [c]EAIRs not available; [d]Sudden death in 54-year old patient with a history of hypertension, aortic regurgitation, electrocardiogram changes of coronary artery disease; no further information available; no autopsy was performed; [e]Most frequent adverse events are those occurring in ≥5% of patients in any study arm; [f]1 oesophageal candidiasis; [g]3 neutropenia; 1 neutrophil count decreased; [h]4 neutropenia; 1 neutrophil count decreased; [i]1 sudden death; 1 cerebral haemorrhage; [j]1 prostate cancer, [k]1 endometrial cancer stage I; 1 gastric cancer recurrent; [l]1 basal cell carcinoma.

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Clin Exp Dermatol 2022;47:1627–35; BE VITAL: https://clinicaltrials.gov/study/NCT04009499?tab=results. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **LCC**, **RBML**, **IBM**, **PJM**, **CTR**, **YT**, **AA**, **FB**, **DDG**, **LG**, **ABG**, **RBW**, **BI**, **RB**, **JC**, **JFM**; Drafting of the publication, or revising it critically for important intellectual content: **LCC**, **RBML**, **IBM**, **PJM**, **CTR**, **YT**, **AA**, **FB**, **DDG**, **LG**, **ABG**, **RBW**, **BI**, **RB**, **JC**, **JFM**; Final approval of the publication: **LCC**, **RBML**, **IBM**, **PJM**, **CTR**, **YT**, **AA**, **FB**, **DDG**, **LG**, **ABG**, **RBW**, **BI**, **RB**, **JC**, **JFM**. **Author Disclosures: LCC:** Grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer and UCB Pharma; Consultant for AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Domain, Eli Lilly, Galapagos, Gilead, Janssen, Moonlake Pharma, Novartis, Pfizer, and UCB Pharma; Speaking fees from AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GSK, Janssen, medac, Novartis, Pfizer, and UCB Pharma. **RBML:** Consultancy fees from AbbVie, AstraZeneca, BMS, Eli Lilly, Novartis, Pfizer, and UCB Pharma; Research grants from AbbVie, Novartis, Pfizer, and UCB Pharma; Owner of Rheumatology Consultancy BV, an AMS company under Dutch law. **IBM:** Consulting fees and honoraria from AbbVie, AstraZeneca, BMS, Boehringer Ingelheim, Cabaletta, Causeway Therapeutics, Celgene, Evelo, Janssen, Lilly, Moonlake, Novartis, and UCB Pharma; Research support from BMS, Boehringer Ingelheim, Celgene, Janssen, Novartis, and UCB Pharma. **PJM:** Research grants from AbbVie, Amgen, BMS, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; Consultancy fees from AbbVie, Acelyrin, Aclaris, Amgen, BMS, Boehringer Ingelheim, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Moonlake Pharma, Novartis, Pfizer, Sun Pharma and UCB Pharma; Speakers' bureau for AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma. **CTR:** Research for AbbVie; Consultant for AbbVie, Amgen, Eli Lilly, Gilead, Janssen, Novartis, Pfizer and UCB Pharma. **YT:** Speaking fees and/or honoraria from AbbVie, AstraZeneca, BMS, Boehringer Ingelheim, Chugai, Eisai, Eli Lilly, Gilead, GSK, Pfizer, Taiho and Taisho; Received grants from Chugai, Eisai, Mitsubishi-Tanabe and Taisho. **AA:** Honoraria and/or research grants from AbbVie, Amgen, BMS, Boehringer Ingelheim, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical Co., and UCB Pharma. **FB:** Consultant and/or speaker and/or investigator for AbbVie, Affibody, Amgen, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, GSK, Janssen, MSD, MoonLake, Novartis, Pfizer, Roche, Sandoz, and Sanofi. **DDG:** Consultant and/or received grant support from Abbvie, Amgen, BMS, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Novartis, Pfizer, and UCB Pharma. **LG:** Grants from AbbVie, Biogen, Lilly, Novartis, Sandoz, UCB Pharma; Personal fees from AbbVie, Amgen, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB Pharma. **ABG:** Received honoraria as an advisory board member and consultant for Amgen, AnaptypsBio, Avotres Therapeutics, BMS, Boehringer Ingelheim, Dice Therapeutics, Eli Lilly, Janssen, Novartis, Sanofi, UCB Pharma and Xbiotech; Received research/educational grants from AnaptypsBio, BMS, Moonlake Immunotherapeutics AG, Novartis and UCB Pharma, (all paid to Mount Sinai School of Medicine). **RBW:** Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, BMS, 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 Therapeutics. **BI:** Shareholder of AbbVie, GSK and UCB Pharma; Employee of UCB Pharma. **RB, JC:** Are employees and shareholders of UCB Pharma. **JFM:** Consultant and/or investigator for AbbVie, Amgen, Biogen, BMS, Dermavant, Eli Lilly, Janssen, LEO Pharma, Pfizer, Novartis, Regeneron, Sanofi, Sun Pharma, and UCB Pharma. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study. 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