Bimekizumab Efficacy and Safety in Biologic DMARD-Naïve Patients with Psoriatic Arthritis was Consistent With or Without Methotrexate: 52-Week Results from the Phase 3 Active Reference Study BE OPTIMAL

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Objective

To report the efficacy and safety of bimekizumab (BKZ) to Week 52 from the phase 3 study BE OPTIMAL in biologic disease-modifying antirheumatic drug-naïve patients with psoriatic arthritis (PsA), with or without concomitant methotrexate.

Background

- Given the chronic nature of psoriatic arthritis, understanding long-term efficacy and safety of biologic monotherapy or therapy in combination with ongoing methotrexate (MTX) is of interest. Studies have shown that tumor necrosis factor inhibitors may have lower efficacy without MTX (– MTX) than with MTX (+ MTX).[1]
- Bimekizumab, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown efficacy and tolerability to 52 weeks in patients with PsA who are biologic disease-modifying antirheumatic drug (bDMARD)-naive.[2]

Methods

- BE OPTIMAL (NCT03895203) comprised a 16-week double-blind, placebo (PBO)-controlled period and a 36-week active treatment-blind period.
- Patients were randomized 3:2:1 to subcutaneous BKZ 160 mg every 4 weeks (Q4W), PBO (with switch to BKZ 160 mg Q4W at Week 16) or reference arm (adalimumab [ADA] 40 mg Q2W); the study was not powered for statistical comparisons of ADA to BKZ or PBO.
- Patients generally could not adjust their background medication, including MTX usage, during the 16-week PBO-controlled period. Efficacy and safety were evaluated by concomitant MTX use at baseline.
- Missing data were imputed using non-responder imputation (discrete) or multiple imputation (continuous).

Results

Baseline patient demographics and disease characteristics

- 770/852 (90.4%) patients completed Week 52 (+ MTX: 458/497 [92.2%]; – MTX: 312/355 [87.9%]), including 9 not on randomized treatment (+ MTX: 4; – MTX: 5). Baseline characteristics were generally similar for +/– MTX patient subgroups (**Table 1**).

Efficacy to Week 52

- To Week 52, the proportions of BKZ-randomized patients who achieved ≥50% improvement in American College of Rheumatology response criteria (ACR50), complete skin clearance (100% improvement in Psoriasis Area and Severity Index) and minimal disease activity (MDA) were similar regardless of baseline MTX use.
  - Fewer patients receiving ADA – MTX achieved ACR50 or MDA at Week 52 compared with the ADA + MTX group (**Figure 1**).
- Other Week 52 efficacy responses on BKZ were generally of a similar magnitude +/– MTX (**Table 2**).

Safety to Week 52

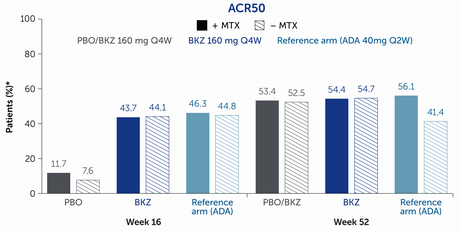
- To Week 52, the proportion of patients with ≥1 treatment-emergent adverse event (TEAE) was similar for BKZ regardless of +/– MTX. More patients receiving ADA – MTX had ≥1 TEAE compared with the ADA + MTX subgroup.
- To Week 52, rates of the most frequent TEAEs were similar between +/– MTX on BKZ, and BKZ was well tolerated regardless of MTX (**Table 3**).

Conclusions

Bimekizumab treatment demonstrated consistent clinical efficacy across disease manifestations to Week 52 in bDMARD-naïve patients with PsA, irrespective of concomitant MTX. Bimekizumab was well tolerated in patients with PsA with or without MTX.

Summary

In BE OPTIMAL, bDMARD-naïve patients with active PsA treated with bimekizumab achieved **consistent clinical efficacy** to Week 52, irrespective of **concomitant MTX**



*The study was not powered for statistical comparisons of ADA to BKZ or PBO, or + MTX and – MTX subgroups.

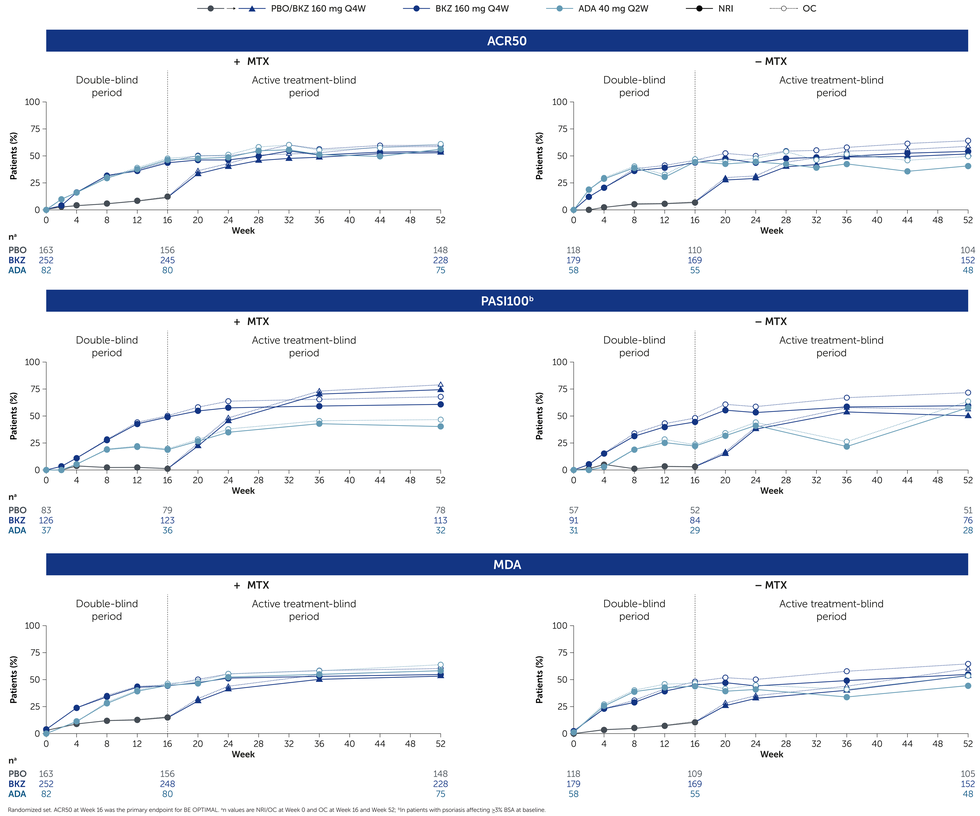
BKZ was **well tolerated** in patients with active PsA **with or without MTX**

Table 1 Baseline characteristics +/– MTX

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference arm (ADA 40 mg Q2W) N=140	
	+ MTX n=163	– MTX n=118	+ MTX n=252	– MTX n=179	+ MTX n=82	– MTX n=58
Age, years, mean (SD)	48.2 (11.5)	49.3 (12.1)	47.8 (12.6)	49.6 (12.4)	49.2 (11.7)	48.8 (14.2)
Male, n (%)	72 (44.2)	55 (46.6)	122 (48.4)	79 (44.1)	41 (50.0)	30 (51.7)
BMI, kg/m^2, mean (SD)	29.4 (6.1)	29.9 (6.0)	29.1 (6.5)	29.4 (7.2)	28.4 (5.7)	28.4 (6.2)
Time since first diagnosis of PsA, years, mean (SD)	5.4 (6.2)	6.0 (7.0)[a]	5.8 (7.3)[a]	6.2 (7.3)[a]	5.9 (6.2)	6.5 (7.6)[a]
≥3% BSA affected by psoriasis, n (%)	83 (50.9)	57 (48.3)	126 (50.0)	91 (50.8)	37 (45.1)	31 (53.4)
PASI score,[a] mean (SD)	7.6 (5.3)	8.4 (6.1)	7.7 (6.4)	8.8 (7.4)	9.6 (8.1)	7.3 (6.8)
TJC (of 68), mean (SD)	16.4 (12.3)	18.0 (12.7)	16.6 (11.8)	17.1 (11.8)	17.8 (13.1)	17.2 (13.1)
SJC (of 66), mean (SD)	10.0 (7.8)	8.8 (6.5)	9.1 (6.4)	8.8 (5.9)	9.8 (7.4)	9.4 (6.7)
Enthesitis,[a] n (%)	36 (22.1)	34 (28.8)	82 (32.5)[a]	61 (34.1)[c]	18 (22.0)[c]	18 (31.0)
LEI score,[a] mean (SD)	2.8 (1.6)	3.0 (1.5)	2.4 (1.4)[a]	2.6 (1.5)[c]	2.2 (1.6)[c]	2.3 (1.6)
Dactylitis,[b] n (%)	22 (13.5)	11 (9.3)	28 (11.1)[b]	28 (15.6)[c]	5 (6.1)[c]	6 (10.3)
LDI score,[c] mean (SD)	46.1 (36.6)	49.9 (50.6)	38.2 (32.0)[b]	55.3 (69.6)[c]	54.1 (37.3)[c]	46.0 (29.8)
Nail psoriasis,[c] n (%)	92 (56.4)	64 (54.2)	146 (57.9)[b]	98 (54.7)[c]	42 (51.2)	33 (56.9)
mNAPSI score,[a] mean (SD)	4.1 (2.2)	3.8 (2.0)	4.0 (2.4)[b]	4.2 (2.5)[c]	3.7 (2.2)	3.8 (2.4)
PGA–PsA, mean (SD)	60.1 (23.7)	56.5 (23.1)	53.1 (23.5)[c]	56.3 (23.3)	57.3 (21.8)	56.7 (22.0)
HAQ-DI, mean (SD)	0.90 (0.60)	0.88 (0.62)	0.78 (0.59)[c]	0.87 (0.58)	0.91 (0.55)	0.79 (0.53)

Randomized set. [a]Data missing for two patients; [b]Data missing for six patients; [c]Data missing for one patient; [d]n patients with psoriasis involving ≥3% BSA at baseline; [e]Patients with LEI >0; [f]Data missing for five patients; [g]n patients with enthesitis at baseline; [h]Patients with LDI >0; [i]n patients with dactylitis at baseline; [j]Patients with mNAPSI >0; [k]n patients with nail psoriasis at baseline.

Figure 1 Patients +/– MTX achieving ACR50, PASI100 and MDA to Week 52 (NRI and OC)



Randomized set. ACR50 at Week 16 was the primary endpoint for BE OPTIMAL. *n values are NRI/OC at Week 0 and OC at Week 16 and Week 52; [b]n patients with psoriasis affecting ≥3% BSA at baseline.

Table 2 Week 52 efficacy endpoints for patients +/– MTX (NRI and MI)

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference Arm (ADA 40 mg Q2W) N=140	
Endpoint	+ MTX n=163	– MTX n=118	+ MTX n=252	– MTX n=179	+ MTX n=82	– MTX n=58
ACR20 [NRI], n (%)	113 (69.3)	78 (66.1)	184 (73.0)	123 (68.7)	65 (79.3)	37 (63.8)
ACR50 [NRI], n (%)	87 (53.4)	62 (52.5)	137 (54.4)	98 (54.7)	46 (56.1)	24 (41.4)
ACR70 [NRI], n (%)	60 (36.8)	41 (34.7)	96 (38.1)	73 (40.8)	36 (43.9)	17 (29.3)
PASI75[a] [NRI], n (%)	71 (85.5)	48 (84.2)	105 (83.3)	72 (79.1)	23 (62.2)	22 (71.0)
PASI90[a] [NRI], n (%)	67 (80.7)	39 (68.4)	89 (70.6)	66 (72.5)	20 (54.1)	21 (67.7)
PASI100[a] [NRI], n (%)	62 (74.7)	29 (50.9)	77 (61.1)	55 (60.4)	15 (40.5)	18 (58.1)
MDA [NRI], n (%)	87 (53.4)	64 (54.2)	138 (54.8)	99 (55.3)	48 (58.5)	26 (44.8)
VLDA [NRI], n (%)	35 (21.5)	27 (22.9)	72 (28.6)	53 (29.6)	25 (30.5)	14 (24.1)
ACR50+PASI100[a] [NRI], n (%)	43 (51.8)	22 (38.6)	61 (48.4)	41 (45.1)	12 (32.4)	12 (38.7)
Enthesitis resolution[b] [NRI], n (%)	24 (66.7)	20 (58.8)	53 (64.6)	34 (55.7)	11 (61.1)	10 (55.6)
Dactylitis resolution[c] [NRI], n (%)	18 (81.8)	11 (100.0)	21 (75.0)	24 (85.7)	4 (80.0)	4 (66.7)
HAQ-DI CfB [MI], mean (SE)	–0.37 (0.04)	–0.38 (0.05)	–0.30 (0.03)	–0.38 (0.04)	–0.49 (0.06)	–0.30 (0.08)
Nail psoriasis resolution[d] [NRI], n (%)	68 (73.9)	43 (67.2)	100 (68.5)	60 (61.2)	24 (57.1)	21 (63.6)

Randomized set. [a]n patients with psoriasis affecting ≥3% BSA at baseline; + MTX: PBO/BKZ n=83, BKZ n=126, ADA n=37; – MTX: PBO/BKZ n=57, BKZ n=91, ADA n=31; [b]n patients with baseline enthesitis (LEI >0); + MTX: PBO/BKZ n=36, BKZ n=82, ADA n=18; – MTX: PBO/BKZ n=34, BKZ n=82, ADA n=18; [c]n patients with baseline dactylitis (LDI >0); + MTX: PBO/BKZ n=22, BKZ n=28, ADA n=5; – MTX: PBO/BKZ n=11, BKZ n=28, ADA n=6; [d]n patients with baseline nail psoriasis (mNAPSI >0); + MTX: PBO/BKZ n=92, BKZ n=146, ADA n=42; – MTX: PBO/BKZ n=64, BKZ n=98, ADA n=33.

Table 3 Safety data to Week 52 for patients +/– MTX

	BKZ 160 mg Q4W N=702[a]		Reference Arm (ADA 40 mg Q2W) N=140	
	+ MTX n=410 PYAR: 355.4	– MTX n=292 PYAR: 247.2	+ MTX n=82 PYAR: 80.7	– MTX n=58 PYAR: 56.1
***n* (%) [EAIR][b]**	325 (79.3) [219.3]	230 (78.8) [227.6]	63 (76.8) [169.2]	50 (86.2) [298.9]
Any TEAEs	325 (79.3) [219.3]	230 (78.8) [227.6]	63 (76.8) [169.2]	50 (86.2) [298.9]
Severe TEAEs	13 (3.2)	10 (3.4)	7 (8.5)	2 (3.4)
Study discontinuation due to TEAEs	10 (2.4) [2.8]	11 (3.8) [4.5]	4 (4.9) [5.1]	3 (5.2) [5.5]
Drug-related TEAEs	133 (32.4)	91 (31.2)	30 (36.6)	24 (41.4)
Serious TEAEs	26 (6.3) [7.5]	20 (6.8) [8.4]	7 (8.5) [9.0]	3 (5.2) [5.4]
Death due to TEAEs	1 (0.2)[c]	0	0	0
Most frequent adverse events[d]				
Nasopharyngitis	41 (10.0) [12.5]	43 (14.7) [19.4]	3 (3.7) [3.8]	9 (15.5) [18.1]
Upper respiratory tract infection	34 (8.3) [10.2]	16 (5.5) [6.7]	4 (4.9) [5.1]	4 (6.9) [7.5]
Urinary tract infection	30 (7.3) [8.7]	13 (4.5) [5.4]	2 (2.4) [2.5]	3 (5.2) [5.5]
Headache	20 (4.9) [5.9]	21 (7.2) [9.0]	4 (4.9) [5.1]	2 (3.4) [3.6]
Oral candidiasis[e]	23 (5.6) [6.7]	15 (5.1) [6.2]	1 (1.2) [1.3]	0
Diarrhea	20 (4.9) [5.8]	16 (5.5) [6.7]	2 (2.4) [2.5]	5 (8.6) [9.5]
Pharyngitis	21 (5.1) [6.1]	11 (3.8) [4.6]	3 (3.7) [3.8]	0
Adjudicated MACE[f]	3 (0.7) [0.9]	1 (0.3) [0.4]	0	0
Adjudicated definite IBD[g]	1 (0.2) [0.3]	1 (0.3) [0.4]	0	0
Malignancies excluding non-melanoma skin cancer				
Colon cancer	1 (0.2) [0.3]	0	0	0
Chronic lymphocytic leukemia stage 0	0	1 (0.3) [0.4]	0	0
Papillary thyroid cancer	0	1 (0.3) [0.4]	0	0
Liver function test changes/enzyme elevations, n/Nsub (%)				
ALT >3x ULN	11/410 (2.7)	4/291 (1.4)	4/82 (4.9)	3/57 (5.3)
AST or ALT >3x ULN	16/410 (3.9)	8/291 (2.7)	5/82 (6.1)	4/57 (7.0)

Safety set. [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]EARIs are reported where available; [c]Cause of death was a motorcycle accident; unrelated to treatment; [d]Most frequent adverse events are those occurring in ≥5% of the BKZ study arm (+/– MTX) reported across all study arms; [e]All infections were mild or moderate and none were serious; 1 BKZ patient (+ MTX) discontinued; [f] + MTX: 1 case each of myocardial infarction, ischemic stroke and thrombotic cerebral infarction. The case of ischemic stroke was deemed by the investigator to be related to study medication. – MTX: 1 case of cerebrovascular accident; [g]Both ulcerative colitis; one in a patient with a prior history of IBD (+ MTX), the other de novo (– MTX).

ACR: American College of Rheumatology; **ACR20/50/70:** American College of Rheumatology response criteria ≥20/50/70% improvement; **ADA:** adalimumab; **ALT:** Alanine aminotransferase; **AST:** Aspartate aminotransferase; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BMI:** body mass index; **BSA:** body surface area; **CfB:** change from baseline; **EAIR:** exposure-adjusted incidence rate; **HAQ-DI:** Health Assessment Questionnaire-Disability Index; **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; **MTX:** methotrexate; **NRI:** non-responder imputation; **OC:** observed case; **PASI:** Psoriasis Area and Severity Index; **PASI75/90/100:** Psoriasis Area and Severity Index ≥75/90/100% improvement; **PBO:** placebo; **PGA–PsA:** Patient's Global Assessment for Psoriatic Arthritis; **PsA:** psoriatic arthritis; **PYAR:** patient-year at risk; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **SD:** standard deviation; **SE:** standard error; **SJC:** swollen joint count; **TEAE:** treatment-emergent adverse event; **TJC:** tender joint count; **ULN:** upper limit of normal; **VLDA:** very low disease activity.

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