SUPPLEMENTARY APPENDIX

Supplementary Appendix 1

UCB-Defined Opportunistic Infection

The definition of opportunistic infections used in this study was: infections caused by uncommon pathogens (e.g., pneumocystis jirovecii, cryptococcosis) or unusually severe infections caused by common pathogens (e.g. cytomegalovirus, herpes zoster).

A prespecified preferred term list of treatment-emergent adverse events (TEAEs) that would be considered opportunistic infections was referred to when classifying infections as opportunistic. Some TEAEs must have also been serious infections to be considered opportunistic infections; others were considered opportunistic infections regardless of seriousness. Some TEAEs must have also been evaluated on a case-by-case basis by the study physician to determine whether or not it was an opportunistic infection.

Supplementary Table 1. Important protocol deviations from Week 16 to Week 52

	PBO/BKZ 160 mg Q4W N=271	BKZ 160 mg Q4W N=414	Reference arm (ADA 40 mg Q2W) N=136	All patients N=821
Any important protocol deviation	10 (3.7)	14 (3.4)	5 (3.7)	29 (3.5)
Inclusion criteria deviation	0	0	0	0
Exclusion criteria deviation	0	0	0	0
Withdrawal criteria deviation	0	0	0	0
Prohibited concurrent medication use	1 (0.4)	2 (0.5)	0	3 (0.4)
Incorrect treatment or dose	0	1 (0.2)	1 (0.7)	2 (0.2)
Treatment non-compliance	0	0	0	0
Procedural non-compliance	9 (3.3)	11 (2.7)	2 (1.5)	22 (2.7)
COVID-19-related important protocol deviation	0	1 (0.2)	2 (1.5)	3 (0.4)
COVID-19 visit deviation	0	1 (0.2)	1 (0.7)	2 (0.2)
COVID-19 treatment deviation	0	0	1 (0.7)	1 (0.1)
COVID-19 termination	0	0	0	0
COVID-19 other important protocol deviation	0	0	0	0
Number of patients excluded from PK-PPS	0	0	0	0

Active treatment-blind set. Patients were summarised according to randomised treatment at baseline in the double-blind treatment period. Placebo-randomised patients switched to BKZ 160 mg Q4W at Week 16. Patients with important protocol deviations affecting the plasma concentration were excluded from the Pharmacokinetic Per Protocol Set. ADA: adalimumab; BKZ: bimekizumab; COVID-19: Coronavirus Disease 2019; PK-PPS: pharmacokinetic per protocol set; Q2W: every two weeks; Q4W: every four weeks.

Supplementary Table 2. Change from baseline in ACR individual components

	PBO (Weeks 0–16) → BKZ 160 mg Q4W (Weeks 16–52) N=281		BKZ 160 mg Q4W (Weeks 0–52) N=431		Reference arm (ADA 40 mg Q2W; Weeks 0–52) N=140	
Component	**Wk 16**	**Wk 52**	**Wk 16**	**Wk 52**	**Wk 16**	**Wk 52**
SJC score change from baseline,[a] mean (SE)	−3.0 (0.5)	−7.8 (0.4)	−6.6 (0.3)	−7.6 (0.3)	−7.5 (0.6)	−8.2 (0.6)
TJC score change from baseline,[b] mean (SE)	−3.1 (0.7)	−11.9 (0.7)	−10.0 (0.5)	−12.5 (0.5)	−10.9 (1.0)	−12.6 (0.9)
HAQ-DI score change from baseline, mean (SE)	−0.09 (0.03)	−0.38 (0.03)	−0.26 (0.02)	−0.34 (0.02)	−0.33 (0.04)	−0.41 (0.05)
PtAAP score change from baseline, mean (SE)	−6.2 (1.5)	−31.8 (1.8)	−23.6 (1.3)	−30.4 (1.4)	−25.7 (2.5)	−32.7 (2.5)
PhGA-PsA score change from baseline, mean (SE)	−12.6 (1.4)	−45.2 (1.2)	−37.4 (1.1)	−44.9 (1.0)	−37.3 (2.0)	−43.0 (2.0)
PGA-PsA score change from baseline, mean (SE)	−7.7 (1.6)	−35.2 (1.9)	−26.4 (1.3)	−33.2 (1.4)	−26.9 (2.5)	−32.9 (2.4)
hs-CRP change from baseline, mean (SE)	−2.4 (1.0)	−6.7 (1.2)	−4.2 (0.6)	−4.1 (0.7)	−3.9 (0.8)	−3.2 (0.9)

Randomised set. [a] The SJC was based on a joint count of 66; [b] The TJC was based on a joint count of 68. ACR: American College of Rheumatology; ADA: adalimumab; BKZ: bimekizumab; HAQ-DI: Health Assessment Questionnaire-Disability Index; hs-CRP: high sensitivity C-reactive protein; PGA-PsA: Patient's Global Assessment of Psoriatic Arthritis; PhGA-PsA: Physician's Global Assessment of Psoriatic Arthritis; PtAAP: Patient's Assessment of Arthritis Pain; Q2W: every two weeks; Q4W: every four weeks; SE: standard error; SJC: swollen joint count; TJC: tender joint count.

Supplementary Table 3. Fungal infections

	Up to Week 16, n (%)			Up to Week 52, n (%) [EAIR/100 PY]	
AEs of Special Monitoring	**PBO N=281** (PYAR: 87.3)	**BKZ 160 mg Q4W N=431** (PYAR: 134.2)	**Reference Arm (ADA 40 mg Q2W) N=140** (PYAR: 43.4)	**BKZ 160 mg Q4W Total N=702[a]** (PYAR: 603.4)	**Reference Arm (ADA 40 mg Q2W) N=140** (PYAR: 136.8)
Fungal Infections, n (%)	4 (1.4)	20 (4.6)	1 (0.7)	82 (11.7) [14.6]	2 (1.4) [1.5]
Candida infections	2 (0.7)	11 (2.6)	0	54 (7.7) [9.3]	1 (0.7) [0.7]
Oral candidiasis	0	9 (2.1)	0	38 (5.4) [6.5]	1 (0.7) [0.7]
Vulvovaginal candidiasis	2 (0.7)	1 (0.2)	0	8 (1.1) [1.3]	0
Oesophageal candidiasis	0	0	0	4 (0.6) [0.7]	0
Skin candida	0	1 (0.2)	0	3 (0.4) [0.5]	0
Oropharyngeal candidiasis	0	0	0	2 (0.3) [0.3]	0
Recurrent candidiasis	0	1 (0.2)	0	12 (1.7)	0
Fungal infections NEC	2 (0.7)	9 (2.1)	0	29 (4.1) [4.9]	0
Fungal skin infection	0	3 (0.7)	0	10 (1.4) [1.7]	0
Oral fungal infection	0	2 (0.5)	0	10 (1.4) [1.7]	0
Vulvovaginal mycotic infection	2 (0.7)	0	0	7 (1.0) [1.2]	0
Tongue fungal infection	0	3 (0.7)	0	3 (0.4) [0.5]	0
Onychomycosis	0	1 (0.2)	0	1 (0.1) [0.2]	0
Oesophagitis fungal infection	0	0	0	1 (0.1) [0.2]	0
Laryngitis fungal	0	0	0	1 (0.1) [0.2]	0
Upper respiratory fungal infection	0	0	0	1 (0.1) [0.2]	0
Tinea infections	0	0	1 (0.7)	7 (1.0) [1.2]	1 (0.7) [0.7]

	Up to Week 16, n (%)			Up to Week 52, n (%) [EAIR/100 PY]	
AEs of Special Monitoring	**PBO N=281** (PYAR: 87.3)	**BKZ 160 mg Q4W N=431** (PYAR: 134.2)	**Reference Arm (ADA 40 mg Q2W) N=140** (PYAR: 43.4)	**BKZ 160 mg Q4W Total N=702[a]** (PYAR: 603.4)	**Reference Arm (ADA 40 mg Q2W) N=140** (PYAR: 136.8)
Tinea versicolour	0	0	1 (0.7)	3 (0.4) [0.5]	1 (0.7) [0.7]
Tinea pedis	0	0	0	2 (0.3) [0.3]	0
Body tinea	0	0	0	1 (0.1) [0.2]	0
Tinea infection	0	0	0	1 (0.1) [0.2]	0
Serious *Candida* infections	0	0	0	0	0
Systemic *Candida* infections	0	0	0	0	0
Candida infections leading to study discontinuation	0	1 (0.2)	0	1 (0.1) [0.2]	0

Safety set (Week 16) and active medication set for the overall study period (Week 52). [a] Includes patients who switched from placebo to BKZ (events after switch only).
ADA: adalimumab; AE: adverse event; BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; NEC: not elsewhere classified; PY: patient-years; PYAR: patient-years at risk; Q2W: every two weeks; Q4W: every four weeks.

Supplementary Table 4. Week 16–52 safety (active treatment-blind period)

	Week 16–52, n (%) [EAIR/100 PY]	
	BKZ 160 mg Q4W Total N=685[a] (PYAR: 467.0)	**Reference Arm (ADA 40 mg Q2W) N=136** (PYAR: 93.1)
Any TEAE	489 (71.4) [206.4]	93 (68.4) [188.5]
Serious TEAEs	39 (5.7) [8.6]	9 (6.6) [10.0]
Study discontinuation due to adverse event	13 (1.9) [2.8]	4 (2.9) [4.4]
Drug-related adverse event	167 (24.4)	37 (27.2)
Severe adverse events	19 (2.8)	7 (5.1)
Deaths	1 (0.1)[b]	0
Most frequent adverse events[c]		
Nasopharyngitis	52 (7.6) [11.7]	6 (4.4) [6.7]
Urinary tract infection	35 (5.1) [7.7]	3 (2.2) [3.3]
Upper respiratory tract infection	33 (4.8) [7.3]	5 (3.7) [5.5]
Oral candidiasis[d]	33 (4.8) [7.3]	1 (0.7) [1.1]
Headache	24 (3.5) [5.3]	5 (3.7) [5.5]
Diarrhoea	23 (3.4) [5.0]	2 (1.5) [2.2]
Hypertension	18 (2.6) [3.9]	5 (3.7) [5.5]
ALT elevation	14 (2.0) [3.0]	4 (2.9) [4.4]
AST elevation	13 (1.9) [2.8]	3 (2.2) [3.2]
Injection site erythema	6 (0.9) [1.3]	6 (4.4) [6.6]
Uveitis	0	0
Adjudicated MACE	4 (0.6) [0.9]	0
Neutropenia	7 (1.0) [1.5]	1 (0.7) [1.1]
Infections		
Serious	5 (0.7) [1.1][e]	2 (1.5) [2.2][e]
Opportunistic	9 (1.3) [2.0]	0
Active TB	0	0
Hypersensitivity	44 (6.4) [9.8]	4 (2.9) [4.4]
Injection site reactions	11 (1.6) [2.4]	9 (6.6) [10.2]
Adjudicated SIB	0	0
Liver function test changes/enzyme elevations		
ALT >3 × ULN	10 (1.5)[f]	5 (3.7)
AST or ALT >3 × ULN	19 (2.8)[f]	6 (4.4)
Definite adjudicated IBD	2 (0.3)[g]	0
Malignancies excluding nonmelanoma skin cancer		

	Week 16–52, n (%) [EAIR/100 PY]	
	BKZ 160 mg Q4W Total N=685[a] (PYAR: 467.0)	**Reference Arm (ADA 40 mg Q2W) N=136** (PYAR: 93.1)
Colon cancer	1 (0.1) [0.2]	0
Chronic lymphocytic leukaemia stage 0	1 (0.1) [0.2]	0
Papillary thyroid cancer	1 (0.1) [0.2]	0
Nonmelanoma skin cancer		
Squamous cell carcinoma	1 (0.1) [0.2]	0
Basal cell carcinoma	2 (0.3) [0.4]	0

Active treatment-blind set. [a] Includes patients who switched from placebo to BKZ; [b] Motorcycle accident; [c] Most frequent adverse events are those occurring in ≥5% of patients in any study arm up to Week 52; [d] All infections were mild or moderate and none were serious, 1 BKZ-treated patient discontinued; [e] 5 serious infections reported on the BKZ treatment arm: 1 cellulitis, 1 gangrene, 1 upper respiratory tract infection, 1 cystitis and 1 urinary tract infection. 2 ADA-treated patients reported serious infections: 1 otitis media and 1 reported both herpes zoster and atypical pneumonia; [f] Data missing for 6 patients; [g] Both ulcerative colitis; one in a patient with a prior history of IBD, the other de novo. ADA: adalimumab; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BKZ: bimekizumab; EAIR: exposure-adjusted incident rate; IBD: inflammatory bowel disease; MACE: major adverse cardiovascular event; PYAR: patient-years at risk; Q2W: every two weeks; Q4W: every four weeks; SIB: suicidal ideation and behaviour; TB: tuberculosis; TEAE: treatment-emergent adverse event; ULN: upper limit of normal.

Supplementary Table 5. ACR responders to Week 52

A) ACR20 (%)

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference arm (ADA 40 mg Q2W) N=140	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	7.8	8.0	27.1	27.6	33.6	34.6
Week 4	13.2	13.6	42.2	42.9	45.0	45.7
Week 8	17.8	18.9	56.6	58.7	58.6	60.3
Week 12	26.7	28.3	56.1	58.2	60.7	63.9
Week 16	23.8	25.2	62.2	64.9	68.6	71.1
Week 20	58.0	62.7	66.8	72.5	68.6	72.2
Week 24	62.3	67.3	65.4	72.9	70.7	75.0
Week 28	64.4	72.4	68.4	76.4	68.6	78.0
Week 32	64.4	72.1	68.0	75.7	66.4	74.4
Week 36	68.3	74.1	67.3	76.1	67.9	76.6
Week 44	69.8	79.0	70.8	80.9	66.4	80.2
Week 52	68.0	76.1	71.2	80.8	72.9	82.9

B) ACR50[a] (%)

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference arm (ADA 40 mg Q2W) N=140	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	1.8	1.8	7.7	7.8	13.6	14.0
Week 4	3.2	3.3	17.6	17.9	21.4	21.7
Week 8	5.7	6.0	33.9	34.9	33.6	34.6
Week 12	7.1	7.5	37.4	38.9	35.0	36.8
Week 16	10.0	10.5	43.9	45.7	45.7	47.4
Week 20	31.3	33.8	47.1	51.4	45.7	48.1
Week 24	35.9	38.8	45.5	50.4	47.1	50.0
Week 28	43.8	48.4	49.0	54.7	50.0	56.9
Week 32	45.6	50.6	52.4	58.5	49.3	55.2
Week 36	49.5	53.9	50.8	57.3	47.9	54.0
Week 44	51.2	57.8	53.4	60.8	44.3	53.4
Week 52	53.0	59.1	54.5	61.8	50.0	56.9

C) ACR70 (%)

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference arm (ADA 40 mg Q2W) N=140	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	0.7	0.7	2.3	2.3	2.9	2.9
Week 4	0.4	0.4	6.3	6.4	5.7	5.8
Week 8	1.1	1.1	14.6	15.1	16.4	16.9
Week 12	2.8	3.0	21.3	22.1	22.1	23.3
Week 16	4.3	4.5	24.4	25.2	27.9	28.9
Week 20	13.5	14.6	29.0	31.6	28.6	30.1
Week 24	18.9	20.4	29.2	32.4	30.0	31.6
Week 28	22.4	24.9	32.9	36.8	30.7	34.7
Week 32	26.0	28.9	36.2	40.3	33.6	37.3
Week 36	28.5	30.9	36.7	41.4	31.4	35.5
Week 44	35.9	40.4	38.5	43.8	34.3	41.0
Week 52	35.9	39.9	39.2	44.6	37.9	43.1

Randomised set. The study was not powered for statistical comparisons of ADA to BKZ or PBO.
[a] ACR50 at Week 16 was the primary endpoint. ACR20/50/70: American College of Rheumatology ≥20%/50%/70% response criteria; ADA: adalimumab; BKZ: bimekizumab; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

Supplementary Table 6. PASI responders to Week 52 (%)

A) PASI75 (%)

	PBO/BKZ 160 mg Q4W N=140		BKZ 160 mg Q4W N=217		Reference arm (ADA 40 mg Q2W) N=68	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	4.3	4.4	19.8	20.6	11.8	12.1
Week 4	5.0	5.1	47.5	48.8	17.6	17.6
Week 8	7.9	8.3	69.6	72.6	42.6	43.3
Week 12	10.0	10.6	77.0	80.7	52.9	57.1
Week 16	12.9	13.7	77.4	81.2	66.2	69.2
Week 20	60.0	65.6	79.7	86.1	61.8	65.6
Week 24	75.7	79.1	81.1	89.8	58.8	63.5
Week 36	85.7	90.2	81.1	90.7	66.2	73.8
Week 52	85.0	92.2	81.6	93.7	66.2	75.0

B) PASI90[a] (%)

	PBO/BKZ 160 mg Q4W N=140		BKZ 160 mg Q4W N=217		Reference arm (ADA 40 mg Q2W) N=68	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	1.4	1.5	5.1	5.3	2.9	3.0
Week 4	4.3	4.3	19.8	20.4	7.4	7.4
Week 8	4.3	4.5	47.9	50.0	26.5	26.9
Week 12	4.3	4.5	57.6	60.4	30.9	33.3
Week 16	2.9	3.1	61.3	64.3	41.2	43.1
Week 20	35.7	39.1	68.2	73.6	44.1	46.9
Week 24	61.4	64.2	72.8	80.6	47.1	50.8
Week 36	75.7	79.7	74.2	83.0	54.4	60.7
Week 52	75.7	82.2	71.4	82.0	60.3	68.3

C) PASI100 (%)

	PBO/BKZ 160 mg Q4W N=140		BKZ 160 mg Q4W N=217		Reference arm (ADA 40 mg Q2W) N=68	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	0.7	0.7	4.1	4.3	0.0	0.0
Week 4	4.3	4.3	12.9	13.3	4.4	4.4
Week 8	2.1	2.3	29.5	30.8	19.1	19.4
Week 12	2.9	3.0	41.9	44.0	23.5	25.4
Week 16	2.1	2.3	47.5	49.8	20.6	21.5
Week 20	20.0	21.9	55.3	59.7	29.4	31.3
Week 24	42.9	44.8	56.2	62.2	38.2	41.3
Week 36	64.3	67.7	59.4	66.5	33.8	37.7
Week 52	65.0	70.5	60.8	69.8	48.5	55.0

Randomised set, in patients with psoriasis affecting ≥3% BSA at baseline. The study was not powered for statistical comparisons of ADA to BKZ or PBO. [a] PASI90 was a ranked secondary endpoint.
ADA: adalimumab; BKZ: bimekizumab; BSA: body surface area; NRI: non-responder imputation; OC: observed case; PASI75/90/100: Psoriasis Area and Severity Index ≥75%/90%/100% improvement; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

Supplementary Table 7. Additional efficacy endpoints (%)

A) MDA[a] (%)

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference arm (ADA 40 mg Q2W) N=140	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 0	1.8	1.8	3.2	3.3	0.7	0.7
Week 4	6.8	6.9	23.4	23.8	17.1	17.4
Week 8	8.9	9.4	32.3	33.3	32.9	33.8
Week 12	10.3	11.0	41.5	43.1	40.7	42.9
Week 16	13.2	14.0	45.0	46.5	45.0	46.7
Week 20	28.5	30.8	47.3	51.3	43.6	45.9
Week 24	37.7	40.8	48.5	53.5	47.9	51.1
Week 36	46.3	50.4	51.7	58.4	46.4	52.0
Week 52	53.7	59.7	55.0	62.4	52.9	60.2

1 **B) VLDA (%)**

	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference arm (ADA 40 mg Q2W) N=140	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 0	0.0	0.0	0.0	0.0	0.0	0.0
Week 4	0.4	0.4	5.3	5.4	3.6	3.6
Week 8	0.7	0.8	8.1	8.4	8.6	8.8
Week 12	2.5	2.6	12.8	13.2	13.6	14.3
Week 16	1.1	1.1	14.6	15.1	15.7	16.3
Week 20	6.4	6.9	20.9	22.6	18.6	19.5
Week 24	11.7	12.7	22.3	24.7	20.0	21.1
Week 36	19.2	20.8	26.9	30.3	22.1	25.2
Week 52	22.1	24.6	29.0	32.9	27.9	32.0

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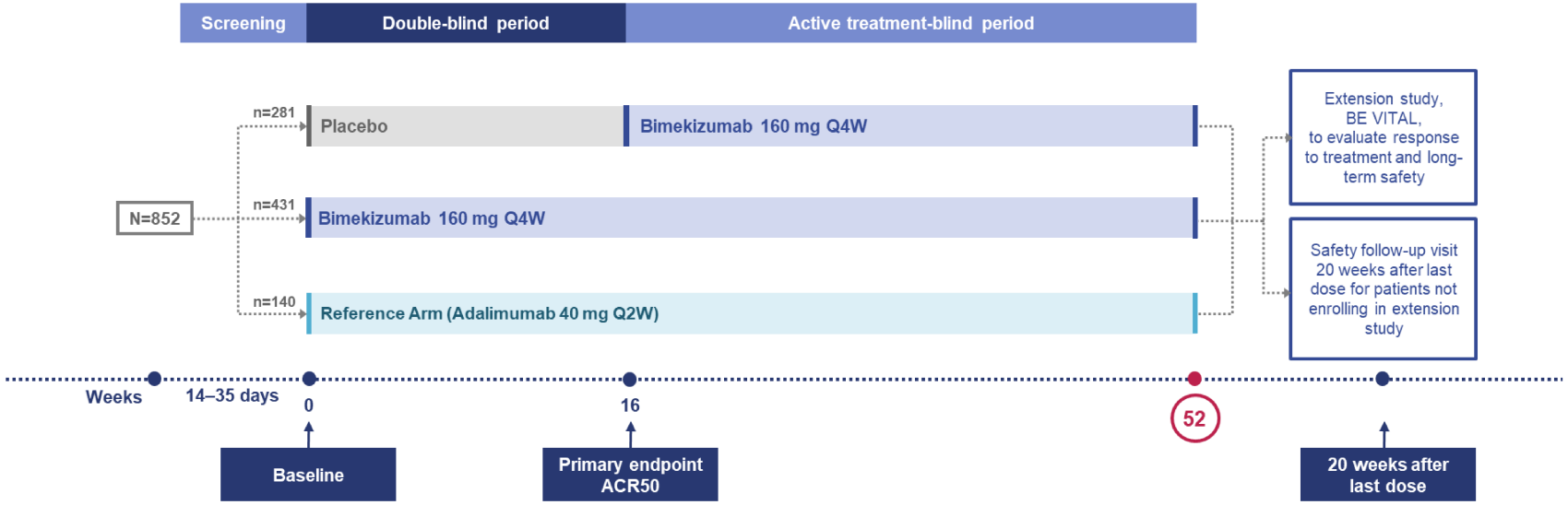
C) ACR50+PASI100[b] (%)

	PBO/BKZ 160 mg Q4W N=140		BKZ 160 mg Q4W N=217		Reference arm (ADA 40 mg Q2W) N=68	
	NRI	**OC**	**NRI**	**OC**	**NRI**	**OC**
Week 2	0.0	0.0	0.0	0.0	0.0	0.0
Week 4	0.0	0.0	5.5	5.6	0.0	0.0
Week 8	0.7	0.7	14.7	15.2	5.9	6.0
Week 12	0.0	0.0	23.0	23.9	16.2	17.5
Week 16	0.0	0.0	27.6	29.0	16.2	16.9
Week 20	11.4	12.5	33.6	36.5	22.1	23.4
Week 24	22.9	23.9	31.3	34.7	25.0	27.0
Week 36	40.7	42.9	42.4	47.7	27.9	31.1
Week 52	46.4	50.4	47.0	53.1	35.3	40.0

Randomised set. The study was not powered for statistical comparisons of ADA to BKZ or PBO. [a] MDA was a ranked secondary endpoint; [b] In patients with psoriasis affecting ≥3% BSA at baseline; PBO/BKZ: n=140; BKZ: n=217; ADA: n=68. ACR50: American College of Rheumatology ≥50% response criteria; ADA: adalimumab; BKZ: bimekizumab; BSA: body surface area; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PASI100: Psoriasis Area and Severity Index 100% improvement; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; VLDA: very low disease activity.

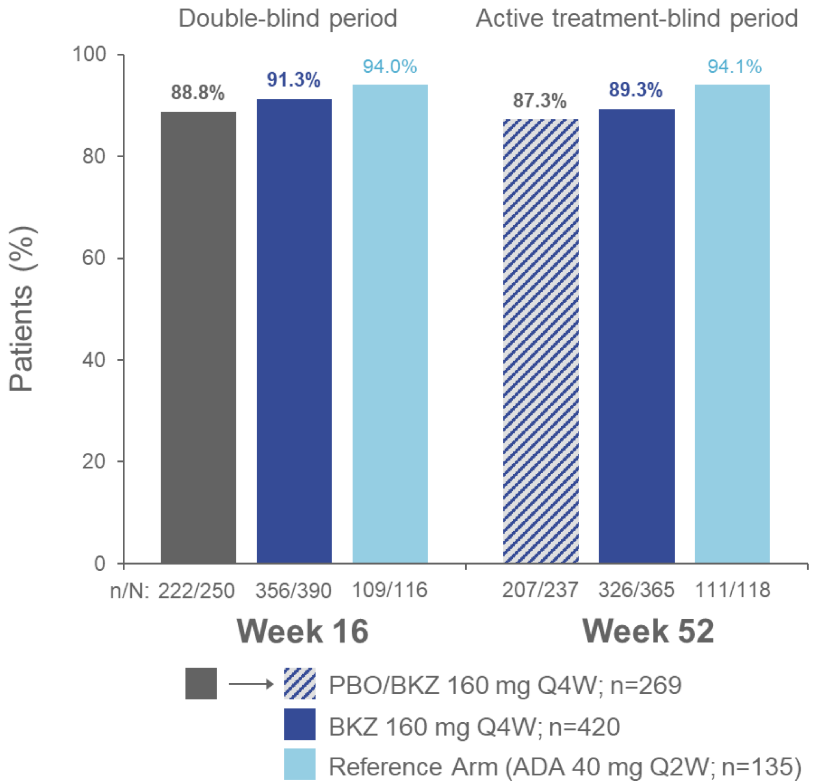
Supplementary Figure 1. Study design



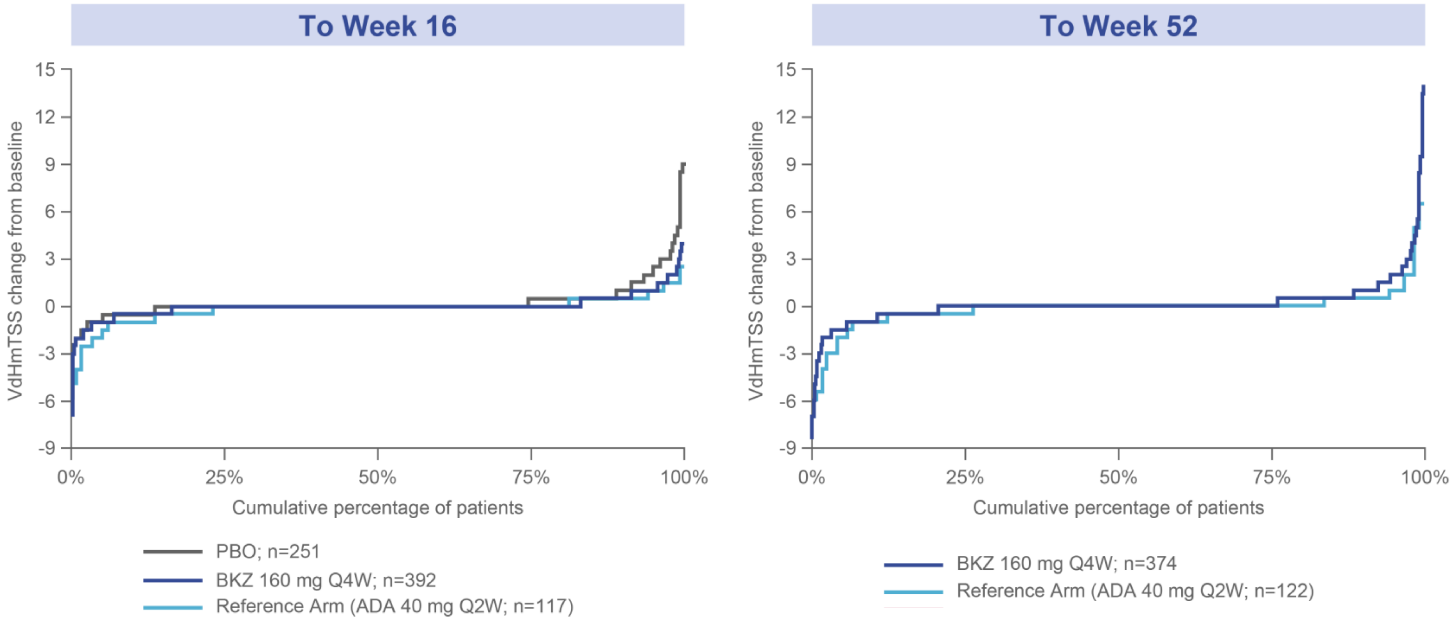
Randomised set. BKZ-treated patients eligible to receive rescue therapy from Week 16 at the discretion of the investigator, while continuing to receive BKZ. ACR50: American College of Rheumatology 50% response criteria; BKZ: bimekizumab; Q2W: every 2 weeks; Q4W: every 4 weeks.

Supplementary Figure 2. Radiographic inhibition outcomes [OC]

(A) Proportion of patients with no radiographic progression (vdHmTSS CfB ≤0.5) at Week 16 and Week 52



(B) Cumulative probability plots of vdHmTSS CfB to Week 16 and Week 16–52



Radiographic set (patients who received ≥1 study drug dose and had valid radiographs of hands and feet, assessed by ≥2 reviewers, at screening). Observed case data reported. Cumulative probability in each dose group in the range of 0–100%. Lower vdHmTSS scores indicate more inhibition achieved. [a] Includes patients randomised to PBO at baseline who switched to BKZ at Week 16. ADA: adalimumab; BKZ: bimekizumab; CfB: change from baseline; OC: observed case; PBO: placebo; Q2W: every two weeks; Q4W: every 4 weeks; vdHmTSS: van der Heijde modified Total Sharp Score.