# Bimekizumab in Patients with Active Psoriatic Arthritis and an Inadequate Response to Tumour Necrosis Factor Inhibitors: 16-Week Efficacy and Safety from BE COMPLETE, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study



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## Disclosures

**JFM:** Consultant and/or investigator for AbbVie, Amgen, Bayer, Biogen, BMS, Celgene, Dermavant, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi-Regeneron Sun Pharma, and UCB Pharma. **IBM:** Consulting fees and honoraria from AbbVie, BMS, Boehringer Ingelheim, Celgene, Janssen, Lilly, Novartis, and UCB Pharma; Research support from BMS, Boehringer Ingelheim, Celgene, Janssen, and UCB Pharma. **CR:** Research grants from AbbVie, Amgen, and UCB Pharma; Consultant for AbbVie, Amgen, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma. **PJM:** Member of the speakers' bureau for AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB Pharma; Consultancy fees from AbbVie, Amgen, BMS, Boehringer Ingelheim, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; Research grants from AbbVie, Amgen, BMS, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma. **RL:** Consultancy fees from Abbott, Ablynx, Amgen, AstraZeneca, BMS, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, and Wyeth; Research grants from Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, and Wyeth; Speaker's bureau from Abbott, Amgen, BMS, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, and Wyeth. **AA:** Honoraria and/or research grants from AbbVie, Amgen, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, and UCB Pharma. **YT:** Member of the speaker's bureaus for AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer-Ingelheim, Chugai, Eisai, Eli Lilly, Gilead, Mitsubishi-Tanabe, and YL Biologics; Research Grants for AbbVie, Asahi-Kasei, Boehringer-Ingelheim, Chugai, Corrona, Daiichi-Sankyo, Eisai, Kowa, Mitsubishi-Tanabe, and Takeda; Consultant fee for AbbVie, Ayumi, Daiichi-Sankyo, Eli Lilly, GSK, Sanofi, and Taisho. **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. **LG:** Research grants from Amgen, Galapagos, Lilly, Pfizer, Sandoz, and UCB Pharma; Consulting fees from: AbbVie, Amgen, BMS, Celltrion, Galapagos, Gilead, GSK, Janssen, Lilly, Novartis, Pfizer, and UCB Pharma. **DDG:** Grants from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB Pharma; Consulting fees from AbbVie, Amgen, BMS, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma. **FB:** Consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Galapagos, Genzyme, GSK, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma. **BI:** Employee of UCB Pharma and a shareholder of GSK and UCB Pharma. **DA, RB, JC:** Employees and stockholders of UCB Pharma. **LCC:** Grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma; Paid consultant for AbbVie, Amgen, Boehringer Ingelheim, BMS, Celgene, Domain, Eli Lilly, Gilead, Galapagos, Janssen, Moonlake, Novartis, Pfizer and UCB Pharma; Paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Medac, Novartis, Pfizer and UCB Pharma.

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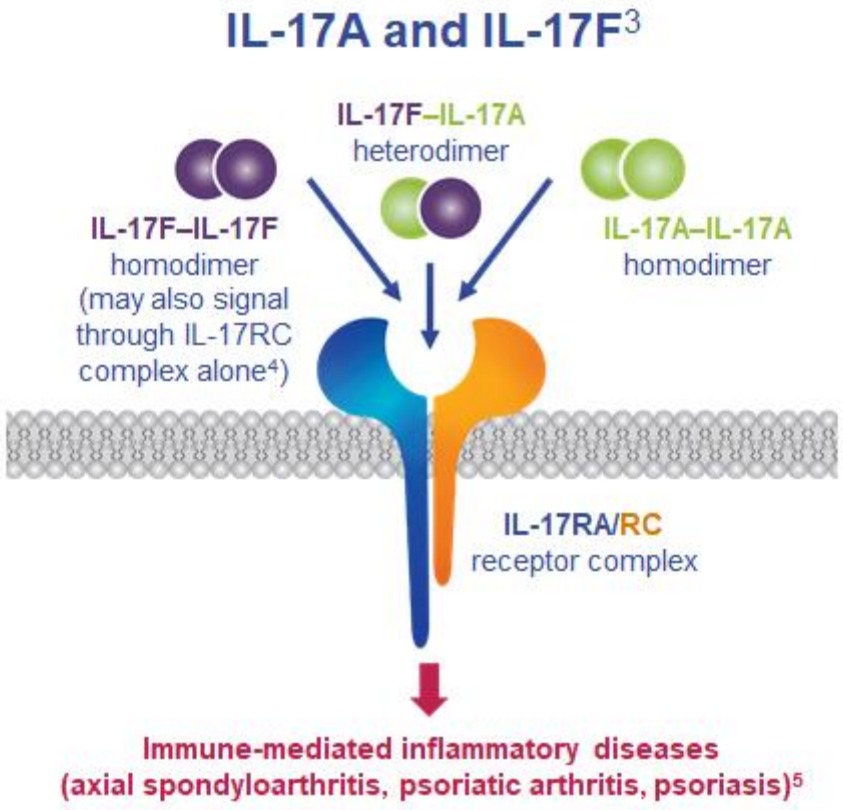
# Background & Objective

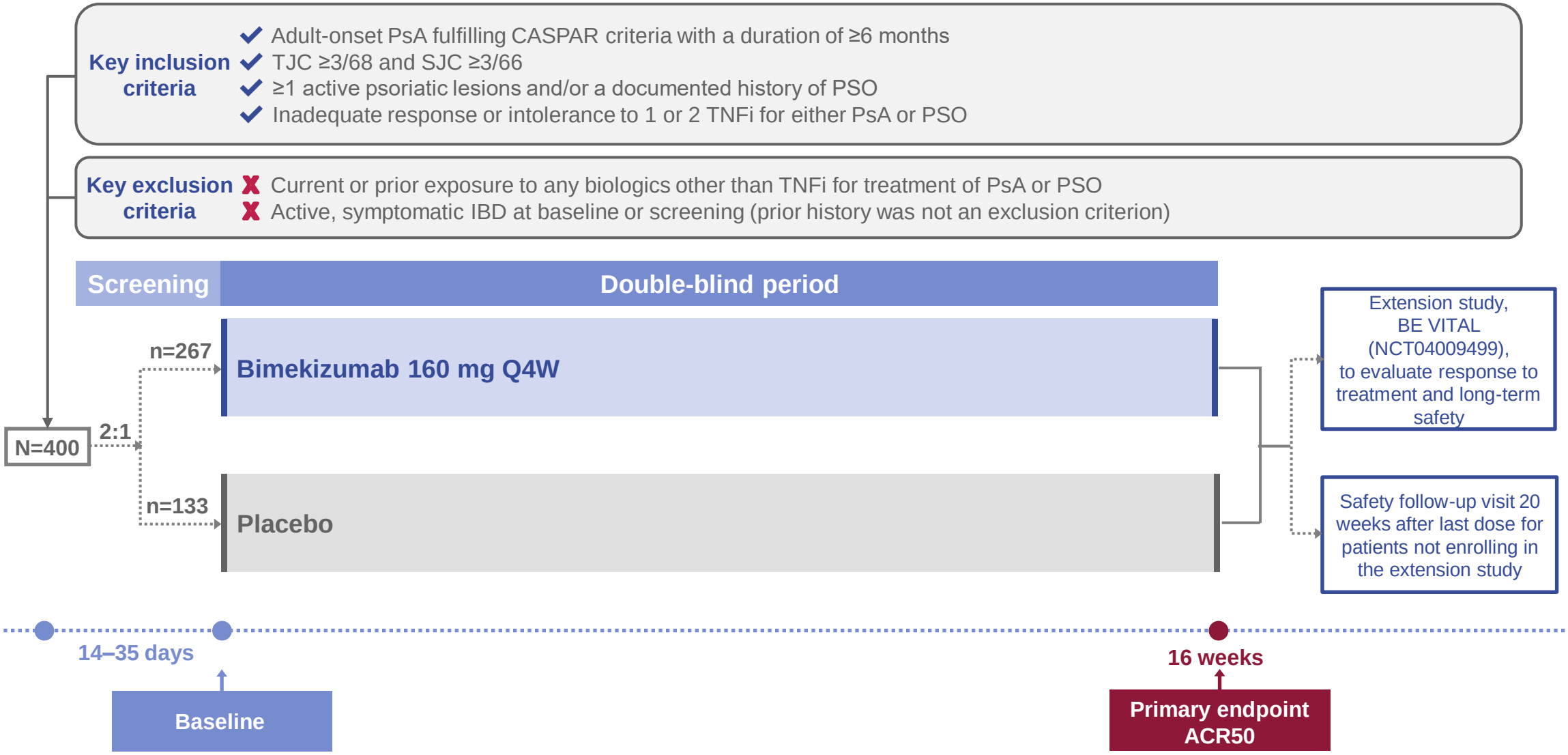
- **Bimekizumab** is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- Bimekizumab has shown rapid and sustained efficacy and was well tolerated up to 152 weeks in a phase 2b study in patients with active psoriatic arthritis (PsA).[1,2]




**OBJECTIVE:** To assess efficacy and safety of subcutaneous bimekizumab vs placebo in patients with active PsA and prior inadequate response or intolerance to tumour necrosis factor inhibitor up to Week 16 in the pivotal phase 3 study, BE COMPLETE

1. Ritchlin CT Lancet 2020;395(10222):427–40; 2. Coates LC Ann Rheum Dis 2021;80:779–80(POS1022); 3. Yang XO J Exp Med 2008;1063–75; 4. Goepfert A Immunity 2020;52(3):499–512.e5;
5. Glatt S Ann Rheum Dis 2018;77:523–32. Ig: immunoglobulin; IL: interleukin; PsA: psoriatic arthritis; RA: receptor A; RC: receptor C.

# Study Design




ACR: American College of Rheumatology; CASPAR: Classification Criteria for Psoriatic Arthritis; IBD: inflammatory bowel disease; PsA: psoriatic arthritis; PSO: psoriasis; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor; Q4W: every 4 weeks.

# Primary, Secondary and Other Endpoints

## Primary endpoint

- ACR50 response at Week 16

## Ranked secondary endpoints

- HAQ-DI CfB at Week 16
- PASI90 response at Week 16
- SF-36 PCS CfB at Week 16
- MDA response at Week 16

## Secondary and other efficacy endpoints

- ACR20 and ACR70 response at Week 16
- PASI75 and PASI100 response at Week 16
- TJC and SJC CfB at Week 16
- Proportion of patients with a decrease in HAQ-DI ≥0.35 at Week 16

## Safety endpoints

- Incidence of TEAEs, treatment-emergent SAEs and TEAEs leading to withdrawal

ACR20/50/70: American College of Rheumatology criteria ≥20/50/70% response; CfB: change from baseline; HAQ-DI: Health Assessment Questionnaire-Disability Index; MDA: minimal disease activity; PASI75/90/100: ≥75/90/100% improvement in PASI; PCS: Physical Component Summary; SAE: serious adverse event; SF-36: Short-Form 36-item Health Survey; SJC: swollen joint count; TEAE: treatment-emergent adverse event; TJC: tender joint count.

# Patient Demographics and Baseline Disease Characteristics

| | Placebo n=133 | BKZ 160 mg Q4W n=267 |
|---|---|---|
| **Age**, years, mean (SD) | 51.3 (12.9) | 50.1 (12.4) |
| **Sex**, male, n (%) | 60 (45.1) | 130 (48.7) |
| **BMI**, kg/m$^2$, mean (SD) | 29.0 (5.4) | 30.1 (6.5) |
| **PsA duration**,[a] years, mean (SD) | 9.2 (8.1) | 9.6 (9.9) |
| **Concomitant methotrexate**, n (%) | 51 (38.3) | 119 (44.6) |
| **Prior TNFi exposure**, n (%)<br>Inadequate response to 1 TNFi<br>Inadequate response to 2 TNFi<br>Intolerance to TNFi | <br>103 (77.4)<br>15 (11.3)<br>15 (11.3) | <br>204 (76.4)<br>29 (10.9)<br>34 (12.7) |
| **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) |
| **Psoriasis BSA ≥3%**, n (%) | 88 (66.2) | 176 (65.9) |
| **PASI score**,[b] mean (SD) | 8.5 (6.6) | 10.1 (9.1) |
| **HAQ-DI**, mean (SD) | 1.0 (0.7) | 1.0 (0.6) |
| **PtAAP**,[c] mean (SD) | 61.7 (24.6) | 58.3 (24.2) |
| **SF-36 PCS**, mean (SD) | 35.9 (0.9) | 36.4 (0.5) |
| **Enthesitis**,[d] n (%)<br>Score, mean (SD) | 36 (27.1)<br>2.9 (1.6) | 106 (39.7)<br>2.6 (1.5) |
| **Dactylitis**,[e] n (%)<br>Score, mean (SD) | 14 (10.5)<br>66.4 (127.6) | 34 (12.7)<br>72.7 (114.4) |

Randomised set. [a] Listed as time since diagnosis of PsA, data missing for one patient receiving placebo and one patient receiving BKZ; [b] In patients with PSO involving ≥3% BSA at baseline; [c] PtAAP VAS 0–100; [d] Leeds Enthesitis Index >0; [e] Leeds Dactylitis Index >0. BKZ: bimekizumab; BMI: body mass index; BSA: body surface area; HAQ-DI: Health Assessment Questionnaire-Disability Index; hs-CRP: high-sensitivity C-reactive protein; PASI: Psoriasis Area and Severity Index; PCS: Physical Component Summary; PsA: psoriatic arthritis; PSO: psoriasis; PtAAP: Patient's Assessment of Arthritis Pain; Q4W: every 4 weeks; SD: standard deviation; SF-36: Short-Form 36-item Health Survey; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor; VAS: visual analogue scale.

# BE COMPLETE Met Primary and All Ranked Secondary Endpoints (Week 16)

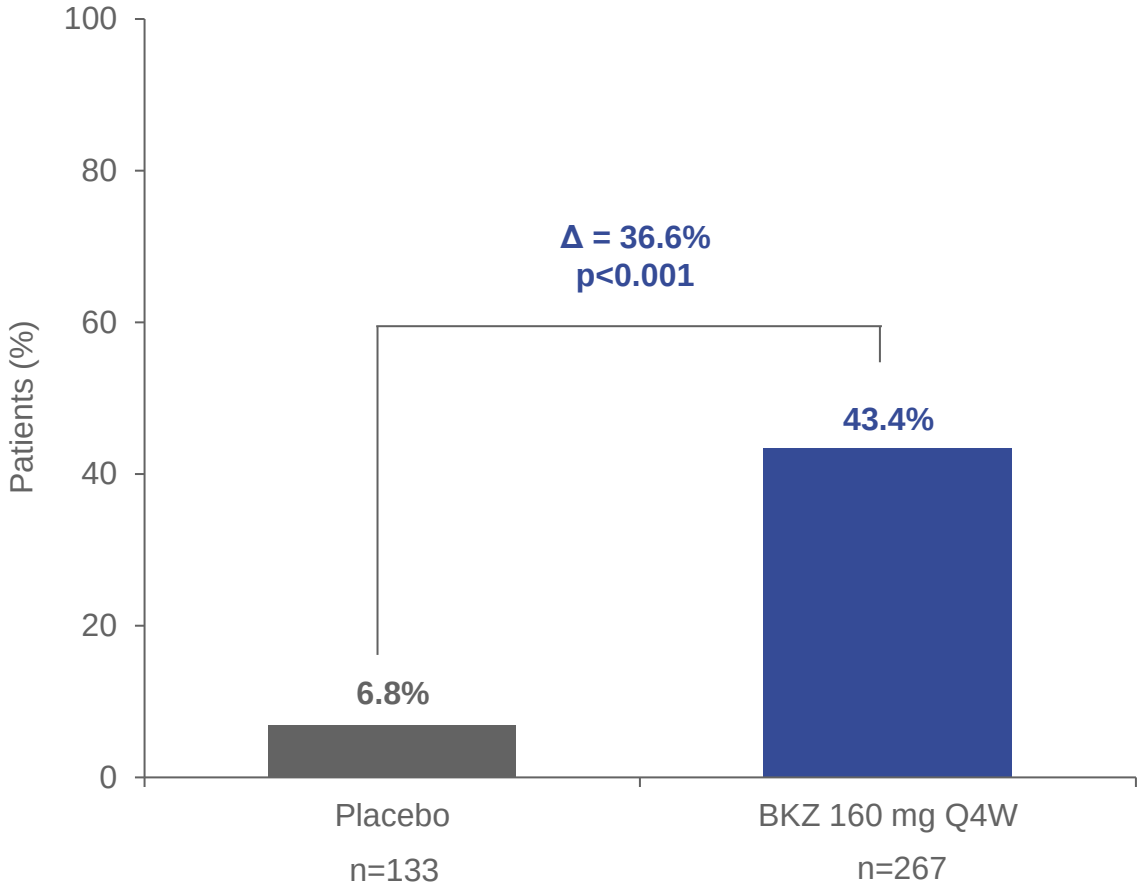
| | Efficacy endpoint | p value[a] | Statistically significant | Odds ratio[a] BKZ vs placebo (95% CI)[b] | Least squares mean difference BKZ vs placebo (95% CI)[b] |
|---|---|---|---|---|---|
| 1 | ACR50 (NRI) | <0.001 | Yes | 11.1 (5.4, 22.9) | – |
| 2 | HAQ-DI CfB (RBMI) | <0.001 | Yes | – | –0.3 (–0.4, –0.2) |
| 3 | PASI90 (NRI)[c] | <0.001 | Yes | 30.2 (12.4, 73.9) | – |
| 4 | SF-36 PCS CfB (RBMI) | <0.001 | Yes | – | +6.0 (+4.4, +7.7) |
| 5 | MDA Response (NRI) | <0.001 | Yes | 13.0 (6.1, 27.9) | – |

Randomised set. For binary variables, p values were obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. For continuous variables, p values were obtained from ANCOVA with treatment, prior TNF inhibitor exposure and region as fixed effects and the baseline value as covariate [a] Tests performed at a 2-sided alpha level of 0.05. [b] Odds ratio for binary variables and least squares mean difference BKZ vs placebo for continuous variables. [c] In patients with PSO involving ≥3% BSA at baseline. ACR50: American College of Rheumatology criteria ≥50% response; ANCOVA: Analysis of Covariance; BKZ: bimekizumab; BSA: body surface area; CfB: change from baseline; CI: confidence interval; HAQ-DI: Health Assessment Questionnaire-Disability Index; MDA: Minimal Disease Activity; NRI: non-responder imputation; PASI90: ≥90% improvement in PASI; PCS: Physical Component Summary; PSO: psoriasis; RBMI: reference-based multiple imputation; SF-36: Short-Form 36-item Health Survey; TNF: tumour necrosis factor.

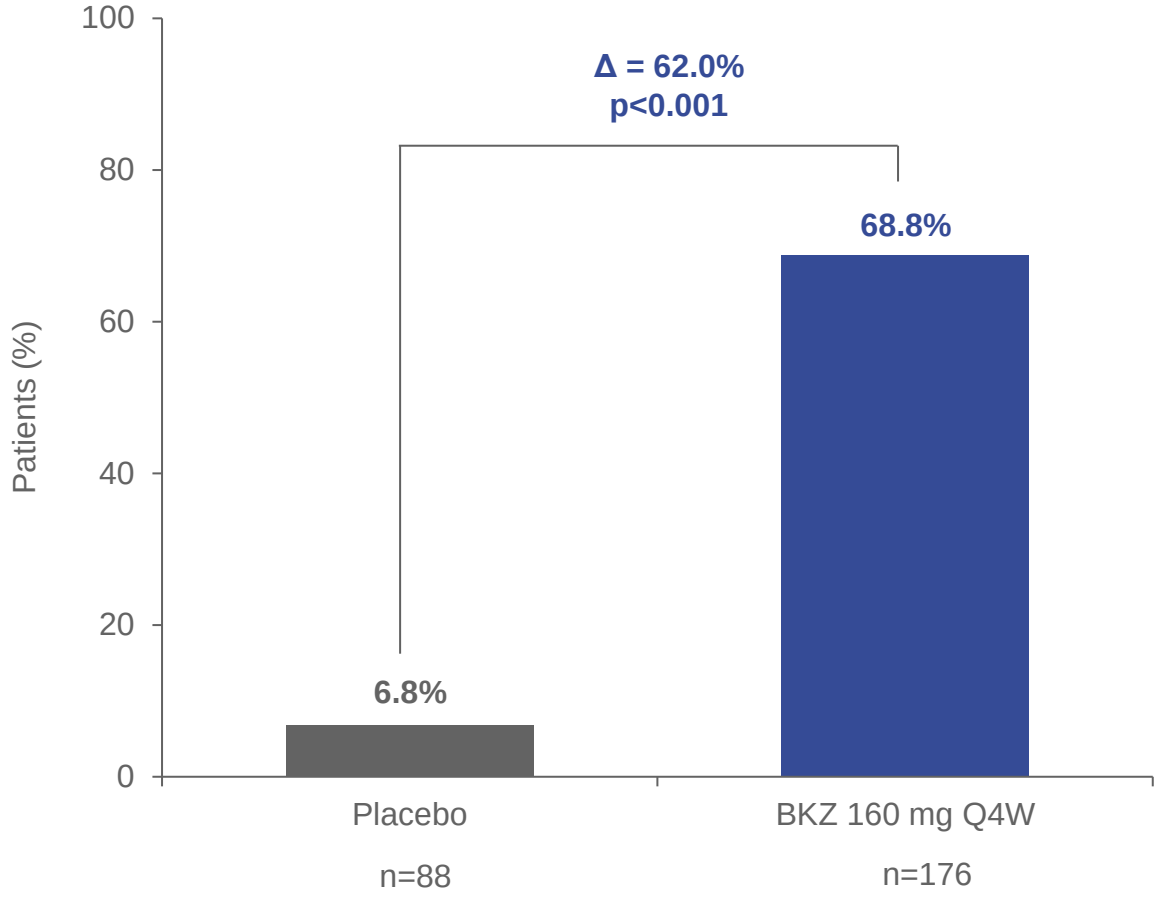
# Efficacy: ACR50 and PASI90 Responses at Week 16 (NRI)

**BKZ demonstrated superiority vs placebo in improvements in joint and skin outcomes at Week 16**

## Primary Endpoint: ACR50



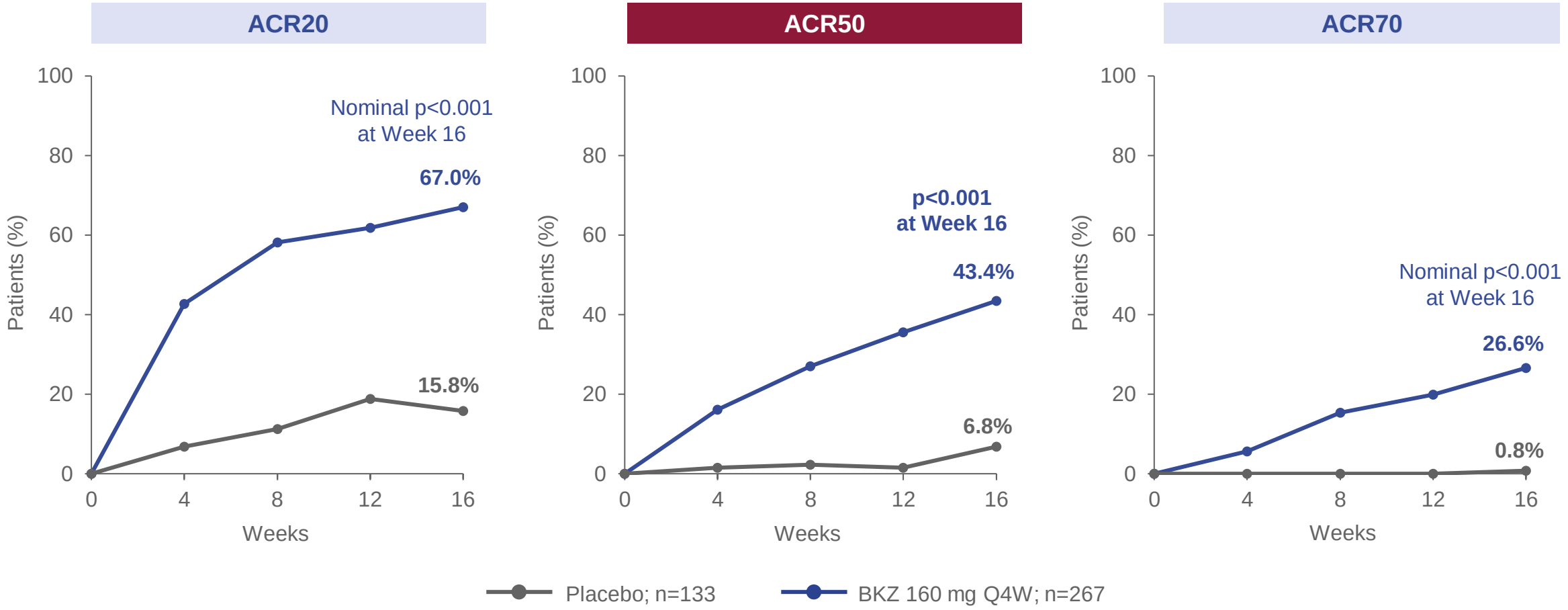

## PASI90[a]




Randomised set. p values were obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. [a] In patients with PSO involving ≥3% BSA at baseline. ACR50: American College of Rheumatology criteria ≥50% response; BKZ: bimekizumab; BSA: body surface area; NRI: non-responder imputation; PASI90: ≥90% improvement in PASI; PSO: psoriasis; Q4W: every 4 weeks.

# Efficacy: ACR Response Criteria to Week 16 (NRI)

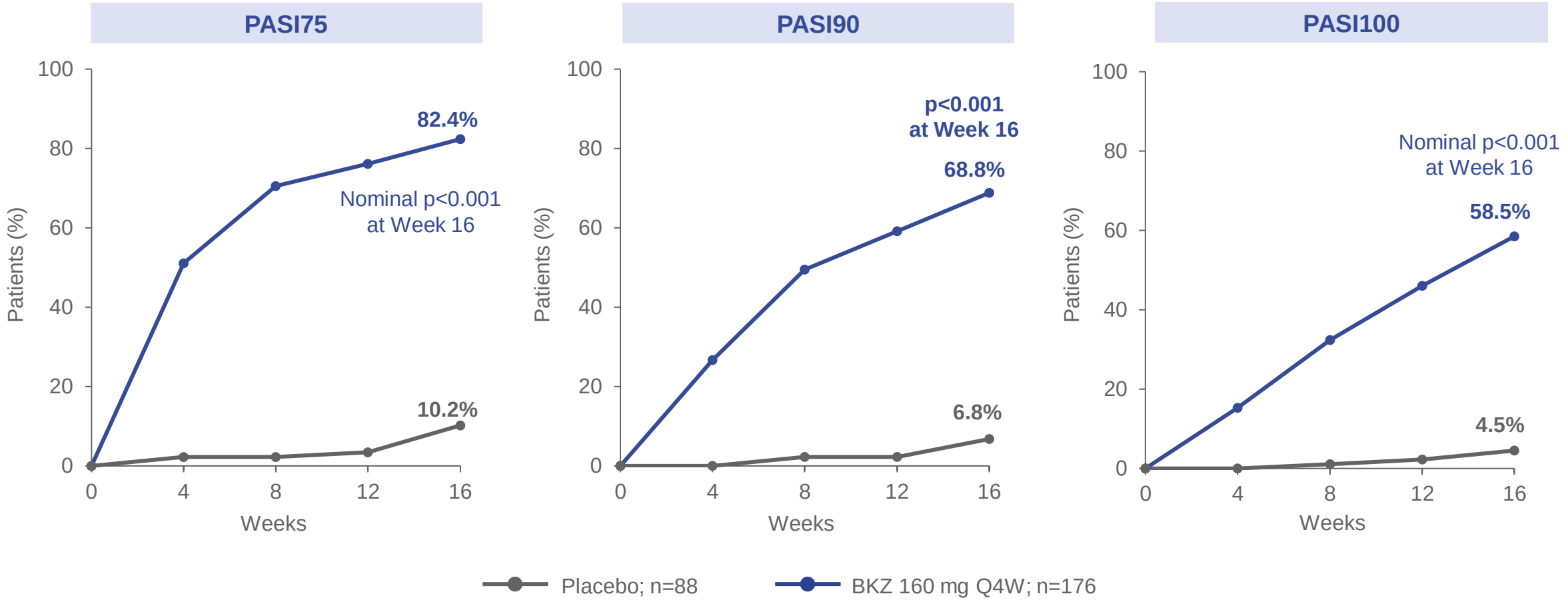
**BKZ demonstrated improvements vs placebo in achievement of all ACR response criteria at Week 16**




Randomised set. p values were obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. Nominal p values were not adjusted for multiplicity. ACR20/50/70: American College of Rheumatology criteria ≥20/50/70% response; BKZ: bimekizumab; NRI: non-responder imputation; Q4W: every 4 weeks; TNF: tumour necrosis factor.

# Efficacy: Psoriasis Area and Severity Index to Week 16 (NRI)

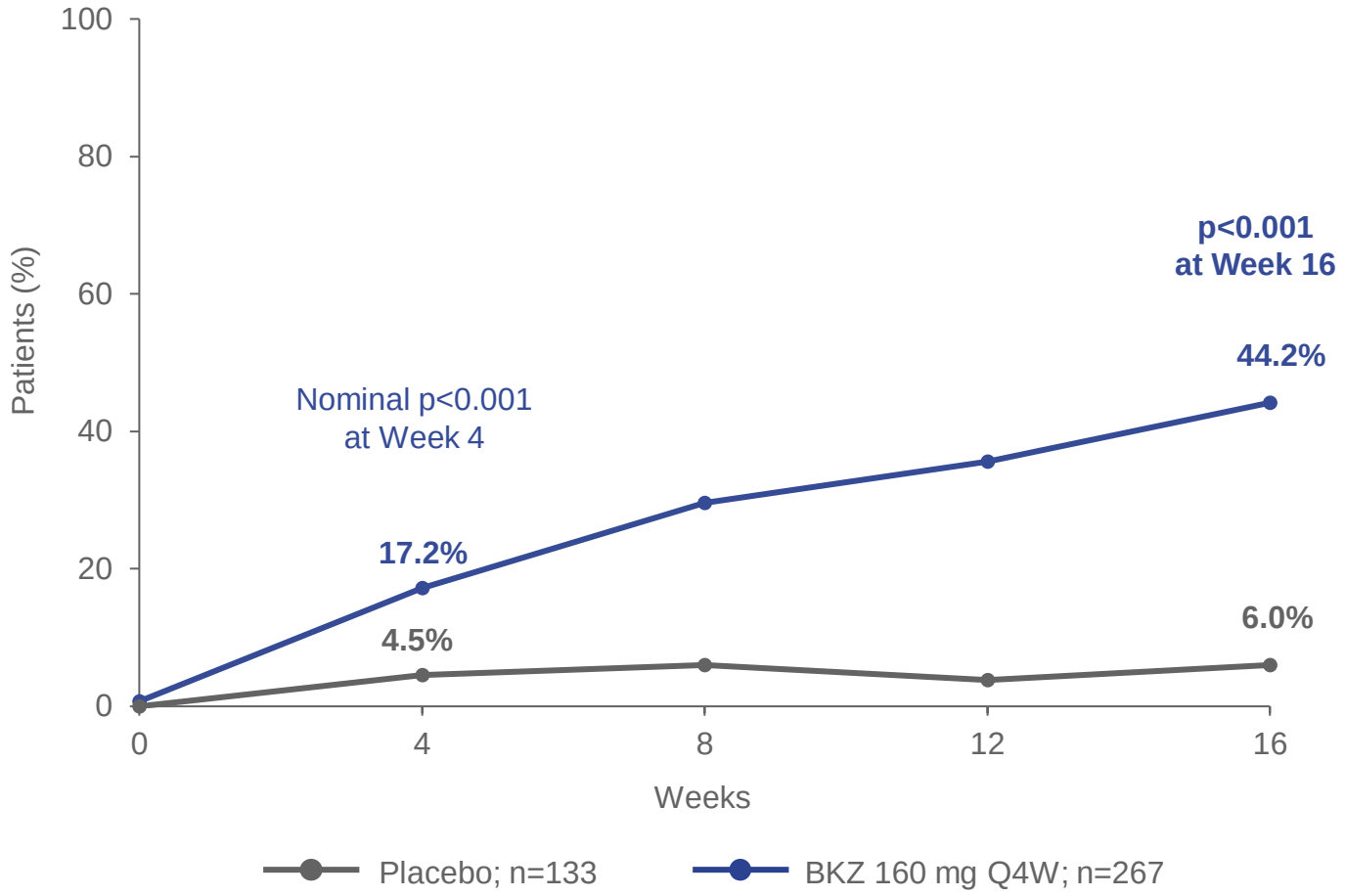
**Over half of BKZ patients achieved complete skin clearance at Week 16**




Randomised set, in patients with PSO involving ≥3% BSA at baseline. p values were obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. Nominal p values were not adjusted for multiplicity. BKZ: bimekizumab; BSA: body surface area; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PASI75/90/100: ≥75/90/100% improvement in PASI; PSO: psoriasis; Q4W: every 4 weeks; TNF: tumour necrosis factor.

# Efficacy: Proportion of Patients Achieving MDA to Week 16 (NRI)

**BKZ demonstrated superiority vs placebo in achievement of MDA response (composite index) at Week 16**




**MDA response defined as achievement of at least 5 of the 7 following criteria:**

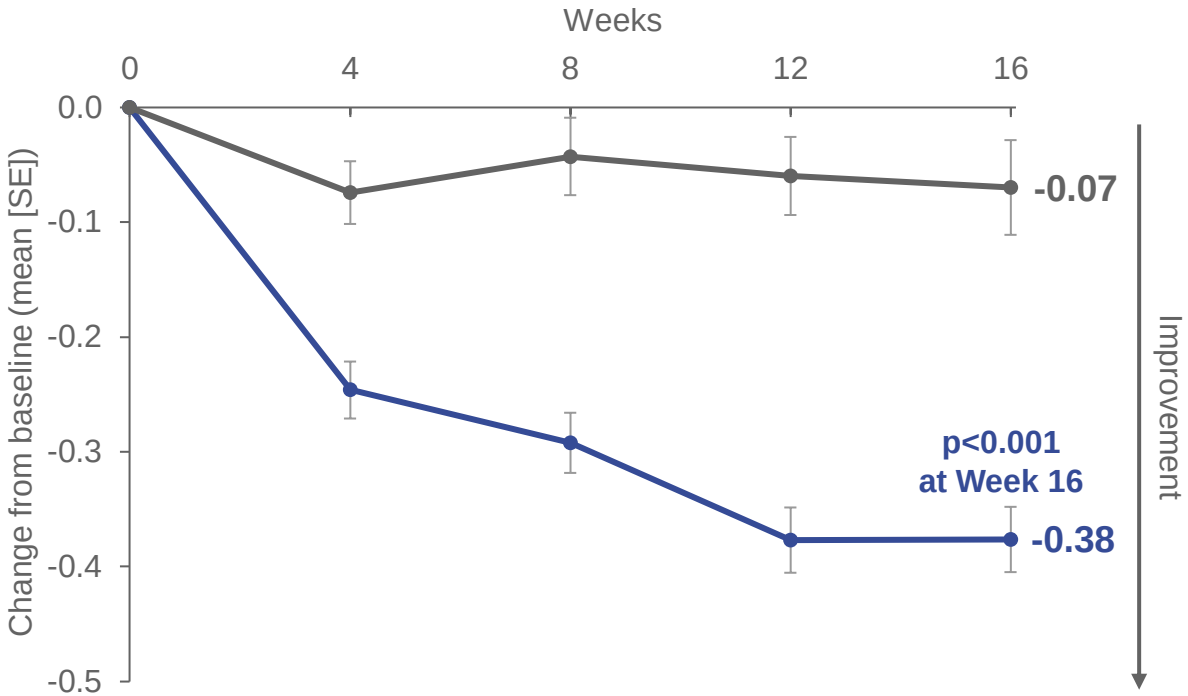
- Tender joint count ≤1
- Swollen joint count ≤1
- Psoriasis Area and Severity Index ≤1[a] or body surface area ≤3%[b]
- Patient's Assessment of Arthritis Pain ≤15 mm
- Patient's Global Assessment-PsA ≤20 mm
- Health Assessment Questionnaire-Disability Index ≤0.5
- Leeds Enthesitis Index ≤1

Randomised set. p value obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. Nominal p values were not adjusted for multiplicity. [a] For patients with PSO involving ≥3% of BSA at baseline. [b] Subjects with PSO involving <3% of BSA at baseline will always meet the criteria PASI ≤1 or BSA ≤3% except in the cases where a BSA score ≥3% is observed. BKZ: bimekizumab; BSA: body surface area; MDA: minimal disease activity; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; PSO: psoriasis; Q4W: every 4 weeks.

# Efficacy: Physical Functioning to Week 16 (MI)

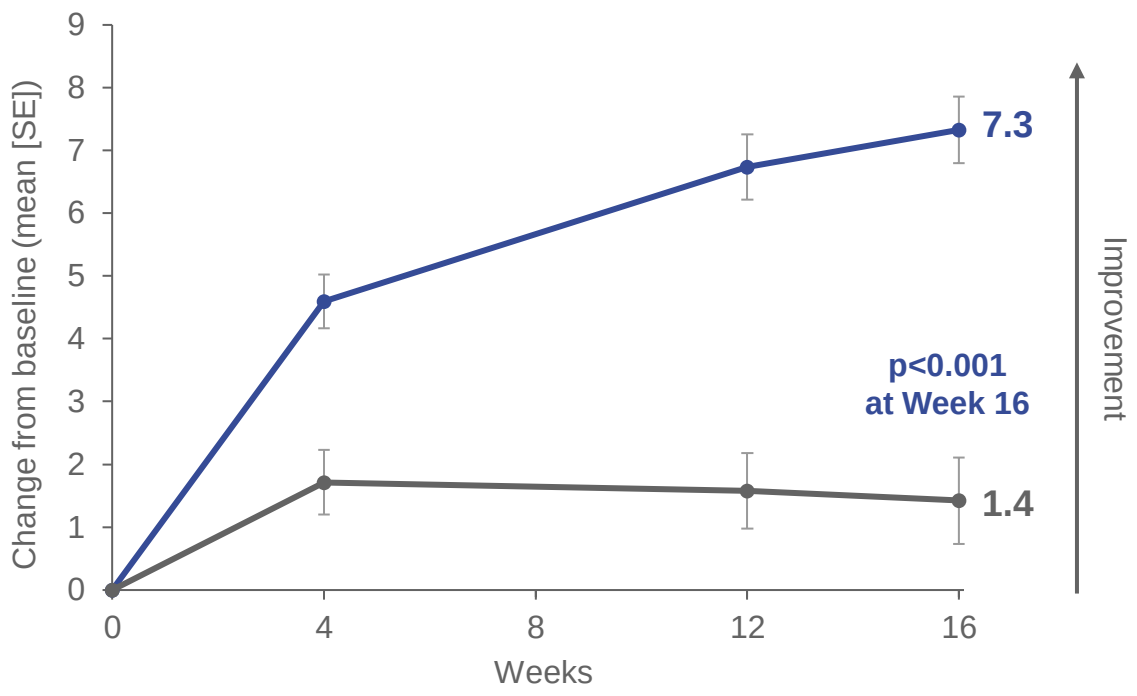
**BKZ demonstrated superiority vs placebo in improvements in physical functioning at Week 16**

## HAQ-DI CfB




| BL HAQ-DI, mean (SD) | 1.0 (0.7) | 1.0 (0.6) |
|---|---|---|

## SF-36 PCS CfB



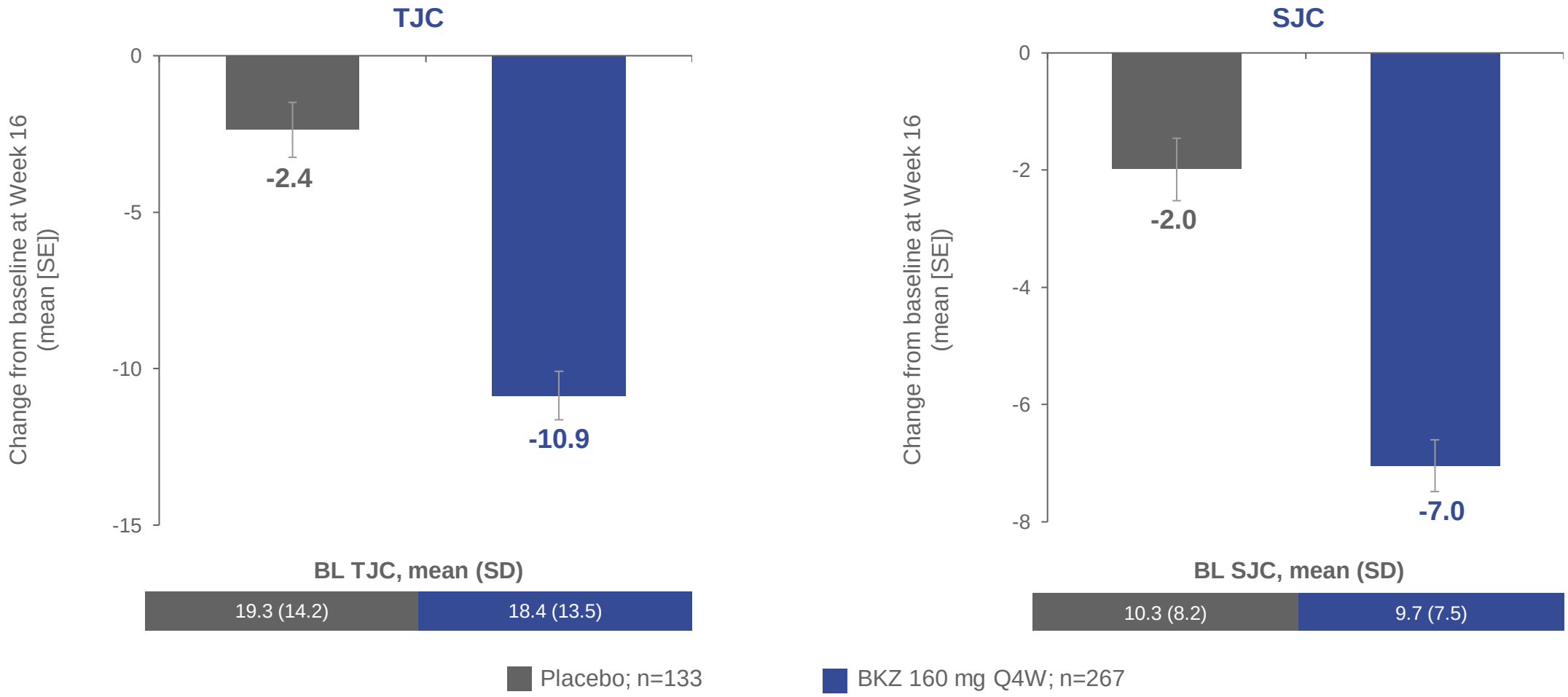

| BL SF-36, mean (SD) | 35.9 (10.2) | 36.4 (9.0) |
|---|---|---|

Placebo; n=133 BKZ 160 mg Q4W; n=267

Randomised set. p value obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. BKZ: bimekizumab; BL: baseline; CfB: change from baseline; HAQ-DI: Health Assessment Questionnaire-Disability Index; MI: multiple imputation; PCS: Physical Component Summary; Q4W: every 4 weeks; SF-36: Short-Form 36-item Health Survey.

# Efficacy: TJC and SJC CfB at Week 16 (MI)

**BKZ demonstrated numerically greater reduction of tender and swollen joints at Week 16**




Randomised set. BKZ: bimekizumab; BL: baseline; CfB: change from baseline; MI: multiple imputation; Q4W: every 4 weeks; SD: standard deviation; SE: standard error; SJC: swollen joint count; TJC: tender joint count.

# Safety: Overall

| n (%) | Placebo n=132[a] | BKZ 160 mg Q4W n=267 |
|---|---|---|
| Any TEAE | 44 (33.3) | 107 (40.1) |
| Serious TEAEs | 0 | 5 (1.9) |
| Discontinuation due to TEAEs | 0 | 2 (0.7) |
| Drug-related TEAEs | 4 (3.0) | 35 (13.1) |
| Severe TEAEs | 0 | 5 (1.9) |
| Deaths | 0 | 0 |
| Most frequently reported TEAEs on the BKZ arm | | |
| Nasopharyngitis | 1 (0.8) | 10 (3.7) |
| Oral candidiasis[b] | 0 | 7 (2.6) |
| Upper respiratory tract infection | 2 (1.5) | 6 (2.2) |
| Fungal infections[c] | 0 | 12 (4.5) |
| Systemic fungal infections | 0 | 0 |
| Neutropenia[d] | 0 | 4 (1.5) |
| Hypersensitivity | 1 (0.8) | 7 (2.6) |
| Anaphylactic reactions | 0 | 0 |
| Dermatitis and eczema | 0 | 4 (1.5) |
| Injection site reactions | 0 | 3 (1.1) |
| Liver function test changes/enzyme elevations | | |
| ALT >3x ULN | 0 | 2 (0.7) |
| AST or ALT >3x ULN | 0 | 4 (1.5) |
| Biochemistry Hy's Law[e] | 0 | 0 |

Safety set. [a] One patient included in the randomised set was not counted in the safety set. [b] 6 out of 7 cases classified by investigator as mild in intensity, 1 out of 7 cases classified as moderate in intensity; one case resulted in discontinuation. [c] All fungal infections were mild to moderate; there were no cases of systemic/disseminated *Candida* infection. [d] Neutropenia were generally transient and not associated with serious infections; 3 patients had neutropenia and 1 had decreased neutrophil count. [e] Patient must experience the elevation in bilirubin and ALT or AST (and the absence of ALP elevation, if applicable) at the same visit. ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BKZ: bimekizumab; MACE: major adverse cardiovascular event; n: number of patients reporting at least one TEAE in that category; Q4W: every 4 weeks; SIB: suicidal ideation behaviour; TEAE: treatment emergent adverse event; ULN: upper limit of normal.

# BE COMPLETE Conclusions

The BE COMPLETE phase 3 study, evaluating dual inhibition of IL-17A and IL-17F with bimekizumab in patients with PsA with inadequate response or intolerance to TNFi, met all its primary and secondary endpoints.

Bimekizumab-treated patients with PsA and inadequate response or intolerance to TNFi showed improvements in joint, skin and HRQoL-related outcomes up to Week 16, compared with placebo.

Furthermore, bimekizumab treatment resulted in improvements in the composite outcome of minimal disease activity, reflecting the efficacy of dual inhibition across PsA disease manifestations.

Bimekizumab treatment led to rapid improvements in signs and symptoms of PsA, with separation from placebo observed by Week 4.

Bimekizumab was well tolerated; the safety profile was consistent with prior studies with no unexpected safety findings.[1,2]

1. Ritchlin CT Lancet 2020;395(10222):427–40; 2. Coates LC Ann Rheum Dis 2021;80:779–80(POS1022). HRQoL: health-related quality of life; IL: interleukin; PsA: psoriatic arthritis; TNFi: tumour necrosis factor inhibitor.

# Thank You

Any Questions?