Head-to-head study of bimekizumab, an IL-17A/IL-17F inhibitor, and risankizumab, an IL-23 inhibitor, in patients with active psoriatic arthritis: Study design and rationale of BE BOLD, a phase 3b, randomized, parallel-group study

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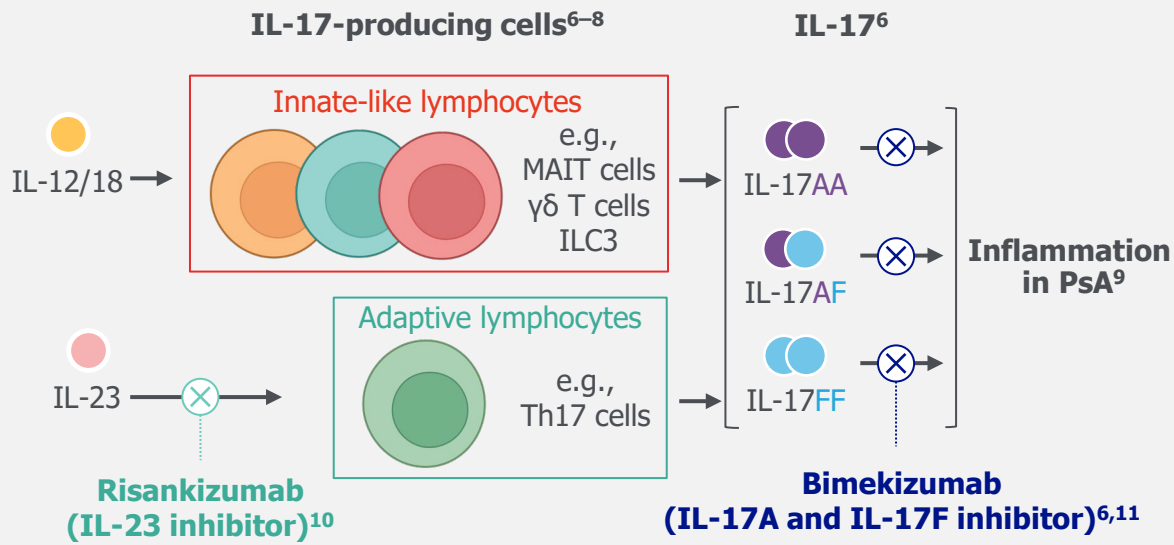
OBJECTIVE

- To describe **BE BOLD**, the **first head-to-head study** designed to compare the **efficacy and safety of bimekizumab (BKZ)** and **risankizumab (RZB)** in patients with active psoriatic arthritis (PsA).

Background

- There are limited data available to guide clinicians in selecting a treatment based on biological mechanism of action in patients with active PsA. To date, no head-to-head studies of biologic treatments[a] using joint efficacy endpoints have shown superiority in PsA.[1]
- BKZ, a monoclonal antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated efficacy and tolerability in PsA.[2] RZB, an IL-23 inhibitor, has also demonstrated efficacy and tolerability in PsA.[3,4]
- IL-23-responsive cells are a significant source of IL-17A and IL-17F. However, **IL-17A and IL-17F**, notably IL-17F, can also be **produced independently of IL-23**, particularly by innate immune cells.[5]
- We hypothesize that BKZ will be superior to RZB in joint efficacy at Week 16, by blocking IL-17A and IL-17F derived from both IL-23-dependent and -independent sources.

Bimekizumab and Risankizumab MoA



[a] Biologic disease-modifying antirheumatic drugs. **1.** Gossec L et al. Ann Rheum Dis 2024;83:706–19; **2.** Mease PJ et al. Rheumatol Ther 2024;11:1363–82 (NCT03895203, NCT03896581, NCT04009499); **3.** Kristensen LE et al. Rheumatol Ther 2024;11:617–32 (NCT03675308); **4.** Östör A et al. Rheumatol Ther 2024;11:633–48 (NCT03671148); **5.** Navarro Compán V et al. Front Immunol 2023;14:1191782; **6.** Tsukazaki H, Kaito T. Int J Mol Sci 2020;21:6401; **7.** Cole S et al. Front Immunol 2020;11:585134; **8.** Łukasik Z et al. Rheumatology (Oxford) 2021;60(Suppl 4):iv16–27; **9.** Wang EA et al. Eur J Rheumatol 2017;4:272–7; **10.** Pang Y et al. Clin Transl Sci 2024;17:e13706; **11.** Glatt S et al. Ann Rheum Dis 2018;77:523–32. BKZ: bimekizumab; IL: interleukin; MAIT: mucosal-associated invariant T; MoA: mechanism of action; PsA: psoriatic arthritis; RZB: risankizumab; Th: T helper.

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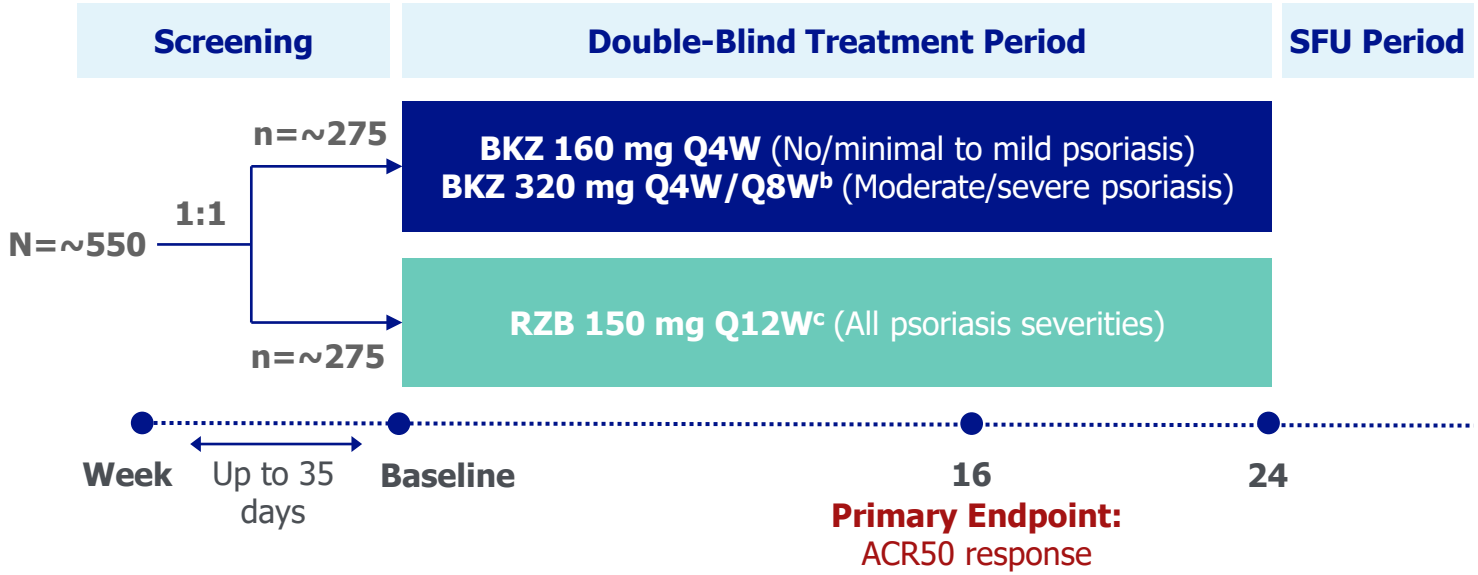
Methods

- BE BOLD (NCT06624228) is a **multicenter, phase 3b, randomized, double-blinded, active-controlled, parallel-group** study.
- Patients will be **dosed according to approved BKZ and RZB labels** for patients with PsA[1–4] **based on psoriasis severity** at baseline.

Psoriasis Severity Definitions

No/minimal psoriasis	BSA <3%
Mild psoriasis	BSA ≥3% to <10% **or** BSA ≥10% and either IGA score <3 or PASI score <12
Moderate/severe psoriasis	BSA ≥10%, IGA score ≥3 and PASI score ≥12

BE BOLD Study Design[a]



Dosing Scheme in Line with Approved Labels

Treatment arm	Week BL	4	8	12	16	20	24
BKZ 160 mg Q4W (No/minimal to mild psoriasis)	●	●	●	●	●	●	End of double-blind period
BKZ 320 mg Q4W/Q8W[b] (Moderate/severe psoriasis)	●	●	●	●	●	○	
RKZ 150 mg Q12W[c] (All psoriasis severities)	●	●	○	○	●	○	

● BKZ or RZB dose ○ Placebo dose (to maintain the blind)

[a] This represents a planned study protocol which may be amended before the study commences; **[b]** 320 mg Q4W to Week 16, then 320 mg Q8W; **[c]** 150 mg at baseline, Week 4, then Q12W. **1.** Bimekizumab EU SmPC. https://www.ema. europa.eu/en/documents/product-information/bimzelx-epar-product-information_en.pdf. Accessed January 2025; **2.** Bimekizumab USPI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761151s005s006s007lbl.pdf. Accessed January 2025; **3.** Risankizumab EU SmPC. https://www.ema.europa.eu/en/documents/product-information/skyrizi-epar-product-information_en.pdf. Accessed January 2025; **4.** Risankizumab USPI. https://www.accessdata. fda.gov/drugsatfda_docs/ label/2024/761105s029,761262s007lbl.pdf. Accessed January 2025. ACR50: ≥50% improvement from baseline in American College of Rheumatology response criteria; BL: baseline; BKZ: bimekizumab; BSA: body surface area; IGA: Investigator's Global Assessment; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; Q4W: every 4 weeks; Q8W: every 8 weeks; Q12W: every 12 weeks; RZB: risankizumab; SFU: safety follow-up.

Key Inclusion and Exclusion Criteria

Inclusion

≥18 years of age

Tested negative for rheumatoid factor and anti-cyclic citrullinated peptide antibodies

Must currently be, or have previously been, on conventional systemic therapy[a]

Active adult-onset PsA, determined by:

≥1 active psoriatic lesion and/or history of chronic plaque-type psoriasis

Fulfilling **CASPAR** (ClASsification criteria for Psoriatic Arthritis)

PsA disease duration ≥6 months prior to screening

Tender joint count ≥3/68 and swollen joint count ≥3/66 at baseline

CASPAR criteria[1]

Inflammatory articular disease (joint, spine, or entheseal) and ≥3 points from the following 5 categories:		Points
Psoriasis	Current psoriasis **or** personal history or family history of psoriasis	2 1
Psoriatic nail dystrophy	Onycholysis, pitting and hyperkeratosis	1
A negative test for rheumatoid factor		1
Dactylitis	Swelling of entire digit or history of dactylitis recorded by a rheumatologist	1
Radiological evidence of juxta-articular new bone formation	Ill-defined ossification near joint margins (excluding osteophyte formation) on plain X-rays of hand or foot	1

Exclusion

Diagnosis of inflammatory conditions other than psoriasis or PsA

A diagnosis of Crohn's disease or ulcerative colitis is permitted, provided that the patient has no active symptomatic disease at screening or baseline

A current or prior exposure to biologic treatments (including BKZ or RZB), with the exception of one prior TNF-inhibitor[b]

[a] Eligible study participants will be allowed to remain on their background medication throughout the study; **[b]** Study participants who have been on a TNF inhibitor previously must have either experienced an inadequate response to previous treatment given at an approved dose for at least 3 months, or been intolerant to administration. **1.** Taylor W et al. Arthritis Rheum 2006;54:2665–73. BKZ: bimekizumab; CASPAR: ClASsification criteria for Psoriatic ARthritis; PsA: psoriatic arthritis; RZB: risankizumab; TNF: tumor necrosis factor.

Key Outcomes[1]

Primary endpoint:

- **ACR50** response at Week 16

Secondary and exploratory endpoints[a]:

- **Minimal Disease Activity** (**MDA**) response at Week 16

MDA

Defined as achievement of ≥5 of the following 7 criteria:

- Tender joint count ≤1
- Swollen joint count ≤1
- PASI ≤1 or BSA ≤3
- Pain VAS ≤15
- PGA-PsA VAS ≤20
- HAQ-DI ≤0.5
- Tender entheseal points (LEI) ≤1

- Composite endpoint of **ACR50+PASI100** response at Week 16[b]
- **ACR50** response at Week 4
- Clinical efficacy outcomes across the domains of PsA
- Patient-reported outcomes
- Health-related quality of life measures
- Work productivity measures

Safety outcomes:

- Incidence of TEAEs
- Incidence of serious AEs
- Incidence of TEAEs leading to withdrawal from study drug

[a] Additional exploratory endpoints other than those listed here may also be included in the study; **[b]** In patients with psoriasis involving ≥3% BSA at baseline. **1.** National Library of Medicine. A Study to Evaluate the Efficacy and Safety of Bimekizumab in Adult Study Participants With Active Psoriatic Arthritis. https://clinicaltrials.gov/study/NCT06624228. Accessed January 2025. ACR50: ≥50% improvement from baseline in American College of Rheumatology response criteria; AE: adverse event; BSA: body surface area; HAQ-DI: Health Assessment Questionnaire-Disability Index; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; PASI: Psoriasis Area and Severity Index; PASI100: 100% improvement from baseline in Psoriasis Area and Severity Index; PGA-PsA: Patient's Global Assessment of Psoriatic Arthritis; PsA: psoriatic arthritis; TEAE: treatment-emergent adverse event; VAS: visual analog scale.

CONCLUSIONS

BE BOLD is the first head-to-head study to test for the superiority of bimekizumab over risankizumab in joint disease, using the clinically meaningful primary endpoint of ACR50 at Week 16.

BE BOLD is also the first trial to evaluate the efficacy and safety of an IL-17A and IL-17F inhibitor vs an IL-23 inhibitor in patients with active PsA.

BE BOLD was designed to utilize approved label dosing for bimekizumab and risankizumab as per the EU SmPC and USPI dosing for PsA.[1–4]

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BI: Shareholder of AbbVie, GSK, and UCB; employee of UCB. **AMa**: Employee of UCB. **JC**: Employee and shareholder of UCB. **LG**: Grants or contracts from AbbVie, Biogen, Eli Lilly and Company, Novartis, and UCB; consulting fees from AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Janssen, MSD, Novartis, Pfizer, and UCB.

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1. Bimekizumab EU SmPC. https://www.ema.europa.eu/en/documents/product-information/bimzelx-epar-product-information_en.pdf. Accessed January 2025; **2.** Bimekizumab USPI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761151s005s006s007lbl.pdf. Accessed January 2025; **3.** Risankizumab EU SmPC. https://www.ema.europa.eu/en/documents/product-information/skyrizi-epar-product-information_en.pdf. Accessed January 2025; **4.** Risankizumab USPI. https://www.accessdata.fda.gov/drugsatfda_docs/ label/2024/761105s029,761262s007lbl.pdf. Accessed January 2025. ACR50: ≥50% improvement from baseline in American College of Rheumatology response criteria; EU: European Union; IL: interleukin; PsA: psoriatic arthritis; SmPC: summary of product characteristics; USPI: United States Prescribing Information.