Rapid, Sustained Improvements in Routine Assessment of Patient Index Data 3 in Bimekizumab-Treated Patients With Psoriatic Arthritis: Post-Hoc Analysis of Two Phase 3 Studies

Arthur Kavanaugh,[1] Alexis Ogdie,[2] Proton Rahman,[3] Barbara Ink,[4] Rajan Bajracharya,[4] Jérémy Lambert,[5] Jason Coarse,[6] Patrick Healy,[6] Heather Edens,[7] William Tillett[8,9]

Objective

To report post-hoc analysis results to 1 year using a Routine Assessment of Patient Index Data 3 (RAPID3) from two bimekizumab (BKZ) phase 3 studies in patients with active psoriatic arthritis (PsA) who were biologic disease-modifying antirheumatic drug (bDMARD)-naïve or had prior inadequate response/intolerance to tumor necrosis factor inhibitors (TNFi-IR)

Background

- BKZ, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown greater efficacy and tolerability at 16 weeks versus placebo (PBO) and sustained efficacy to Week 52 across disease domains in patients with active PsA who were bDMARD-naive or TNFi-IR.[1–3]
- RAPID3, a composite index of patient-reported outcomes, assesses physical function, pain and patient global estimate of disease activity (each scored 0–10, for a total of 0–30).[4]

Methods

- BE OPTIMAL (NCT03895203; bDMARD-naïve) and BE COMPLETE (NCT03896581; TNFi-IR) were phase 3 trials of BKZ 160 mg every 4 weeks (Q4W) in patients with active PsA. Both were double-blind and PBO-controlled to Week 16, after which patients on PBO received BKZ (PBO/BKZ).[1–3]
- BE OPTIMAL included a reference arm (adalimumab 40 mg every 2 weeks; data not shown). BE OPTIMAL Week 52 and BE COMPLETE Week 16 completers could enroll in BE VITAL (NCT04009499; open-label extension); BE COMPLETE plus BE VITAL is hereafter referred to as "BE COMPLETE."[1–3]
- In this post-hoc analysis, change from baseline in RAPID3 (calculated using the Health Assessment Questionnaire–Disability Index [HAQ-DI] for physical function, scored 0–3, along with the pain visual analog scale [VAS] and patient global assessment of PsA, both scored 0–100, all collected separately and rescored from 0–10) was evaluated to Week 52 in patients on BKZ, including stratification for patients with or without (±) concomitant methotrexate (MTX) use at baseline. Disease activity states for RAPID3 were calculated to 1-year treatment with BKZ as remission (REM; RAPID3 ≤3), low disease activity (LDA; 3< RAPID3 ≤6), moderate disease activity (MoDA; 6< RAPID3 ≤12) or high disease activity (HDA; RAPID3 >12).
- The proportion of patients achieving the minimal clinically important difference (MCID) for RAPID3 (score decrease of ≥3.8 points from baseline) to Week 52 was also measured.[5]
- For each component variable of the RAPID3 endpoint, missing data or non-missing data preceded by a treatment discontinuation were imputed before deriving RAPID3. Data were reported using observed cases (OC), multiple imputation (MI) or non-responder imputation (NRI) for continuous variables and worst-category imputation (WCI) for RAPID3 categories.

Results

Patient disposition

- In BE OPTIMAL, 388/431 (90.0%) BKZ and 257/281 (91.5%) PBO/BKZ patients completed Week 52, while in BE COMPLETE, 236/267 (88.4%) BKZ and 111/133 (83.5%) PBO/BKZ patients completed Week 52.

Change from baseline in RAPID3 to Week 52

- Improvements in RAPID3 with BKZ were numerically larger by Week 4 compared with PBO, continued to Week 16 and sustained to Week 52. PBO/BKZ patients achieved similar improvement in RAPID3 to BKZ patients by Week 52 (**Figure 1**).

Change from baseline in RAPID3 to Week 52 ± concomitant MTX

- Improvements in RAPID3 were observed in BKZ-treated patients ± concomitant MTX (**Figure 2**).

Disease activity states and MCID responders for RAPID3 at Week 52

- Evaluation of RAPID3 disease activity states showed that at Week 52, REM or LDA was achieved by 235/431 (54.5%) BKZ and 151/281 (53.7%) PBO/BKZ patients in BE OPTIMAL, and by 131/267 (49.1%) BKZ and 48/133 (36.1%) PBO/BKZ patients in BE COMPLETE (**Figure 3**).
- At Week 52 in the BKZ group, 273/431 (63.3%) and 177/267 (66.3%) patients achieved the MCID for RAPID3 in BE OPTIMAL and BE COMPLETE, respectively (**Figure 4**).

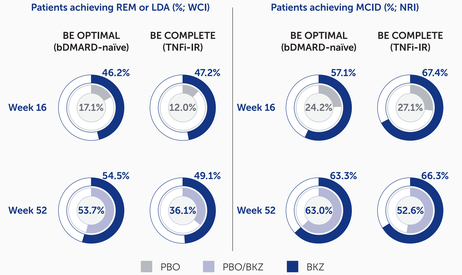
Conclusions

In this post-hoc analysis of BE OPTIMAL and BE COMPLETE, bimekizumab treatment resulted in quick RAPID3 improvement that was sustained to 1 year in patients with active PsA who were previously bDMARD-naïve or TNFi-IR, regardless of concomitant MTX use.

Summary

RAPID3 assesses physical function, pain and patient global estimate of disease activity

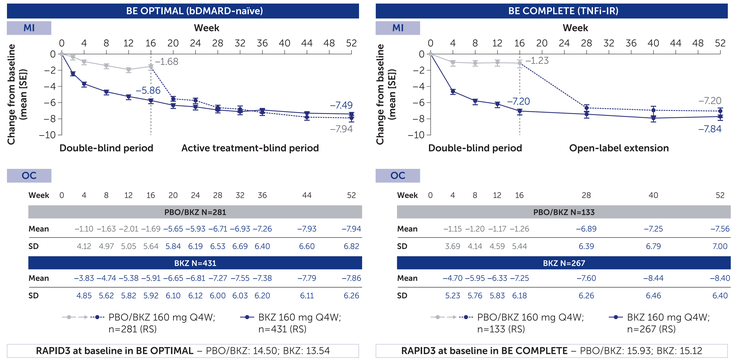
In a post-hoc analysis of two phase 3 trials, **RAPID3**[a] was assessed in **BKZ-treated patients with active PsA**



Clinically relevant implications: Fast improvement was observed **in RAPID3 at Week 16** and was **sustained to Week 52**, regardless of prior TNFi exposure or concomitant MTX use

[a]RAPID3 was comprised of the HAQ-DI for physical function (scored 0–3), together with the pain VAS and patient global assessment of PsA (both scored 0–100). Each endpoint was rescored from 0–10 for calculation of RAPID3.

Figure 1 Mean change from baseline in RAPID3 over time to Week 52 (MI; OC)[a,b]

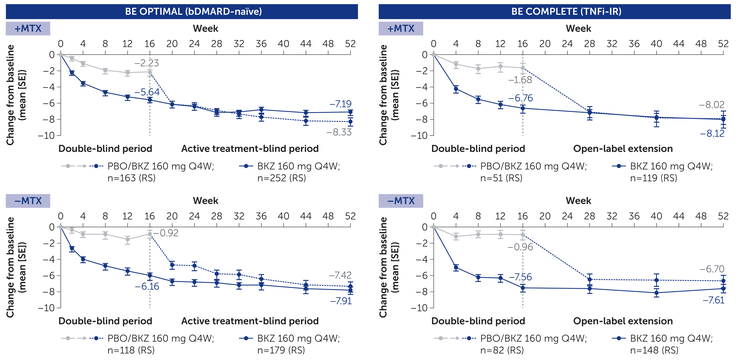


RAPID3 at baseline in BE OPTIMAL – PBO/BKZ: 14.50; BKZ: 13.54

RAPID3 at baseline in BE COMPLETE – PBO/BKZ: 15.93; BKZ: 15.12

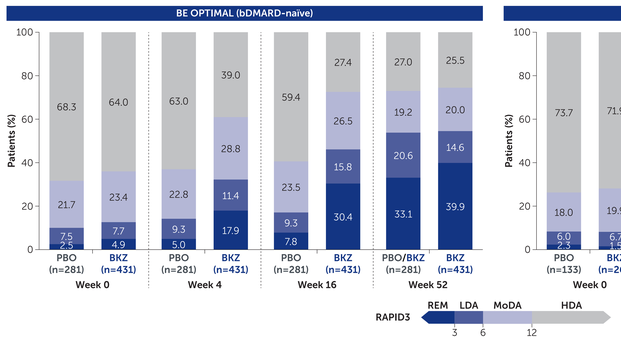
[a]Baseline was defined as the last available value before the first dose of study drug. [b]Patients with missing baseline values were not included in the OC counts. OC did not use the estimand approach. Only observed data on treatment are presented.

Figure 2 Mean change from baseline in RAPID3 over time to Week 52 ± concomitant MTX use at baseline (MI)[a]



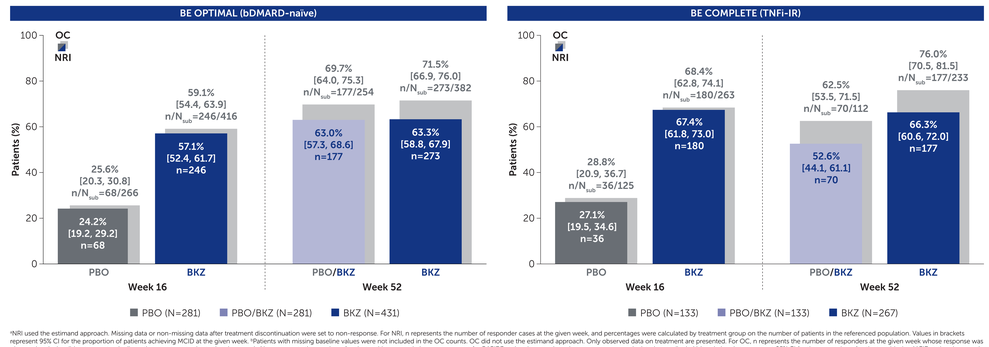
[a]Baseline was defined as the last available value before the first dose of study drug.

Figure 3 Disease activity states for RAPID3 over time to Week 52 (WCI)[a]



[a]WCI used the estimand approach. Missing data or non-missing data after treatment discontinuation were considered in the worst category (HDA).

Figure 4 Proportion of patients achieving MCID (score decrease of ≥3.8 points from baseline) for RAPID3 at Weeks 16 and 52 (NRI; OC)[a,b]



[a]NRI used the estimand approach. Missing data or non-missing data after treatment discontinuation were set to non-response. For NRI, n represents the number of responder cases at the given week, and percentages were calculated by treatment group on the number of patients in the referenced population. Values in brackets represent 95% CI for the proportion of patients achieving MCID at the given week. [b]Patients with missing baseline values were not included in the OC counts. OC did not use the estimand approach. Only observed data on treatment are presented. For OC, n represents the number of responders at the given week whose response was observed and who did not prematurely discontinue treatment prior to the given week. N_{sub} represents the number of patients with a non-missing measurement for RAPID3 at the given week, and percentages were calculated accordingly. Values in brackets represent 95% CI for the proportion of patients achieving MCID at the given week.

±: with or without; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **CI:** confidence interval; **HAQ-DI:** Health Assessment Questionnaire–Disability Index; **HDA:** high disease activity; **IL:** interleukin; **LDA:** low disease activity; **MCID:** minimal clinically important difference; **MI:** multiple imputation; **MoDA:** moderate disease activity; **MTX:** methotrexate; **NRI:** non-responder imputation; **OC:** observed cases; **PBO:** placebo; **PBO/BKZ:** patients who were PBO–controlled until Week 16, after which they received BKZ; **PsA:** psoriatic arthritis; **Q4W:** every 4 weeks; **RAPID3:** Routine Assessment of Patient Index Data 3; **REM:** remission; **RS:** randomized set; **SD:** standard deviation; **SE:** standard error; **TNFi-IR:** inadequate response/intolerance to tumor necrosis factor inhibitors; **VAS:** visual analog scale; **WCI:** worst-category imputation.

Institutions: [1]Division of Rheumatology Allergy and Immunology, University of California San Diego School of Medicine, La Jolla, CA, USA; [2]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [3]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St John's, NL, Canada; [4]UCB Pharma, Slough, UK; [5]UCB Pharma, Colombes, France; [6]UCB Pharma, Morrisville, NC, USA; [7]UCB Pharma, Smyrna, GA, USA; [8]Royal National Hospital of Rheumatic Diseases, Bath, UK; [9]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, UK.

References: [1]McInnes IB. Lancet 2023;401(10370):25–37. [2]Ritchlin CT. Ann Rheum Dis 2023;82(11):1404–1414. [3]Merola JF. Lancet 2023;401(10370):38–48. [4]Coates LC. Arthritis Care Res 2018;70(8):1198–1205. [5]Ogdie A. Ann Rheum Dis 2022;81(Suppl 1):1582. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **AK**, **AO**, **PR**, **BI**, **RB**, **JL**, **JC**, **PH**, **HE**, **WT**; drafting of the publication, or reviewing it critically for important intellectual content: **AK**, **AO**, **PR**, **BI**, **RB**, **JL**, **JC**, **PH**, **HE**, **WT**; final approval of the publication: **AK**, **AO**, **PR**, **BI**, **RB**, **JL**, **JC**, **PH**, **HE**, **WT**. **Author Disclosures: AK:** Research grants from Abbott, Amgen, Bristol Myers Squibb, Pfizer, Roche, Janssen and UCB Pharma. **AO:** Grant/research support from AbbVie, Amgen, Janssen, Novartis and Pfizer; consultant for AbbVie, Amgen, Bristol Myers Squibb, Celgene, CorEvitas, Eli Lilly and Company, GSK, Gilead, Janssen, Novartis, Pfizer, Takeda and UCB Pharma. **PR:** Consulting fees from Abbott, AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Janssen, Novartis, Pfizer and UCB Pharma; received research grants from Janssen and Novartis. **BI:** Employee of UCB Pharma; shareholder of AbbVie, GSK and UCB Pharma. **HE**, **RB**, **PH**, **JL**, **JC:** Employees and shareholders of UCB Pharma. **WT:** Research grants, consulting fees, speaking fees and/or honoraria from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly and Company, GSK, Janssen, MSD, Novartis, Ono Pharma, Pfizer and UCB Pharma. **Acknowledgments:** This study was funded by UCB Pharma. We would like to thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Quinn Ho, PhD, and M. Elizabeth Wegman, BA, at Costello Medical, Boston, MA, for medical writing, and the Creative team at Costello Medical for design support. All costs associated with development of this poster were funded by UCB Pharma.