Identification of Responder and Disease Activity Thresholds for the Psoriatic Arthritis Impact of Disease-12 (PsAID-12) Questionnaire Using Pooled Data from Two Phase 3 Trials of Bimekizumab in Patients with Psoriatic Arthritis

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Objective

To determine clinically meaningful within-patient improvement thresholds to be used as responder thresholds, and to explore preliminary disease activity/impact bands for the Psoriatic Arthritis Impact of Disease-12 total and single-item domain scores for patients with active psoriatic arthritis.

Background

- The Psoriatic Arthritis (PsA) Impact of Disease-12 (PsAID-12) questionnaire is a 12-item patient-reported outcome measure developed to assess the impact of PsA on 12 physical, social and psychological domains.[1,2]
- Previous thresholds have been published for the PsAID-12 total score;[1,3] however, thresholds are also needed for the single-item domain scores.

Methods

- Blinded pooled data were analysed from two double-blind, placebo-controlled phase 3 trials (BE OPTIMAL [NCT03895203] and BE COMPLETE [NCT03896581]) of subcutaneous bimekizumab (BKZ) 160 mg every 4 weeks in patients with PsA. BE OPTIMAL included an adalimumab reference arm.
- Analyses were conducted on observed scores for all randomised patients with ≥1 non-missing PsAID-12 single-item domain between baseline and Week 16 (N=1,252).
- **Week 16 clinically meaningful within-patient (CMWP) improvement thresholds** were determined by triangulating results from:
  - Anchor-based analyses (using American College of Rheumatology [ACR] response criteria and PsA Disease Activity Score [PASDAS]) divided patients into response groups based on the level of change.
  - Empirical cumulative distribution function (eCDF) curves of changes in PsAID-12 scores from baseline to Week 16 guided selection of CMWP improvement thresholds.
  - Supportive distribution-based analyses (one standard error of measurement and half of the baseline standard deviation [SD]) were conducted.
- **Disease activity thresholds** were determined using the maximum Youden index values from the receiver operating characteristic (ROC) curve analyses (using PASDAS and Disease Activity Index for PsA [DAPSA] scores as anchors).

Results

- Patient characteristics at baseline are presented in **Table 1**.
- Mean PsAID-12 total and single-item domain scores at baseline and Week 16 are presented in **Figure 1**.
- Anchor-based and distribution-based approaches supported the use of 2-point reduction in the PsAID-12 total score to represent a marked CMWP improvement.
- For eight PsAID-12 single-item domain scores, CMWP improvement thresholds were identified as 3-point reduction in scores:
  - CMWP improvement thresholds could not be determined for four single item domains due to high proportions of patients scoring 0 (no symptoms) at baseline: anxiety, fear and uncertainty; embarrassment and/or shame; social participation; and depression.
- Findings from the eCDF curves supported the use of the above CMWP estimates (**Figure 2**).
- The ROC curves used to determine disease/impact activity thresholds for the PsAID-12 total score using PASDAS disease activity categories are shown in **Figure 3**; the identified disease activity/impact activity thresholds for the PsAID-12 total and single-item domain scores are presented in **Figure 4**.

Summary

This analysis identified **interpretation thresholds** for the **PsAID-12 total** and **single-item domain scores** to assess treatment efficacy and disease impact in patients.

Clinically meaningful within-patient improvement threshold:

- Total score (0–10 scale): 2-point decrease
- Single-item domain scores (0–10 scale): 3-point decrease

Disease activity thresholds:

- Initial thresholds for remission, low, moderate and high disease activity identified

Conclusion

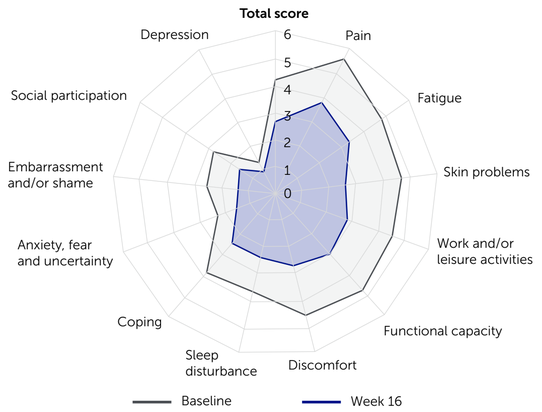
Clinically meaningful within-patient improvements and disease activity thresholds were identified for the **PsAID-12 total score** and **eight single-item domain scores,** including **pain, fatigue and skin problems,** which can be used to assess treatment efficacy and disease impact in patients.

Table 1 Baseline patient demographics and disease characteristics

Characteristics	Pooled (bDMARD-naïve + TNFi-IR)[a] N=1252
Age, years, mean (SD)	49.3 (12.4)
Male, n (%)	589 (47.0)
BMI, kg/m^2, mean (SD)	29.4 (6.3)
TJC (of 68 joints), mean (SD)	17.5 (12.8)
SJC (of 66 joints), mean (SD)	9.4 (7.1)
hs-CRP, mean (SD)	10.2 (16.9)
Psoriasis affecting ≥3% BSA, n (%)	689 (55.0)
PsAID-12 total score,[b] mean (SD)	4.2 (1.9)
PASDAS,[c] mean (SD)	5.5 (1.0)
DAPSA,[b] mean (SD)	48.5 (27.7)

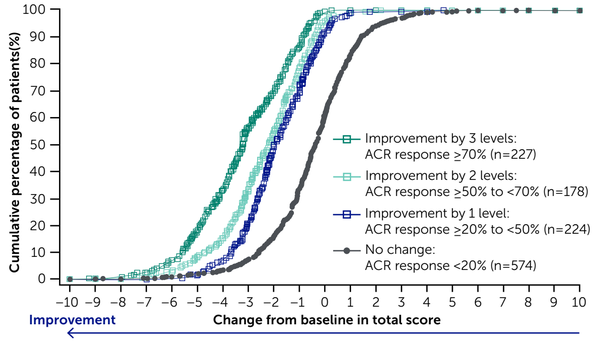
PsAID-12 analysis set (all randomised patients who had ≥1 non-missing PsAID-12 single-item domain score at any scheduled visit). [a]BE OPTIMAL included bDMARD-naïve patients (N=852); BE COMPLETE included TNFi-IR patients (N=400); [b]Data missing for 1 patient (BE OPTIMAL); [c]Data missing for 12 patients (BE OPTIMAL), 1 patient (BE COMPLETE).

Figure 1 Mean PsAID-12 total and single-item domain scores at baseline and Week 16



PsAID-12 analysis set (all randomised patients who had ≥1 non-missing PsAID-12 single-item domain score at any scheduled visit). PsAID-12 score ranges from 0–10 (higher scores indicate worse status). Baseline N=1,251; Week 16 N=1,204.

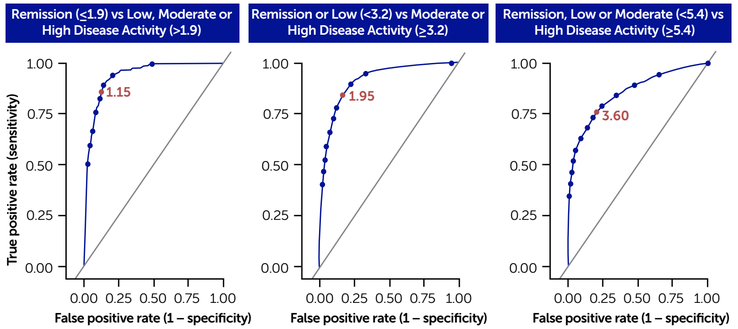
Figure 2 eCDF curves of changes in PsAID-12 total score from baseline to Week 16 by ACR response category



	−10	−9	−8	−7	−6	−5	−4	−3	−2	−1	0	1	2	3	4	5	6	7	8	9	10
ACR response ≥70%	0.0	0.4	7.0	33.0	70.5	99.6	100	100	100	100	100										
ACR response ≥50% to <70%	0.0	0.0	2.8	15.2	55.6	96.1	99.4	100	100	100	100										
ACR response ≥20% to <50%	0.0	0.0	0.0	6.7	49.6	92.0	99.6	99.6	100	100	100										
No change: ACR response <20%	0.0	0.2	1.0	3.3	15.9	62.0	94.3	99.0	99.8	100	100										

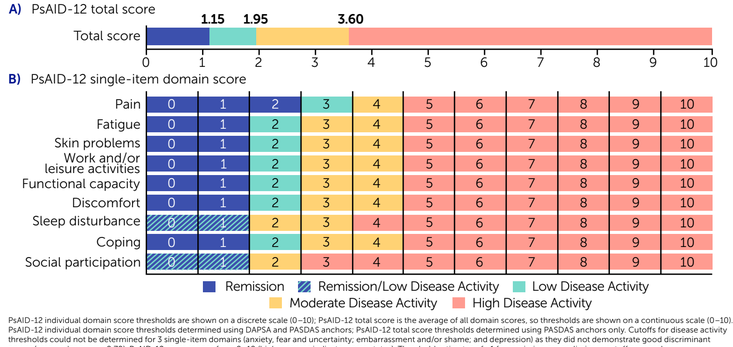
PsAID-12 analysis set (all randomised patients with ≥1 non-missing PsAID-12 single-item domain score at any scheduled visit). Patients were divided into different response groups based on the ACR response (No change: ACR response <20%; ACR response ≥20% to <50%; ACR response ≥50% to <70%; ACR response ≥70%).

Figure 3 ROC curves for determination of disease activity thresholds for the PsAID-12 total score using PASDAS-based disease activity categories



Orange markers indicate cutoffs corresponding to the maximum Youden index values. ROC analyses used data from the PsAID-12 Analysis Set pooled across baseline, Week 4 and Week 16 study visits.

Figure 4 Disease activity threshold estimates for PsAID-12 total and single-item domain scores determined using DAPSA and PASDAS as anchors



PsAID-12 individual domain score thresholds are shown on a discrete scale (0–10); PsAID-12 total score is the average of all domain scores, so thresholds are shown on a continuous scale (0–10). PsAID-12 individual domain score thresholds determined using DAPSA and PASDAS anchors only. Cutoffs for disease activity thresholds could not be determined for 3 single-item domains (anxiety, fear and uncertainty; embarrassment and/or shame; and depression) as they did not demonstrate good discriminant power (area under curve <0.70). PsAID-12 score ranges from 0–10 (higher scores indicate worse status). Threshold estimates of ≤1 for remission are preliminary cutoff proposals.

ACR: American College of Rheumatology; **ACR response <20%/≥20% to <50%/≥50% to <70%/≥70%:** <20%/≥20% to <50%/≥50% to <70%/≥70% improvement from baseline in ACR criteria; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BMI:** body mass index; **BSA:** body surface area; **CMWP:** clinically meaningful within-patient; **DAPSA:** Disease Activity Index for Psoriatic Arthritis; **eCDF:** empirical cumulative distribution function; **hs-CRP:** high sensitivity C-reactive protein; **PASDAS:** Psoriatic Arthritis Disease Activity Score; **PsA:** psoriatic arthritis; **PsAID-12:** Psoriatic Arthritis Impact of Disease-12; **ROC:** Receiver Operating Characteristic; **SD:** standard deviation; **SJC:** swollen joint count; **TJC:** tender joint count; **TNFi-IR:** inadequate response or intolerance to tumour necrosis factor-α inhibitor.

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References: [1]Gossec L. Ann Rheum Dis 2014;73:1012–9; [2]Orbai AM. J Rheumatol 2019;46(8):990–5; [3]Holland R. Ann Rheum Dis 2018;77:343–7. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **LG, LCC, AMO, MdW, CGP, JL, VC, BI, VT, DDG;** Drafting of the publication, or revising it critically for important intellectual content: **LG, LCC, AMO, MdW, CGP, JL, VC, BI, VT, DDG;** Final approval of the publication: **LG, LCC, AMO, MdW, CGP, JL, VC, BI, VT, DDG.** **Author Disclosures: LG:** Grants from AbbVie, Biogen, Lilly, Novartis, Sandoz, UCB Pharma; Personal fees from AbbVie, Amgen, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sandoz and UCB Pharma. **LCC:** Grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer and UCB Pharma; Paid consultant for AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Domain, Eli Lilly, Galapagos, Gilead, 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. **AMO:** Research grants to Johns Hopkins University from AbbVie, Amgen and Janssen; Consulting fees from BMS, Janssen, Sanofi and UCB Pharma. **MdW:** Over the last five years Stichting Tools has received fees for lectures or consultancy provided by MdW from Celgene, Eli Lilly, Janssen-Cilag, Pfizer and UCB Pharma. **CGP:** Employee of Evidera, a part of Thermo Fisher Scientific that receives funding for research from UCB Pharma. **JL, VC:** Employee and shareholder of UCB Pharma. **BI:** Employee and shareholder of UCB Pharma and shareholder of AbbVie and GSK. **VT:** Employee of UCB Pharma. **DDG:** Consultant and/or received grant support from Abbvie, Amgen, BMS, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB Pharma. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to these studies. The authors acknowledge Heather Edens, PhD, UCB Pharma, Smyrna, Georgia, USA, for publication coordination, David Morgan, PhD, Costello Medical, Manchester, UK for medical writing and editorial assistance, and the Costello Medical Creative team for design support. This study was funded by UCB Pharma. All costs associated with development of this presentation were funded by UCB Pharma.

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