Psychometric Validation of the P-SIM, a Novel Patient-Reported Outcome Instrument for Patients with Plaque Psoriasis

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Objective

To assess psychometric properties of the Psoriasis Symptoms and Impacts Measure (P-SIM), a novel patient-reported outcome (PRO) instrument developed to capture key signs, symptoms and impacts of plaque psoriasis, using blinded data from the BE VIVID and BE READY bimekizumab phase 3 trials.

Background

- Plaque psoriasis has negative impacts on patients' quality of life and emotional wellbeing.[1–3] Understanding patients' experiences of plaque psoriasis is key to supporting treatment needs.
- The P-SIM is a novel PRO instrument developed to capture patients' experiences of signs, symptoms and impacts of plaque psoriasis. We assessed its psychometric properties when measured daily in BE VIVID (NCT03370133) and BE READY (NCT03410992) and propose a responder definition (RD) threshold for assessing treatment effects.

Methods

Pooled, blinded data from 1,002 patients were analysed through Weeks 0–16 of BE VIVID and BE READY. Average weekly scores (missing if >3 daily scores for a given week were missing) were derived for the 14 P-SIM items.

- Test-retest reliability was evaluated using intraclass correlation coefficients (ICCs).
- Convergent validity was assessed at baseline and Week 16 between P-SIM and relevant PRO and clinician-reported outcome (ClinRO) scores
  - PROs: Dermatology Life Quality Index (DLQI), DLQI Item 1 (skin symptoms), Patient Global Assessment of Psoriasis (PGAP)
  - ClinROs: Investigator's Global Assessment (IGA), Psoriasis Area and Severity Index (PASI).
- Known-groups validity was evaluated by comparing P-SIM scores at baseline and Week 16 between patient subgroups based on PRO/ClinRO scores.
- Correlations were calculated between changes from baseline to Week 16 in P-SIM and PRO/ClinRO scores to assess sensitivity to change.
- Anchor-based analyses were performed to propose P-SIM item RD thresholds indicating within-patient marked clinically meaningful improvement. Empirical cumulative distribution function (eCDF) curves were examined to verify these thresholds.

Results

- 16-week average completion rate was 85.2%.
- P-SIM inter-item correlations were strong (coefficient >0.5) at baseline and Week 16, apart from "Choice of Clothing" with "Pain" and "Burning" at baseline (both 0.49).
- All ICCs were between 0.91 and 0.98 (acceptability threshold: 0.70), demonstrating excellent test-retest reliability.
- All P-SIM scores were moderately-to-strongly correlated with other PROs and ClinROs at Week 16, demonstrating convergent validity. Correlations were less strong with ClinROs at baseline which had low variability.
- P-SIM scores discriminated between patient subgroups at Week 16 **(Figure 1)**, showing good known-groups validity.
- 16-week changes from baseline in P-SIM and other PRO scores were strongly correlated (>0.5; moderate with ClinROs), establishing sensitivity to change **(Table 1)**.
- Mean change scores from anchor-based analyses and eCDF curves determined a 4-point decrease in each item score as indicative of marked clinically meaningful improvement **(Figure 2)**; lower thresholds (1.98–2.86; "Itch", "Pain", "Scaling" scores) were previously determined in phase 2b analyses.

Summary

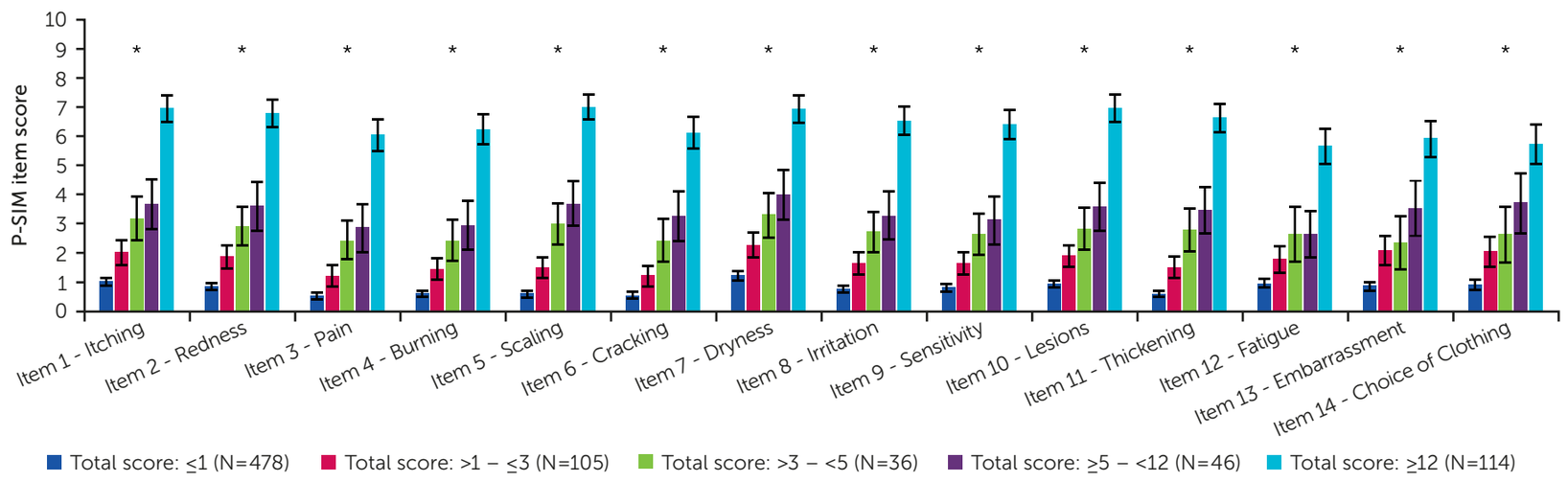
The 14-item P-SIM was completed daily using a handheld electronic PRO device

Each item was scored for severity/impact level over the previous 24 hours on a scale from 0 (no symptom/impact) to 10 (very severe)

Individual items were scored daily and weekly average scores were derived for each

If scores were missing for >3 days in a week, the weekly score was considered missing

Figure 1 Between-subgroup differences in P-SIM item scores at Week 16 by PASI total score subgroup



*p<0.05; between-groups differences calculated by Kruskal-Wallis test. 95% confidence intervals for mean scores within each group are displayed as error bars. Similar results were seen for patient subgroups based on IGA score, DLQI total score, DLQI Item 1 score and PGAP score.

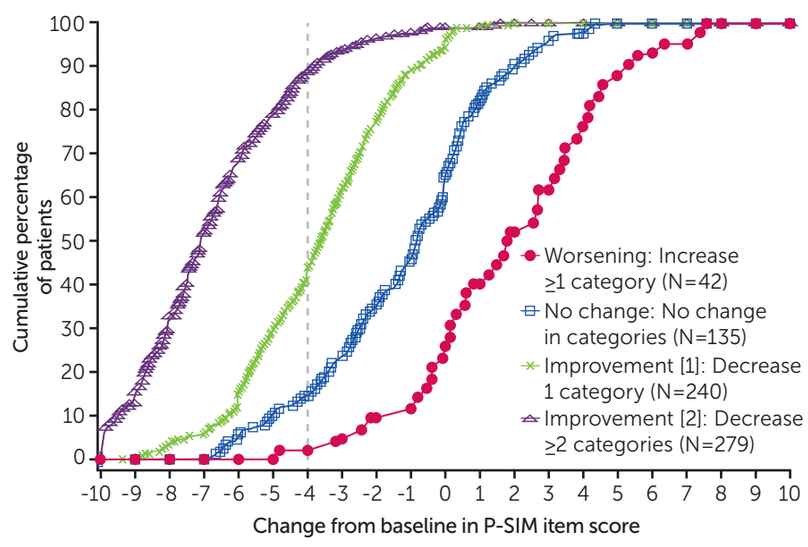
Table 1 Spearman correlations between changes from baseline to Week 16 in P-SIM item scores and in PRO/ClinRO scores

P-SIM item	Spearman correlation coefficient				
	PASI total score N=698	DLQI total score N=698	DLQI Item 1 score N=696	IGA score N=698	PGAP score[a] N=314
Item 1 – Itching	0.42	0.61	0.74	0.48	0.72
Item 2 – Redness	0.45	0.61	0.68	0.50	0.74
Item 3 – Pain	0.44	0.60	0.69	0.46	0.68
Item 4 – Burning	0.44	0.61	0.70	0.48	0.69
Item 5 – Scaling	0.49	0.61	0.66	0.53	0.73
Item 6 – Cracking	0.43	0.60	0.65	0.47	0.68
Item 7 – Dryness	0.44	0.60	0.68	0.49	0.75
Item 8 – Irritation	0.44	0.63	0.70	0.49	0.73
Item 9 – Sensitivity	0.44	0.61	0.68	0.48	0.70
Item 10 – Lesions	0.45	0.62	0.65	0.49	0.72
Item 11 – Thickening	0.44	0.61	0.64	0.49	0.71
Item 12 – Fatigue	0.38	0.61	0.54	0.44	0.60
Item 13 – Embarrassment	0.38	0.69	0.56	0.46	0.61
Item 14 – Choice of Clothing	0.38	0.68	0.50	0.46	0.59

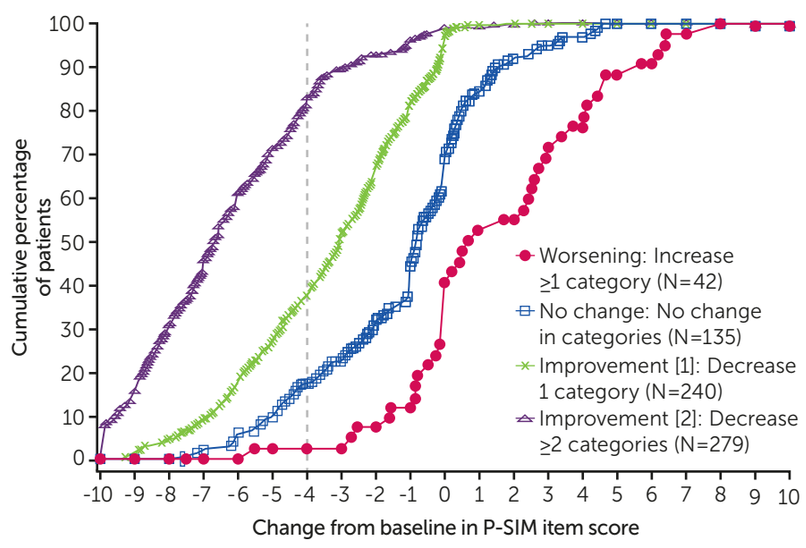
[a]Changes from baseline to Week 12 were used for PGAP due to substantial amounts of missing data at Week 16. Blue cells indicate correlation coefficients that were strong (>0.5).

Figure 2 RD analysis – eCDF curves

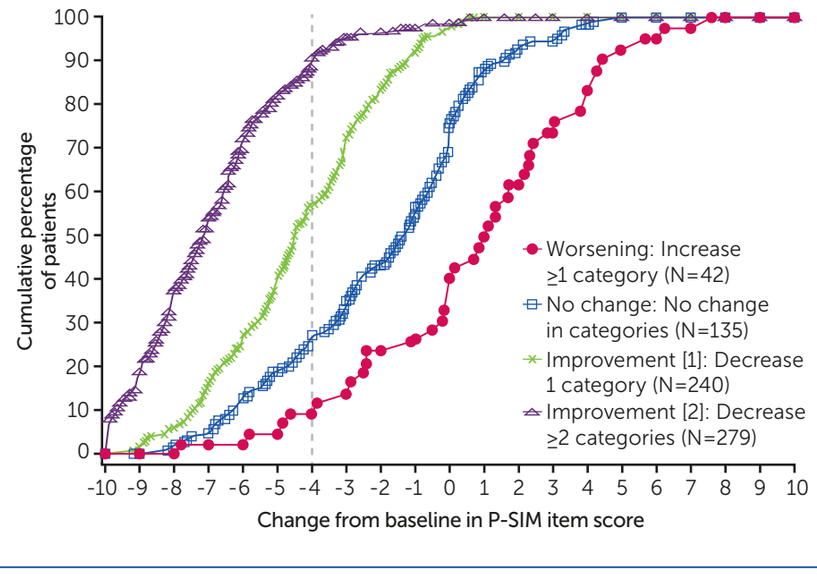
A) eCDF curves of observed change from baseline to Week 16 in P-SIM Item 1 (Itching) by DLQI Item 1 change score category



B) eCDF curves of observed change from baseline to Week 16 in P-SIM Item 3 (Pain) by DLQI Item 1 change score category



C) eCDF curves of observed change from baseline to Week 16 in P-SIM Item 5 (Scaling) by DLQI Item 1 change score category



DLQI Item 1 was prioritised for the RD anchor-based analysis as it is patient-reported, measured on a directly interpretable ordinal scale, and its change from baseline to Week 16 had the highest correlation with those in P-SIM items. Negative changes from baseline in P-SIM item scores indicate improvement. eCDFs for Itching, Pain and Scaling items are shown as these items were used as efficacy endpoints in the BE VIVID and BE READY trials; findings for other items were similar.

Conclusions

P-SIM scores demonstrated good test-retest reliability, convergent and known-groups validity, and sensitivity to change. A 4-point RD threshold could be used to assess 16-week treatment effects.

CI: confidence interval; ClinRO: clinician-reported outcome; DLQI: Dermatology Life Quality Index; eCDF: empirical cumulative distribution function; ICC: intraclass correlation coefficient; IGA: Investigator's Global Assessment; PASI: Psoriasis Area and Severity Index; PGAP: Patient Global Assessment of Psoriasis; PRO: patient-reported outcome; P-SIM: Psoriasis Symptoms and Impacts Measure; RD: responder definition.

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References: [1]Armstrong AW *et al.* PLOS ONE 2012;7:e52935; [2]Kimball AB *et al.* Am J Clin Dermatol 2005;6:383–392; [3]Augustin M, Radtke MA. Expert Rev Pharmacoecon Outcomes Res 2014;14:559–568. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **RBW**, **ABG**, **JFM**, **LG**, **CC**, **LP**, **CP**, **VC**; Drafting of the publication, or revising it critically for important intellectual content: **RBW**, **ABG**, **JFM**, **LG**, **CC**, **LP**, **CP**, **VC**; Final approval of the publication: **RBW**, **ABG**, **JFM**, **LG**, **CC**, **LP**, **CP**, **VC**. **Author Disclosures:** **RBW**: Consulting fees from AbbVie, Almirall, Amgen, Arena, Avillion, Boehringer Ingelheim, BMS, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants from AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, and UCB Pharma; **ABG**: Honoraria as an advisory board member and consultant for Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, BMS, Eli Lilly, Incyte, Janssen, LEO Pharma, Novartis, Sun Pharma, UCB Pharma, and XBiotech (only stock options which she has not used); research/educational grants (paid to Mount Sinai Medical School) from Boehringer Ingelheim, Incyte, Janssen, Novartis, Sun Pharma, UCB Pharma, and XBiotech; **JFM**: Consultant and/or investigator for AbbVie, Arena, Avotres, Biogen, BMS, Dermavant, Eli Lilly, EMD-Serono, Janssen, LEO Pharma, Merck, Novartis, Regeneron, Sanofi, Sun Pharma, Pfizer, and UCB Pharma; **LG**, **LP**, **VC**: Employees of UCB Pharma; **CC**: Employee and shareholder of UCB Pharma; **CP**: Salaried employee of Evidera, which received funding from UCB Pharma to conduct the study. **Acknowledgements:** This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Susanne Wiegratz, UCB Pharma, Monheim am Rhein, Germany, for publication coordination, Eva Cullen, UCB Pharma, Brussels, Belgium, for critical review, Dan Smith, Costello Medical, Cambridge, UK, for medical writing and editorial assistance, and Shien Guo, Weiqin Liao and Xiaomei Ye, Evidera, Waltham, MA, USA, for their support in data analysis. All costs associated with development of this poster were funded by UCB Pharma.