PCR205

Determination of Ranges of HSSDD & HSSQ Scores Defining Clinically Meaningful Within-Patient Improvement Thresholds and Severity Levels

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Objective

To determine clinically meaningful within-patient change thresholds for improvement (often used in the responder definition) and severity thresholds, to categorise patients across disease activity/impact bands, for Hidradenitis Suppurativa (HS) Symptom Daily Diary (HSSDD) and HS Symptom Questionnaire (HSSQ) individual item scores.

Background

- HS is a chronic inflammatory skin disease, characterised by painful and recurrent skin lesions.[1]
- HSSDD and HSSQ assess patients' perceptions of the core symptoms of HS using 11-point numeric rating scales (0–10); higher scores indicate higher symptomology levels.
  - The HSSDD assesses 5 items (worst skin pain, average skin pain, itch, smell or odour, and drainage or oozing from HS lesions) over the past 24 hours (scores averaged weekly);
  - The HSSQ assesses 4 items (skin pain, itch, smell or odour, and drainage or oozing from HS lesions) over the past 7 days.
- Here, we determined the clinically meaningful within-patient improvement and severity thresholds to guide interpretation of HSSDD and HSSQ item scores for patients with HS.

Methods

- Pooled, blinded data from two randomised phase 3 trials, BE HEARD I & II, of bimekizumab 320 mg every 2/4 weeks or placebo were used to estimate HSSDD and HSSQ thresholds in patients with moderate to severe HS.[2,3]
- The HSSDD was completed daily from screening to the Week 16 visit. The HSSQ was completed during study visits (baseline and Weeks 16–48).
- Threshold analyses were conducted on observed scores for all randomised patients with ≥1 non-missing item score at any scheduled assessment visit.
- Thresholds for clinically meaningful within-patient improvement for Week 16 were determined and assessed by triangulating threshold estimates from the following analyses:
  - Anchor-based analyses, using Patient Global Impression of Severity of HS (PGI-S-HS) or Skin Pain (PGI-S-SP), to divide patients into response groups and describe HSSDD and HSSQ score changes from baseline as a basis for the thresholds;
  - Empirical cumulative distribution function (eCDF) plot of changes in item scores from baseline to Week 16 to support selection of the final thresholds;
  - Distribution-based analyses (one standard error of measurement and half of the baseline standard deviation [SD]) to support the relevance of the thresholds.
- Disease activity thresholds were determined using the maximum Youden index values from the receiver operating characteristic (ROC) analyses with PGI-S-HS or PGI-S-SP as the anchor.

Results

- The analysis sets for HSSDD and HSSQ included 934 patients and 1,007 patients, respectively, from BE HEARD I & II.
- The mean ages of patients in the HSSDD and HSSQ analysis sets were 37.1 and 36.7 years, while the mean disease durations were 8.0 and 7.9 years, respectively (**Table 1**). Most included patients were female.
- For HSSDD, the identified clinically meaningful within-patient improvement threshold ranges were:
  - Worst and average skin pain item scores: 3- to 4-point decrease;
  - Smell or odour, itch, and draining or oozing item scores: 2- to 3-point decrease.
- For HSSQ, the identified clinically meaningful within-patient improvement threshold ranges were:
  - Skin pain item score: 4- to 5-point decrease;
  - Smell or odour, and draining or oozing item scores: 3- to 4-point decrease;
  - Itch item score: 3-point decrease.
- Findings from the eCDF plot supported the use of the aforementioned improvement threshold estimates; a plot of changes in HSSDD worst skin pain is shown in **Figure 1**.
- The ROC curves used to determine disease severity thresholds for HSSDD worst skin pain using PGI-S-SP categories are shown in **Figure 2**.
- Disease severity thresholds of none, mild, moderate, severe and very severe were identified for both HSSDD (**Figure 3**) and HSSQ items (**Figure 4**).

Conclusions

This analysis defined clinically meaningful within-patient improvement and severity thresholds for HSSDD and HSSQ item scores. These novel HS-specific symptom instruments can assess treatment efficacy and disease impacts in patients with HS.

Summary

This analysis defined **clinically meaningful within-patient improvement** and **severity thresholds** for **HSSDD** and **HSSQ** item scores

The thresholds were identified by evaluating HSSDD and HSSQ scores and changes in scores against the severity levels from established patient-reported disease severity anchor measures

HSSDD clinically meaningful within-patient improvement thresholds:

- **Worst** and **average skin pain**: 3- to 4-point decrease
- **Smell or odour, itch,** and **draining or oozing:** 2- to 3-point decrease

HSSQ clinically meaningful within-patient improvement thresholds:

- **Skin pain:** 4- to 5-point decrease
- **Smell or odour,** and **draining or oozing:** 3- to 4-point decrease
- **Itch:** 3-point decrease

Disease severity thresholds:

- Thresholds of **none, mild, moderate, severe and very severe** were identified for both **HSSDD** and **HSSQ**

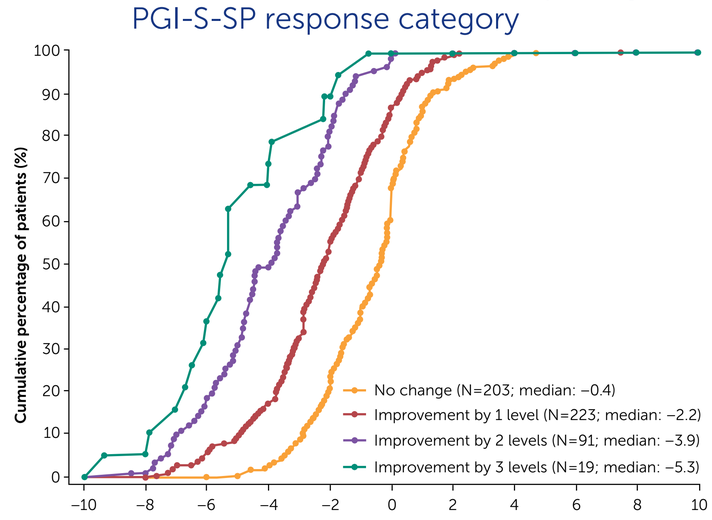
These **novel, HS-specific symptom instruments can help** to assess treatment efficacy and disease impacts in patients with HS

Table 1 Baseline characteristics

	HSSDD Analysis Set (N=934)	HSSQ Analysis Set (N=1,007)
Age, years, mean (SD)	37.1 (12.2)	36.7 (12.2)
Female, n (%)	525 (56.2)	569 (56.5)
Race, n (%)		
White	722 (77.3)	771 (76.6)
Black or African American	88 (9.4)	103 (10.2)
Asian	37 (4.0)	41 (4.1)
Other or Mixed	40 (4.3)	42 (4.2)
Region, n (%)		
North America	350 (37.5)	382 (37.9)
Western Europe	271 (29.0)	290 (28.8)
Central and Eastern Europe	243 (26.0)	260 (25.8)
Asia and Australia	70 (7.5)	75 (7.5)
BMI, kg/m², mean (SD)	33.0 (8.1)	33.1 (8.1)
Duration of disease, years, mean (SD)	8.0 (7.8)	7.9 (7.8)
AN count, mean (SD)	16.4 (16.5)	16.2 (16.1)
DT count, mean (SD)	3.5 (4.2)	3.6 (4.3)
Hurley Stage, n (%)[a]		
II	524 (56.1)	561 (55.7)
III	409 (43.8)	446 (44.3)
Symptom item scores, mean (SD)		
Worst skin pain	5.5 (2.5)	N/A[b]
Average skin pain	4.8 (2.5)	N/A[b]
Skin pain	N/A[b]	5.8 (2.4)
Smell or odour	4.4 (3.0)	4.6 (3.0)
Itch	4.7 (2.7)	5.0 (2.8)
Drainage or oozing	4.5 (2.8)	5.0 (2.8)

Data presented for HSSDD analysis set (all randomised patients with ≥1 non-missing HSSDD weekly symptom item score at any scheduled assessment visit) and HSSQ analysis set (all randomised patients with ≥1 non-missing HSSQ item score at any scheduled assessment visit). Percentages may not sum to 100 due to rounding. [a]Only patients with Hurley Stage II and III were included at baseline, as per the BE HEARD I & II eligibility criteria. [b]HSSDD assesses worst skin pain and average skin pain, while HSSQ assesses skin pain.

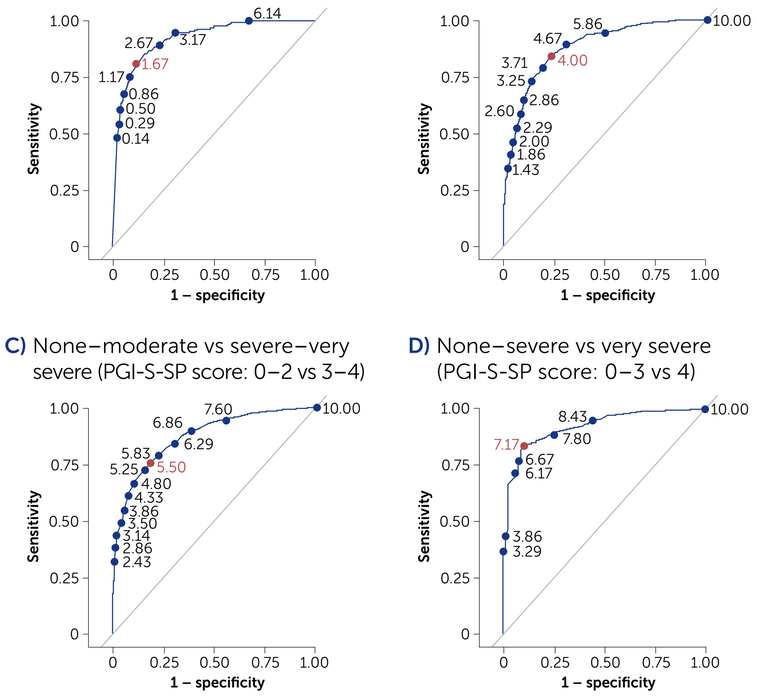
Figure 1 eCDF plot of changes from baseline to Week 16 in HSSDD worst skin pain by PGI-S-SP response category



No change (%)	0.0	0.0	0.0	2.5	22.7	68.5	93.1	99.5	100	100	100
Improvement by 1 level (%)	0.0	0.0	5.8	17.5	55.6	87.4	99.1	99.6	100	100	100
Improvement by 2 levels (%)	0.0	1.1	18.7	49.5	80.2	98.9	100	100	100	100	100
Improvement by 3 levels (%)	0.0	5.3	36.8	68.4	89.5	100	100	100	100	100	100

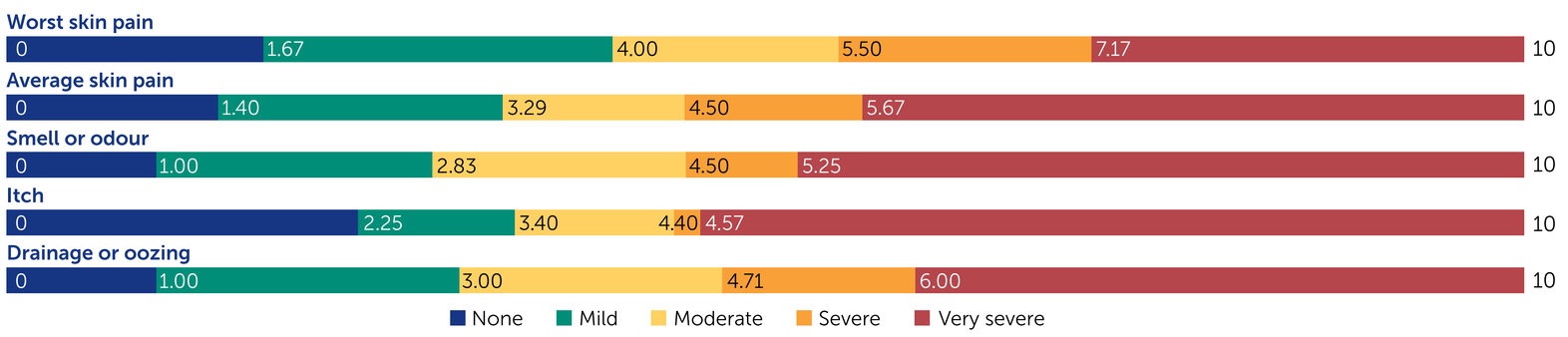
HSSDD analysis set (all randomised patients with ≥1 non-missing HSSDD weekly symptom item score at any scheduled assessment visit). Patients were divided into different response groups based on the PGI-S-SP response from baseline to Week 16.

Figure 2 ROC curves for determination of disease severity thresholds for HSSDD worst skin pain using PGI-S-SP response categories



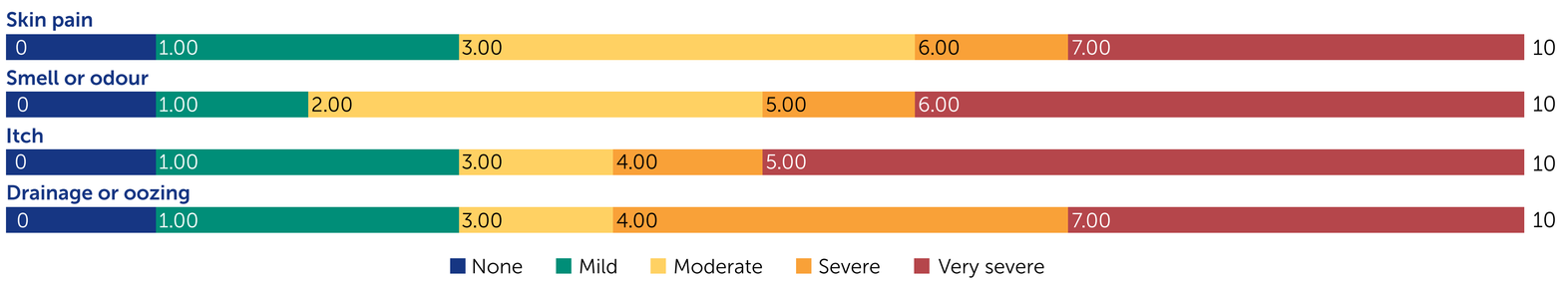
HSSDD analysis set (all randomised patients with ≥1 non-missing HSSDD weekly symptom item score at any scheduled assessment visit). Each target scale cut-off threshold for a given severity level was estimated from the highest Youden index of the ROC curve, using data pooled across visits at baseline, Week 4, Week 16, Week 32 and Week 48. Red markers indicate cut-offs corresponding to the maximum Youden index values.

Figure 3 Severity thresholds for HSSDD symptom item scores



Numbers within the coloured bars indicate the lower score for each severity threshold. Score categories were determined by a ROC analysis using PGI-S-SP (HSSDD worst skin pain and average skin pain items) and PGI-S-HS (HSSDD smell or odour, itch, and drainage or oozing items) as anchors.

Figure 4 Severity thresholds for HSSQ symptom item scores



Numbers within the coloured bars indicate the lower score for each severity threshold. Score categories were determined by a ROC analysis using PGI-S-SP (HSSQ skin pain item) and PGI-S-HS (HSSQ smell or odour, itch, and drainage or oozing items) as anchors.

AN: abscess and inflammatory nodule; **BMI:** body mass index; **DT:** draining tunnel; **eCDF:** empirical cumulative distribution function; **HS:** hidradenitis suppurativa; **HSSDD:** Hidradenitis Suppurativa Symptom Daily Diary; **HSSQ:** Hidradenitis Suppurativa Symptom Questionnaire; **PGI-S-HS:** Patient Global Impression of Severity of HS; **PGI-S-SP:** Patient Global Impression of Severity of Skin Pain; **ROC:** receiver operating characteristic; **SD:** standard deviation.

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References: [1]Ingram JR et al. J Eur Acad Dermatol Venereol 2022;36:1597–605; [2]BE HEARD I: www.clinicaltrials.gov/study/NCT04242446; [3]BE HEARD II: www.clinicaltrials.gov/study/NCT04242498. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **JRI**, **JSK**, **JL**, **RR**, **EM**, **IP**, **CGP**; Drafting of the publication, or reviewing it critically for important intellectual content: **JRI**, **JSK**, **JL**, **RR**, **EM**, **IP**, **CGP**; Final approval of the publication: **JRI**, **JSK**, **JL**, **RR**, **EM**, **IP**, **CGP**. **Author Disclosures: JRI:** Receives a stipend as Editor-in-Chief of the British Journal of Dermatology and an authorship honorarium from UpToDate; consultant for AbbVie, Boehringer Ingelheim, ChemoCentryx, Citryll, MoonLake Immunotherapeutics, Novartis, UCB Pharma and Union Therapeutics; has served on advisory boards for Insmed, Kymera Therapeutics and Viela Bio; co-copyright holder of HiSQOL© and HS-IGA; his department receives income from copyright of the Dermatology Life Quality Instrument (DLQI) and related instruments. **JSK:** Reports personal fees from AbbVie, ChemoCentryx, CSL Behring, DermTech, Incyte, Insmed, Janssen, MoonLake Immunotherapeutics, Novartis and UCB Pharma; personal fees and grants from Incyte; co-copyright holder of HiSQOL©; consultant for and received honoraria from AbbVie, Alumis, DermTech, Incyte, Insmed, Janssen, MoonLake Immunotherapeutics, Novartis and UCB Pharma; has been a speaker for AbbVie, Janssen, Novartis and UCB Pharma. **JL**, **RR**, **EM**, **IP:** Employees and shareholders of UCB Pharma. **CGP:** Employee of Evidera, a part of Thermo Fisher Scientific that receives funding for research from UCB Pharma. **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, MSc, UCB Pharma, Monheim, Germany for publication coordination, Jack Wardle, MSc, Costello Medical, Cambridge, UK for medical writing and editorial assistance and the Creative team at Costello Medical for graphic design assistance. All costs associated with development of this poster were funded by UCB Pharma.

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Poster ID: PCR205
Link expiration: 29 November 2023

Presented at ISPOR Europe 2023 | Copenhagen, Denmark | 12–15 November 2023