Validation of the HS-IGA: A Novel Hidradenitis Suppurativa-Specific Investigator Global Assessment for Use in Interventional Trials

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Objective

To assess the cross-sectional and longitudinal psychometric properties of the Hidradenitis Suppurativa Investigator Global Assessment (HS-IGA) tool using clinical data from a phase 2 randomised double-blind placebo-controlled active-reference arm trial (NCT03248531).

Background

- Unlike other dermatologic conditions, hidradentis suppurativa (HS) does not have a global assessment measure that is easy to use in both clinical trials and real-world clinical practice.[1]
- A global assessment of disease activity has been identified by the HS Core Outcome Set Collaboration (HiSTORIC) as one of several core domains to measure in future HS trials alongside pain, symptoms, physical signs, HS-specific quality of life and disease progression.[2]
- HS-IGA is a novel global assessment tool that has been developed and initially validated by HiSTORIC to assess disease severity and intervention responsiveness.[3]
- HS-IGA does not require raters to distinguish among lesion types, limits counting to 21 lesions and consolidates anatomic regions. These features may allow for improved operational performance and ease of rater use in HS trials.[3]

Methods

- Psychometric properties of the HS-IGA were assessed using blinded data from 88 adult participants enrolled in a phase 2 randomised double-blind placebo-controlled active-reference arm trial that assessed the efficacy, safety and pharmacokinetics of bimekizumab in moderate to severe HS (NCT03248531) (**Table 1**).
- HS-IGA is a 6-point dichotomous scale in which the score is derived as a number between 0 and 5 based on maximum lesion count in either the lower body or upper body, whichever sum is greater, as shown in **Table 2**. Response is defined as a 2-point improvement from baseline.[3]
- Convergent validity was assessed by computing Spearman's rank correlation coefficients at baseline and Week 12 between HS-IGA score and other clinician-rated measures of HS severity (International HS Severity Score System [IHS4][4] and HS Physician's Global Assessment [HS-PGA]).[5]
- Divergent validity was assessed by computing Spearman's rank correlation coefficients at baseline and Week 12 between HS-IGA and patient-reported outcome measures (Dermatology Life Quality Index [DLQI] and Patient's Global Assessment of average and worst skin pain [PtGA-ASK and PtGA-WSK, respectively]).
- Test-retest reliability was assessed by calculating an intraclass correlation coefficient (ICC) between screening and baseline visits.
- Responsiveness was evaluated by comparing HS-IGA with HS Clinical Response endpoint (HiSCR), a clinician-rated measure of HS severity.[6] Proportions of HS-IGA responders and $HiSCR_{50/75/90}$ responders and non-responders were compared at Week 12 using contingency tables with chi-square tests of independence.
- The ability of HS-IGA to predict dichotomic anchors ($HiSCR_{50/75/90}$ response and HS-PGA clear or minimal) was assessed over time using the area under the curve (AUC) of the receiver operating characteristic constructed with a mixed effects logistic regression model.

Results

- HS-IGA exhibited strong convergent validity with IHS4 and HS-PGA both at baseline (Spearman's rank correlation 0.86 [p<0.001] and 0.74 [p<0.001], respectively) and at Week 12 (Spearman's rank correlation 0.73 [p<0.001] and 0.64 [p<0.001], respectively).
- Divergent validity was as expected, with weaker correlation coefficients between HS-IGA and DLQI, PtGA-ASK and PtGA-WSK both at baseline (Spearman's rank correlation 0.15 [p=0.156], <0.4, <0.4, respectively) and at Week 12 (Spearman's rank correlation 0.20 [p=0.082],<0.4, <0.4, respectively).
- HS-IGA scores showed very good test-retest reliability (ICC 0.92) between screening and baseline visits.
- HS-IGA responders were associated with $HiSCR_{50/75/90}$ responders at Week 12 (χ^2 of 18.45 [p<0.001], 18.11 [p<0.001], and 20.83 [p<0.001], respectively), supporting the good ability of the HS-IGA to detect change over time (i.e., responsiveness) (**Table 3**).
- HS-IGA scores showed good predictive validity compared with $HiSCR_{50/75}$ (AUC 0.69/0.73) and with HS-PGA clear or minimal (AUC 0.71) response at Week 12; the closest alignment was with $HiSCR_{90}$ (AUC 0.85).
- While data from a phase 2 randomised controlled trial were used to assess psychometric properties of the HS-IGA, some subgroups had a smaller number of participants for analysis, and this may have also influenced patient-centredness performance.

Conclusions

HS-IGA demonstrates very good psychometric properties and may be considered for use as an endpoint in clinical trials, supporting drug development efforts in HS; it also has potential for use in clinical practice. As advanced treatments are developed, alignment with the stringent $HiSCR_{90}$ indicates HS-IGA may be less susceptible to ceiling effects.

Summary

The HS-IGA assessment tool demonstrates very good psychometric properties when compared with currently utilised clinician-reported outcome measures, as illustrated by the measures of convergent validity (Spearman's rank correlation coefficients), test-retest reliability (ICC) and predictive validity (AUC) reported here.

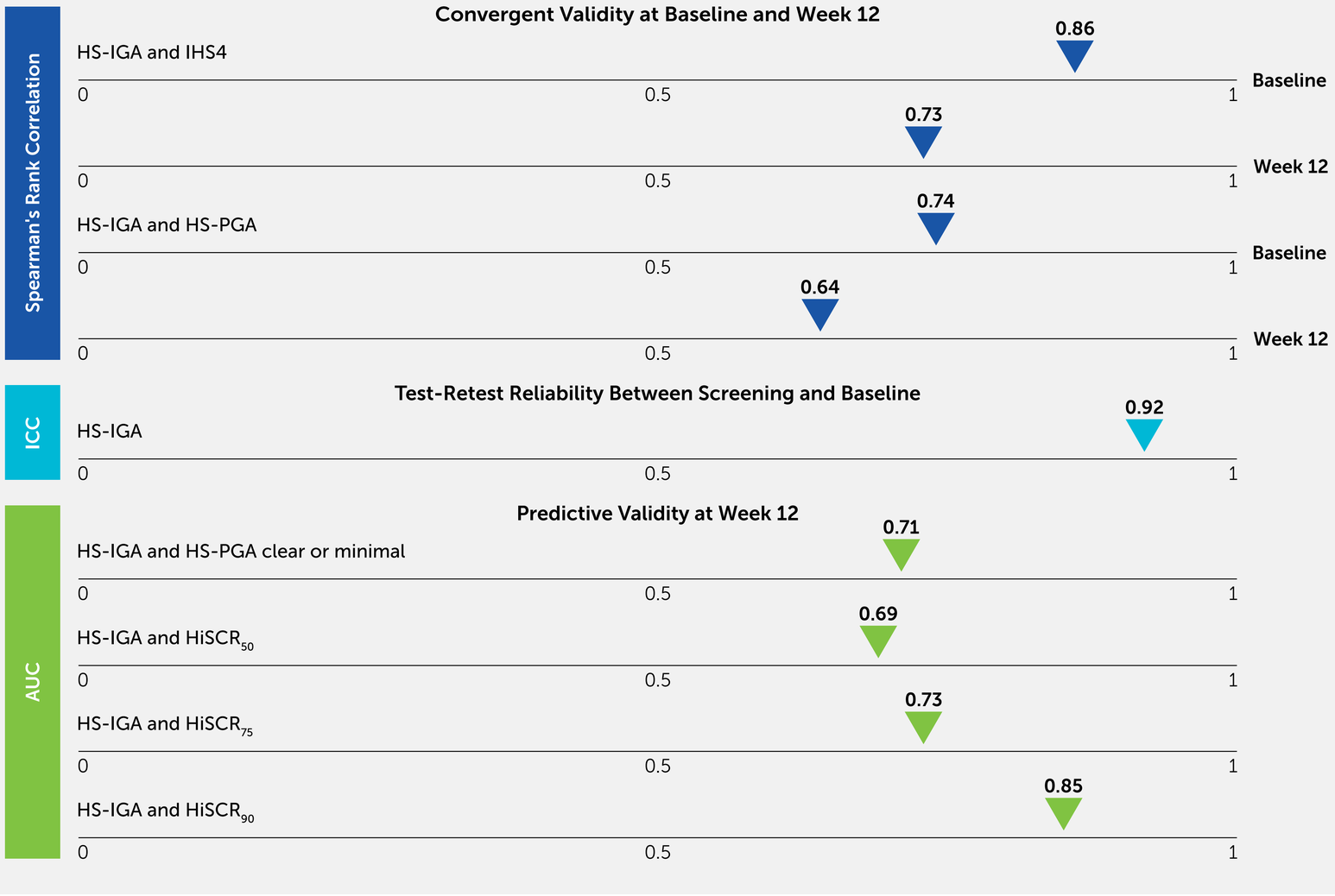

Table 1 Demographics and clinical characteristics of study population

Characteristic	Full Analysis Set (N=88)
Age, years, mean (SD)	36.7 (12.0)
Female, n (%)	61 (69.3)
Race, n (%)	
Caucasian	61 (69.3)
Black or African American	20 (22.7)
Asian	4 (4.5)
Other or mixed	3 (3.4)
Region, n (%)	
Australia	19 (21.6)
Europe	25 (28.4)
United States	44 (50.0)
Clinical Characteristics at Baseline	
HS-IGA, mean (SD)	3.8 (1.4)
HS-PGA,[a] n (%)	
Clear	0 (0.0)
Minimal	0 (0.0)
Mild	1 (1.1)
Moderate	28 (31.8)
Severe	4 (4.5)
Very severe	55 (62.5)
HS-PGA, mean (SD)	4.3 (1.0)
IHS4,[b] mean (SD)	43.1 (30.1)
Clinical Characteristics at Week 12	
$HiSCR_{50}$,[c] n/N (%)	42/79 (53.2)
$HiSCR_{75}$,[c] n/N (%)	29/79 (36.7)
$HiSCR_{90}$,[c] n/N (%)	17/79 (21.5)

[a]The HS-PGA score ranges from clear to very severe;[5] [b]A higher IHS4 score signifies greater HS severity; the score is the sum of the number of nodules (multiplied by 1), the number of abscesses (multiplied by 2) and the number of draining tunnels (multiplied by 4);[4] [c]$HiSCR_{50}$ represents at least 50% reduction in total abscess and inflammatory nodule count with no increase from baseline in abscess or draining fistula count, with $HiSCR_{75}$ and $HiSCR_{90}$ representing at least 75% and 90% reductions, respectively.[6]

Table 2 HS-IGA score

HS-IGA Score[a]	Maximum Lesion Count in Upper or Lower Body
0	0–1
1	2–5
2	6–10
3	11–15
4	16–20
5	>20

[a]The HS-IGA is a 6-point dichotomous scale scored between 0 and 5 based on total abscess, fistula (draining and non-draining) and nodule (inflammatory and non-inflammatory) count, either in the upper body area or the lower body area, whichever sum is greater.[3]

Table 3 Responsiveness: contingency table of HiSCR and HS-IGA responses at Week 12

	HS-IGA Response[a]		
	No	Yes	Chi-square Test
	n (%)		
$HiSCR_{50}$[b]			
No	33 (64.7)	4 (14.3)	χ^2 (1, 79)=18.45 p<0.001
Yes	18 (35.3)	24 (85.7)	
$HiSCR_{75}$[b]			
No	41 (80.4)	9 (32.1)	χ^2 (1, 79)=18.11 p<0.001
Yes	10 (19.6)	19 (67.9)	
$HiSCR_{90}$[b]			
No	48 (94.1)	14 (50.0)	χ^2 (1, 79)=20.83 p<0.001
Yes	3 (5.9)	14 (50.0)	

[a]HS-IGA response is defined as a 2-point reduction in score relative to baseline; [b]$HiSCR_{50}$ represents at least 50% reduction in total abscess and inflammatory nodule count with no increase from baseline in abscess or draining fistula count, with $HiSCR_{75}$ and $HiSCR_{90}$ representing at least 75% and 90% reductions, respectively.[6]

AUC: area under the curve; **DLQI:** Dermatology Life Quality Index; **HiSCR:** Hidradenitis Suppurativa Clinical Response scale; **HiSTORIC:** Hidradenitis Suppurativa Core Outcomes Set International Collaboration; **HS:** hidradenitis suppurativa; **HS-IGA:** Hidradenitis Suppurativa Investigator Global Assessment; **HS-PGA:** Hidradenitis Suppurativa Physician's Global Assessment; **ICC:** intraclass correlation coefficient; **IHS4:** International Hidradenitis Suppurativa Severity Score System; **PtGA-ASK:** Patient's Global Assessment of Average Skin Pain; **PtGA-WSK:** Patient's Global Assessment of Worst Skin Pain; **SD:** standard deviation.

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