Performance of the Scleroderma Skin Patient-reported Outcome (SSPRO) in a Phase 2 Trial with Lenabasum

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Poster # FRI0334

Abstract

Background/Purpose: Skin involvement is a distressing feature of systemic sclerosis (SSc). The severity and extensiveness of skin thickening, as traditionally assessed by mRSS, may not directly correlate with its effect on patients' health related quality of life (HRQoL). The Scleroderma Skin Patient-reported Outcome (SSPRO) was specifically developed to assess the skin-related HRQoL in SSc. No skin-specific PRO in SSc has been prospectively validated in a clinical trial.
Objective: Validate the SSPRO prospectively in a clinical trial.
Methods: The SSPRO, Patient Global Assessment (PtGA), Physician Global Assessment (MDGA), HAQ-DI, mRSS, FVC % predicted, PROMIS-29 questionnaire, and ACR CRISS were assessed prospectively in a Phase 2 study of lenabasum in dcSSc. SSPRO has 18 items that assess four SSc skin-related HRQoL domains. The Phase 2 study of lenabasum had a 4-month double-blind portion (N = 38 completers) followed by an open-label extension (N = 36 entered). Spearman correlations of baseline values and change values were determined for SSPRO and other outcome measures. Mean change in SSPRO scores were determined in subjects with different levels of improvement in other efficacy outcomes.
Results: At baseline, SSPRO correlated moderately with all other outcome measures except for FVC %, as expected, with strongest correlations with PtGA, HAQ-DI, and PROMIS-29 pain interference and social role domains. The mean change in SSPRO scores at 3 and 12 months correlated mostly moderately (r = 0.25 to 0.62) with the mean change in other outcome scores, but correlations were low or inconsistent with change in mRSS, FVC%, and PROMIS-29 anxiety domain. Significance of correlations in some outcomes was hampered by small magnitudes of change.
Conclusion: SSPRO score correlates with both physician and patient-reported outcomes at baseline, though correlations with the latter were stronger. Change in SSPRO reflects changes in how the patient feels (PtGA, PROMIS-29 pain interference and depression domains) and functions (HAQ-DI, PROMI-29 physical function and social role domains) and less consistently with physician-assessed outcomes. Subjects with improvement ≥ MID levels of −0.250 in HAQ-DI, -1 in PtGA, and −5 in mRSS had SSPRO improvements of -22 to -23 points at 12 months.

Background

- It is clinically relevant to measure health-related quality of life (HRQOL) when testing clinical benefit of potential treatments for diffuse cutaneous systemic sclerosis (dcSSc).
- Skin involvement is a distressing feature of dcSSc.
- The Scleroderma Skin Patient-reported Outcome (SSPRO) was specifically developed to assess the skin-related HRQoL in patients with SSc. Patient input was central to all phases of its development.
- The SSPRO was previously shown to be reliable and valid with high internal consistency, and construct, content and face validity.[2]
- The hypothesis of this study was that SSPRO score is a valid measure of HRQoL in SSc patients.
- The objective of this study was to show, that in the context of a Phase 2 study in dcSSc patients:
  - Baseline SSPRO score correlates with other baseline HRQoL measures.
  - Change in SSPRO score correlates with change in other HRQoL measures.
  - Patients with medically meaningful improvement in mRSS and Health Assessment Questionnaire-Disability Index (HAQ-DI) have greater improvements in SSPRO scores than patients with less or no improvement.

Methods

- JB101-SSc-001 is a Phase 2 study of lenabasum in subjects with dcSSc, with a 4-month double-blind placebo-controlled Part A followed by an open-label extension (OLE).
- The SSPRO, Patient Global Assessment (PtGA), Physician Global Assessment (MDGA), HAQ-DI, mRSS, FVC % predicted, PROMIS-29 questionnaire, and ACR CRISS were assessed prospectively in this study.
- Spearman correlations of baseline values and change values were determined for SSPRO and other outcome measures.
- Mean change in SSPRO scores were determined in subjects with increasing levels of improvement in other patient-reported outcomes.

SSPRO Items and Scales

Question	Scale
1. How tight has your skin felt?	PS
2. How dry has your skin been?	PS
3. How painful has your skin been?	PS
4. How discolored has your skin been?	PS
5. How itchy has your skin felt?	PS
6. How self-conscious have you been because of your skin?	EE
7. How worried have you been about your skin?	EE
8. How depressed have you been about your skin?	EE
9. How much have you not felt like your true self because of the way your skin is?	EE
10. How frustrated have you been about your skin?	EE
11. How much have you felt like you lack control over your skin's condition?	EE
12. How much difficulty have you had doing things with your hands because of skin tightness?	PF
13. How much difficulty have you had with opening or closing your mouth because of skin tightness?	PF
14. How much difficulty have you had with moving parts of your body because of skin tightness?	PF
15. How much has your skin's condition interfered with your daily activities (examples: work, study, leisure activities)?	PF
16. How much has your skin prevented you from going out to socialize?	SE
17. How much has your skin interfered with your interactions with people?	SE
18. How much has your skin affected the clothes you wear?	SE
PS = Physical Symptoms, EE = Emotional Effects, PF = Physical Function, SE = Social Effects	

Table 1. SSPRO Items and Scales The SSPRO has18 items that represent 4 HRQoL scales: physical symptoms, social effects, emotional effects, and physical function. Each item is scored on a 7-point Likert scale. The scores for individual items are added to determine scores for the 4 scales and total SSPRO score.

Baseline Demographics and Disease Characteristics

- Baseline demographics and disease characteristics of subjects who had Baseline measurements in study JBT101-SSc-001 are given in **Table 2**.
- Subjects were mostly middle-aged, White females with moderate skin thickening and moderate overall disease activity as assessed by subjects and physicians, with moderate-severe disability as assessed by HAQ-DI. The majority of subjects were on stable doses of background immunosuppressive treatments.

Characteristic	Lenabasum (N = 27)	Placebo (N = 15)
Age in years, mean (SD)	49 (10.42)	47 (11.05)
Female sex, n (%)	23 (85.2)	9 (60.0)
White, n (%)	22 (81.5)	12 (80.0)
mRSS, mean (SD)	24 (10.40)	26 (11.12)
Disease duration in months, mean (SD)	34 (16.61)	33 (17.91)
Patient Global Assessment, mean (SD)	4.9 (2.28)	4.9 (2.81)
Physician Global Assessment, mean (SD)	4.6 (1.76)	5.2 (2.11)
HAQ-DI, mean (SD)	1.51 (0.793)	1.26 (0.809)
Concomitant immunosuppressive medicines (%)	93%	80%

Table 2. Baseline demographics and disease characteristics

Results

Correlations between SSPRO Total Score and Other Efficacy Measures

For purposes of discussion in this poster and without regard to direction, correlation coefficients are considered low for r < 0.25, moderate for r ≥ 0.25 to < 0.60, and high for r ≥ 0.60.

At Baseline:

- Directionally correct correlations between SSPRO total score and all other PRO were moderate to high at baseline
- Directionally correct correlations between SSPRO with mRSS and MDGA were moderate. There was no correlation with FVC % predicted
- SSPRO was not redundant with these other baseline efficacy measures, with r < 0.80 for all correlations

At 3 and 12 Months:

- Directionally correct correlations between change in SSPRO total score and change in physician-related assessments were generally low (MDGA and mRSS)
- Directionally correct correlations between change in SSPRO total score and change in patient reported function were generally moderate at 3 and 12 months, and corrections between change in SSPRO total score and ACR CRISS score and change in FVC % predicted with moderate at 12 months
- Correlations between change in SSPRO and change in mRSS, a physician assessment of skin thickening were low. This indicates that SSPRO provides additional information beyond change in mRSS

Time	Change in Patient-Reported Outcomes							Change in Other Outcomes			
	HAQ-DI	PtGA	PROMIS-29					ACR CRISS Score	mRSS	MDGA	FVC %
			Physical Function	Social Role	Pain Interference	Depression	Anxiety				
Baseline	0.52 0.0005	0.61 <0.0001	-0.33 0.034	-0.57 0.0001	0.62 <0.0001	0.51 0.0007	0.41 0.008		0.44 0.004	0.51 0.0007	-0.07 0.670
3 months	0.29 0.083	0.26 0.124	-0.46 0.004	-0.40 0.015	0.46 0.005	0.33 0.044	0.14 0.395	-0.20 0.235	0.02 0.932	0.30 0.067	-0.12 0.483
12 months	0.25 0.145	0.28 0.103	-0.25 0.152	-0.62 < 0.0001	0.41 0.014	0.27 0.119	0.21 0.234	-0.48 0.004	0.20 0.251	0.15 0.394	-0.53 0.001

Table 3. Spearman Correlations between SSPRO Total Score and Other Efficacy Outcomes at Baseline and between Change in SSPRO Total Score and Change in Other Efficacy Outcomes at 3 months, and 12 months, (r, P-value) Subjects with that improvement vs. those without. ACR CRISS score is absolute, not change, score

Degree of Improvement in SSPRO Total Score by Degree of Improvement in Other Efficacy Measures

Mean SSPRO total score generally increased in subjects with increasing levels of improvement in HAQ-DI, PtGA, mRSS, and ACR CRISS score (**Table 4**).

Efficacy Outcome	HAQ-DI Improvement at least				PtGA Improvement at least			mRSS Improvement at least				ACR CRISS score at least			
	None	-0.125	-0.250	-0.500	None	-1	-2	None	-3	-5	-8	< 0.30	≥ 0.30	≥ 0.60	≥ 0.90
3 months	-9.9	-17.6	-20.2	-22.5	-11.9	-15.3	-16.5	-11.0	-14.7	-16.3	-10.3	-10.2	-17.8	-17.1	-14.5
12 months	-17.9	-20.2	-22.7	-27.2	-16.5	-21.9	-21.5	-11.6	-19.6	-23.2	-23.1	-13.0	-23.5	-26.6	-27.3

Table 4. Mean SSPRO Total Score by Degree of Improvement in Other Efficacy Outcomes at 3 and 12 Months

Results

Correlations between SSPRO Total Score and Other Efficacy Measures

Effect sizes of SSPRO and other efficacy outcomes were determine at 3 months in the double-blinded, placebo-controlled part of study JBT101-SSc-001.

- Effect size for SSPRO total score and the 4 scales of SSPRO were similar to those for other efficacy outcomes (**Table 5**).

Efficacy Outcome	Effect Size
SSPRO	
Total	0.51
Physical Symptoms	0.57
Emotional Effects	0.39
Physical Function	0.57
Social Effects	0.42
mRSS	0.38
PtGA	0.35
MDGA	0.57
HAQ-DI	0.25

Table 5. Effect Sizes of Efficacy Outcomes in Lenabasum-treated Subjects at 3 Months

Summary and Conclusions

- SSPRO was prospectively validated in this small Phase 2 study
  - SSPRO total cores correlates with patient-reported outcomes and other efficacy outcomes at baseline
  - Change in SSPRO total scores also correlate better with patient-reported outcomes than physician-related outcomes at 3 and 12 months
  - Subjects with minimal important differences in HAQ-DI (Δ−0.250), PtGA (Δ-1, 0-10 range), and mRSS (Δ−5) had improvements in SSPRO total scores of ~ -15 to -20 points at 3 months and ~-22 to -23 points at 12 months
  - Effect sizes of SSPRO total score and its scales were better than effect sizes of other efficacy outcomes at 3 months
- Additional prospective validation in a larger and longer double-blind, placebo-controlled trial is warranted

Thank You

❖ To the people with SSc who participated in this study
❖ To the investigators and study staff for this study
❖ The JBT101-SSc-001 study was sponsored by Corbus Pharmaceuticals, Inc.

Please see a related presentation: Abstract # OP0325, Spiera R et al, Safety and Efficacy Of Lenabasum in an Open-Label Extension of a Phase 2 Study in Diffuse Cutaneous Systemic Sclerosis; 14/06/2019, 3:30 – 5 pm

References

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Presented at the European Congress of Rheumatology 2019 Madrid, Spain, June 12-15, 2019