# Health Assessment Questionnaire Disability Index (HAQ-DI) and Patient Global Assessment of Health (PtGA) Correlate with Changes (Δ) in Patient-Reported Outcomes (PROs)

*R. Spiera[*1], L. Hummers[2], L. Chung[3], T. Frech[4], R. Domsic[5], V. Hsu[6], D. E. Furst[7], J. Gordon[1], M. Mayes[8], R. Simms[9], E. Lee[10], S. Constantine[10], B. Conley[10], Q. Dinh[10], B. Bloom[10], B. White[10]*

[1]Hospital for Special Surgery, New York City; [2]Johns Hopkins, Baltimore; [3]Stanford, Palo Alto; [4]University of Utah, Salt Lake City; [5]University of Pittsburgh, Pittsburgh; [6]Robert Wood Johnson Medical School; [7]Pacific Arthritis Associates and UCLA, Los Angeles; University of Washington, Seattle, University of Florence, Italy; [8]University of Texas, Houston; [9]Boston University, Boston; [10]Corbus Pharmaceuticals, Inc., Norwood, United States

Abstract #158

## Abstract

**Introduction:** Health Assessment Questionnaire Disability Index (HAQ-DI) and Patient Global Assessment of Health (PtGA) are the most consistently used patient-reported outcomes (PRO) in recent trials in diffuse cutaneous systemic sclerosis (dcSSc). There is limited information on whether HAQ-DI and PtGA baseline and change scores correlate with each other and other PROs used in trials. The hypothesis was HAQ-DI scores would correlate with PROs that assess patent function and PtGA would correlate with PROs that assess patient symptoms.

**Methods:** Baseline and change (Δ) scores for HAQ-DI and PtGA were correlated (Spearman) with each other, PROMIS-29 domain scores, and Systemic Sclerosis Skin Symptoms Patient-reported Outcome (SSPRO) scores in the double-blind placebo-controlled (Part A) study of lenabasum in SSc (N = 42) and its open-label extension (OLE, N = 36). Change scores were correlated at Month 3 of Part A (N = 38) and Months 6, 12, 18, and 24 (N = 36, 31, 30, and 24, respectively) of the OLE. For descriptive purposes in this abstract, correlations coefficients (r) were categorized as no (0 to 0.19), weak (0.20 to 0.34), moderate (0.35 to 0.59), strong (0.60 to 0.79) correlations, and very strong (≥ 0.80) correlations.

**Results:** All correlations were directionally correct (**Table 1**). All moderate, strong, or very strong correlations were statistically significant, p ≤ 0.05, except p = 0.06 for a few moderate correlations. Baseline HAQ-DI and PtGA values correlated moderately or strongly with each other and all other PRO except PROMIS-29 sleep disturbance in Part A, but not the OLE. HAQ-DI and PROMIS-29 physical function were redundant at baseline in Part A, r = 0.80. Change in HAQ-DI consistently correlated most strongly with Δ PROMIS-29 physical function and social role in Part A and the OLE (p < 0.01), except not with Δ social role at 3 months in Part A. Δ PtGA correlated moderately and occasionally strongly with Δ patient symptoms as assessed by Δ PROMIS-29 anxiety, depression, fatigue, and pain interference domains in Part A and the OLE, at all visits.

**Conclusion:** The correlations between changes in HAQ-DI and other patient-reported functioning and between change in PtGA and patient-reported symptoms were notable for their consistency over 2 years in this study. Both Δ HAQ-DI and Δ PtGA are included in the calculation of the ACR Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) score, suggesting this composite score may reflect both patient function and symptoms.

## Background

- Systemic sclerosis (SSc) is a potentially life-threatening autoimmune disease characterized by thickened skin resulting from inflammation, edema, and fibrosis (Denton and Khanna, 2017) with significant effects on health-related quality of life (HRQOL) (Morrisroe et al, 2018).
- Lenabasum is a novel rationally designed oral agonist of cannabinoid receptors (CB) that activates the ECS with preferential activity at $CB_2$ (Burstein, 2018).
- In a Phase 2 study, lenabasum demonstrated improved efficacy outcomes with a favorable safety profile among 42 participants with dcSSc (Spiera et al, 2020).
- The Scleroderma Skin Patient-reported Outcome (SSPRO) was specifically developed as a reliable and valid instrument to assess the skin-related HRQoL in patients with SSc (Man et al, 2017).
- ACR CRISS is a composite outcome designed to evaluate improvement from baseline in clinical trial subjects with diffuse cutaneous SSc.
- ACR CRISS includes change from baseline in 2 PROs, HAQ-DI (patient function) and PtGA (patient overall assessment of health).
- The question is whether inclusion of HAQ-DI and PtGA in ACR CRISS also represents changes in other PROs, making ACR CRISS more broadly representative of patient opinion of clinical benefit

## Objective

- The objective of this analysis was to determine:
  - If HAQ-DI scores were correlated with PROs that assess patient function
  - If PtGA scores were correlated with PROs that assess patient symptoms

## Methods

- In this Phase 2 study of lenabasum, subjects with dcSSc were enrolled in a 4-month double-blind placebo-controlled study, followed by an open-label extension (OLE) (**Figure 1**).

**Figure 1. Design for Phase 2 Study of Lenabasum in dcSSc**


### Subject Selection Criteria

- Adults with dcSSc were included if they had disease duration ≤ 3 years or > 3 and ≤ 6 years if mRSS ≥ 16 or CRP or IL-6 were high.
- Stable doses of concomitant medicines, including immunosuppressive drugs, was allowed.
- Study treatment during double-blind phase
  - Month 1: Lenabasum 5 mg once daily, 20 mg once daily, 20 mg twice daily or placebo
  - Months 2-3: Lenabasum 20 mg twice daily or placebo
- Off Study Drug Phase: Background immunosuppressant medications were continued, but no study drug was given (Mean 20.2 weeks).
- OLE: Lenabasum 20 mg twice daily was continued for subjects who completed the double-blind phase with lenabasum or placebo.

### Study Analysis

- Assessments
  - SSPRO – Patient-reported answers to 18 questions about how scleroderma affects the skin and how those skin problems affect how the person feels and does things.
  - Patient Global Assessment (PtGA) – Visual analog scale where the patient selects a whole number (0 through 10) that best reflects overall health
  - Physician Global Assessment (MDGA) - Visual analog scale where the physician selects a whole number (0 through 10) that best reflects overall health
  - HAQ-DI – Patient-reported assessment of functional disability
  - PROMIS-29 questionnaire – Measures what participants are able to do and how they feel by asking questions
- Spearman correlations of baseline values and change values were determined for SSPRO and other outcome measures.
- Mean change in SSPRO scores was determined in subjects with increasing levels of improvement in other PROs.
- Spearman correlations between baseline values and mean change (Δ) scores for HAQ-DI and PtGA, PROMIS-29 domain scores, and SSPRO scores were determined in the
  - Double-blind, placebo-controlled study (N = 42)
  - Open-label extension (OLE, N = 36)
- Correlations between mean change scores for each assessment were determined for:
  - Double-blind, Month 3 (N = 38)
  - OLE, Months 6, 12, 18, and 24 (N = 36, 31, 30, and 24, respectively)
- For descriptive purposes, correlations coefficients (r) were categorized as:
  - None (0 to 0.19)
  - Low (0.20 to 0.34)
  - Moderate (0.35 to 0.59)
  - Strong (0.60 to 0.79)
  - Very strong (≥ 0.80)

## Results

- Baseline demographics and disease characteristics for the overall study population are shown in **Table 1**.
- Subjects were mostly middle-aged, white females with moderate skin thickening and moderate overall disease activity as assessed by participants and physicians, with moderate-severe disability as assessed by HAQ-DI.
- The majority of subjects were on stable doses of background immunosuppressive treatments.

**Table 1. Baseline Characteristics of Study Population**

| Characteristic | Lenabasum (N = 27) | Placebo (N = 15) |
|---|---|---|
| Age, years* | 49 ± 10.4 | 47 (11.1) |
| Female sex, n (%) | 23 (85.2) | 9 (60.0) |
| White, n (%) | 22 (81.5) | 12 (80.0) |
| mRSS* | 24 ± 10.4 | 26 ± 11.1 |
| Disease duration, months* | 34 ± 16.6 | 33 ± 17.9 |
| Patient Global Assessment* | 4.9 ± 2.3 | 4.9 ± 2.8 |
| Physician Global Assessment* | 4.6 ± 1.8 | 5.2 ± 2.1 |
| HAQ-DI* | 1.5 ± 0.8 | 1.3 ± 0.8 |
| Concomitant immunosuppressive medicines (%) | 93% | 80% |

* Mean ± standard deviation

- All correlations were directionally correct (**Tables 2 and 3**).
- All moderate, strong or very strong correlations were statistically significant, p ≤ 0.05, except p = 0.06 for some moderate correlations.
- Baseline HAQ-DI and PtGA values correlated moderately or strongly with each other and all other PROs except PROMIS-29 sleep disturbance in the double-blind study, but not the OLE.
- HAQ-DI and PROMIS-29 physical function were redundant at baseline in the double-blind study, r = 0.80.

**Table 2. Correlations Between Change Scores for HAQ-DI and Patient-reported Outcomes**

| Correlations between HAQ-DI | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time (months) | PtGA | SSPRO | PROMIS-29 Domain | | | | | | |
| | | | Physical Function | Social Role | Anxiety | Depression | Fatigue | Sleep | Pain Interference |
| 3 | 0.37* | 0.31+ | -0.68*** | -0.02 | 0.65*** | 0.57*** | 0.29 | 0.15 | 0.25 |
| 6 | 0.43** | 0.43** | -0.68*** | -0.48** | 0.48** | 0.55*** | 0.55*** | 0.34* | 0.50** |
| 12 | 0.35+ | 0.41* | -0.75*** | -0.59*** | 0.35+ | 0.36* | 0.52** | 0.19 | 0.43* |
| 18 | 0.47** | 0.36+ | -0.73*** | -0.52** | 0.37* | 0.51** | 0.61*** | 0.27 | 0.50** |
| 24 | 0.43* | 0.51* | -0.70*** | -0.58** | 0.38 | 0.44* | 0.25 | 0.26 | 0.34 |

*p ≤ 0.05; ** p ≤ 0.01;*** p ≤ 0.001; +p ≤ 0.06

### Between Group Correlations

- Change in HAQ-DI consistently correlated most strongly with Δ PROMIS-29 physical function and social role in the double-blind study and the OLE (p < 0.01), with the exception of Δ social role at 3 months in the double-blind study (**Table 2**).
- Change in PtGA correlated moderately and occasionally strongly with change in subject symptoms as assessed by Δ PROMIS-29 anxiety, depression, fatigue, and pain interference domains in the double-blind study and the OLE, at all visits (**Table 3**).

**Table 3. Correlations Between Change Scores for PtGA and Patient-reported Outcomes**

| Correlations with PtGA | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time (months) | HAQ-DI | SSPRO | PROMIS-29 Domain | | | | | | |
| | | | Physical Function | Social Role | Anxiety | Depression | Fatigue | Sleep | Pain Interference |
| 3 | 0.37* | -0.27 | -0.14 | -0.28 | 0.55*** | 0.64*** | 0.46** | 0.23 | 0.50** |
| 6 | 0.43** | 0.33+ | -0.37* | -0.15 | 0.53*** | 0.50** | 0.59*** | 0.37* | 0.56*** |
| 12 | 0.35+ | 0.34+ | -0.25 | -0.16 | 0.43* | 0.54** | 0.63*** | 0.39* | 0.64*** |
| 18 | 0.47** | 0.3 | -0.59*** | -0.46* | 0.55** | 0.56** | 0.65*** | 0.37* | 0.57** |
| 24 | 0.43* | 0.66*** | -0.22 | -0.53** | 0.46** | 0.62** | 0.56** | 0.50* | 0.61** |

*p ≤ 0.05; ** p ≤ 0.01; ***p ≤ 0.001; +p ≤ 0.06

## Summary and Conclusions

- Correlations between changes in the HAQ-DI and other patient-reported functioning and between change in PtGA and patient-reported symptoms were notable for their consistency across 2 years in this study.
- Directionally correct change in HAQ-DI and in PtGA are included in the calculation of the ACR Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) score.
- Correlations observed between change scores for HAQ-DI, PtGA and other PROs suggest that inclusion of changes in HAQ-DI and PtGA in ACR CRISS may be adequate to allow ACR CRISS to broadly reflect changes in PROs, making it a useful efficacy endpoint for studies that look holistically for improvement in subjects with dcSS.
- Results from the Phase 3 RESOLVE-1 study of lenabasum will provide further data for the correlations between PROs and may further support for the use of ACR CRISS as the primary efficacy endpoints in randomized, controlled trials of subjects with dcSSc.

## References

Burstein SH. The cannabinoid acids, analogs and endogenous counterparts. *Bioorg Med Chem.* 2014;22(10):2830-43.

Man A, Correa JK, Ziemek J, Simms RW, Felson DT, Lafyatis R. Development and validation of a patient-reported outcome instrument for skin involvement in patients with systemic sclerosis. *Ann Rheum Dis.* 2017;76:1374–80.

Morrisroe K, Hudson M, Baron M, de Vries-Bouwstra J, Carreira PE, Wuttge DM, Wang M, Frech TM, Stevens W, Proudman SM, Nikpour M; International Systemic Sclerosis Inception Cohort (INSYNC) collaboration. Determinants of health-related quality of life in a multinational systemic sclerosis inception cohort. *Clin Exp Rheumatol.* 2018;36 Suppl 113(4):53-60.

Spiera R. Hummers L, Chung L, Frech TM, Domsic R, Hsu V, et al. Safety and efficacy of lenabasum in a phase 2 randomized, placebo-controlled trial in adults with systemic sclerosis. *Arthritis Rheum.* 2020 in press.

Poster presented at the 6th Systemic Sclerosis World Congress; 5-7 March 2020; Prague, Czech Republic