Patient and Physician Opinions of Clinical Benefit at 3 Months in a Clinical Trial Correlate with Patient-Reported Outcomes (PROs)

R. Spiera,* L. Hammond,* L. Chenq,† F. Protat,* B. Domais,* V. Hart,‡ D. E. F. Ugris†,† G. Jourdàn,‡ M. Mayapo,‡ R. Simona,‡ E. Lee,‡ S. Constantinou,‡ B. Conroy,* G. Dillé,* B. Bloom,* W. White‡

*Hospital for Special Surgery, New York City, †Joslin Diabetes, Baltimore, ‡Stanford, Palo Alto; †University of Utah, Salt Lake City, ‡University of Pittsburgh, Pittsburgh; *Weill Medical College of Cornell University, New York City; ‡Scripps, La Jolla, Los Angeles, Los Angeles, California, United States; †University of Florence, Florence, Italy; University of Texas, Houston; *Boston University, Boston, **Cymbal Pharmaceuticals, Inc., Norwood, United States

Abstract

Introduction

Scleroderma (ScS) is a potentially life-threatening autoimmune disease characterized by a triad of chronic inflammation, fibrosis, and vascular damage (Sepúlveda et al, 2019). ScS results in impaired health status, a greater chronic disease burden, and increased mortality (Morrisroe et al, 2017; Zhou et al, 2019).

The endocannabinoid system (ECS) is a naturally occurring neuroimmune modulatory system that regulates innate immune responses and associated repair, regeneration, and neuroinflammation (Buckley et al, 2014; Serhan, 2014) (Figure 1).

Lambdasum is a novel, selective, CB2 agonist that activates proresolving innate immune responses (Tepner et al, 2014) (Figure 2).

In a Phase 2 study of patients with dcSSc, lambdasum was well tolerated and was associated with improvements in the American College of Rheumatology (ACR) Combined Response Index in diffuse cutaneous Scleroderma (CRISS) score (Spiera et al, 2020). Disease-specific and non-specific patient reported outcomes (PROs) are used to assess how people with SSc feel and function.

The opinion of the patient and treating physician of the clinical benefit of lambdasum in early treatment of dcSSc (4 months) correlated with change in PROs and efficacy outcomes. Longer studies will further elucidate which PROs reflect ScS patients’ assessment of clinical benefit from treatment.

Objective

This was a secondary analysis from a Phase 2 study of lambdasum in patients with dcSSC (Spiera et al, 2020) to evaluate the correlation between patient and physician assessments of the clinical benefit of lambdasum in early treatment (3 months) with the change in PROs.

Methods

Study Design

This was a double-blind, randomized, placebo-controlled Phase 2 study conducted at ninetofive SSC centers (Figure 3).

In the 159 patients completing 3 months dosing, the PROs included HAQ-DI, PROMIS Physical Function, Social Role, Pain, and Interference.

The opinion of the patient and treating physician of the clinical benefit of lambdasum was safe and well tolerated. The PROs included HAQ-DI, PROMIS Physical Function, Social Role, Pain, and Interference.

Results

The baseline characteristics of the study population were similar between groups (Table 1).

Table 2. Correlation of Physician and Patient Opinions of Clinical Benefit with Patient-Reported Outcomes (PROs) at 3 Months

<table>
<thead>
<tr>
<th>Opinion of Clinical Benefit</th>
<th>Lambdasum (n = 77)</th>
<th>Placebo (n = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR CRISS Score (higher)</td>
<td>0.74</td>
<td>0.62</td>
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</table>
| mRSS                       | ≤ 6 years duration who were on stable standard care treatment received lambdasum for 3 months. 49 patients completed 3 months dosing.
| mRSS                       | 0.03              | 0.22            |
| ACR CRISS Score (lower)    | 0.03              | 0.22            |

Lambdasum reduces the acute and chronic phases of the resolution phase of inflammation.

Leukocytes within the body
- Systemic Graft vs Host disease
- Enhancing bacterial clearance
- Keppel cellular activation
- Peptide coupled receptors
- Pain function
- Enhance chemotactic clearance
- Regulates multiple physiologic processes

Leukocytes within the body
- Inflammation and Pro
- Cytokines and chemokines
- Proresolving Effects of
- Scleroderma Skin Symptoms Patient Reported Outcome (SSPRO) questionnaire, and PROMIS-29 questionnaire domain T1 scores for physical function, social role fatigue, sleep disruptions, interferences, anxiety, and depression domains.

ACR CRISS score and mRSS were measured. Safety and efficacy assessments were performed at weeks 4, 12, and 28.

Summary and Conclusions

Both physician and patient opinion of the clinical benefit of lambdasum at 3 months correlated with the overall assessment of health related to SSc and change in skin symptoms.

Larger studies will further elucidate the value of specific PROs to reflect the clinical benefit from lambdasum.

The ongoing RESOLVE-1 study is a 52-week, randomized, placebo-controlled study evaluating lambdasum for the treatment of patients with dcSSC.

To confirm these initial findings, results from RESOLVE-1 will include correlations between patient and physician assessments of benefit and changes in efficacy outcomes and ACR CRISS.

References


