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Baseline European Patient Demographics and Disease Characteristics in a Phase 3 Study of Safety and Efficacy of Lenabasum, a CB2 Agonist, in Diffuse Cutaneous Systemic Sclerosis

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on behalf of RESOLVE-1 Study Investigators

Background:

We previously presented on the baseline characteristics of a large cohort of diffuse cutaneous systemic sclerosis (dcSSc) patients enrolled in a Phase 3 trial of lenabasum, a selective cannabinoid receptor type 2 (CB2) agonist. Lenabasum, was safe and well-tolerated in a prior Phase 2 study in dcSSc patients and associated with improvements in ACR Combined Response Index Systemic Sclerosis (CRISS) score and multiple secondary efficacy outcomes.

Objectives:

We now report on the background standard of care and baseline disease characteristics of European (EU) patients in order to assess variability by geographic regions.

Methods:

The RESOLVE-1 Phase 3 study was designed with input from study investigators and regulatory authorities. An important intent of the design was to have eligibility criteria that allow testing of efficacy and safety of lenabasum in an inclusive group of dcSSc subjects to maximize relevance to patients in current practice. The study is ongoing and remains blinded.

Results:

Primary efficacy outcome is the ACR CRISS score at 12 months, comparing lenabasum 20 mg BID to placebo. Key inclusion criteria are males and females ≥ 18 years of age with dcSSc and disease duration ≤ 6 years who are on stable standard of care medicines, with background stable immunosuppressive mediations allowed. Baseline mRSS needed to be ≥ 15 if disease duration was > 3 to ≤ 6 years at enrollment. The study enrolled 110 EU subjects over 15 months who received ≥ 1 dose of study drug at 20 sites in 7 countries. Baseline characteristics as shown in Table 1. The majority were middle-aged, female, and white, and 80% were on immunosuppressive drugs in EU region; methotrexate (MTX) used in 30% of subjects, mycophenolate/mycophenolic acid (MMF) used in 46% of subjects, and 43% of subjects took ≥ 2 concurrent immunosuppressive drugs. There were regional

differences in background immunosuppressive with use of MTX, MMF and corticosteroids highest in EU, NA and Asia, respectively.

Conclusion:

This is the first Phase 3 study to use ACR CRISS as the primary efficacy outcome, a composite outcome of multiple clinically relevant measures of SSc, and the largest interventional study to date in diffuse cutaneous SSc. While the use of background immunosuppressive therapies is significant irrespective of geographic regions, MTX use is highest in the EU. Benefits of having inclusive eligibility criteria are that they facilitated timely full enrollment and will make the study more relevant to real-world practice. This study provides a model for future Phase 3 trials in dcSSc and will afford valuable information regarding scleroderma care in practice as well as evaluating the efficacy and safety of lenabasum.

Table 1. Patient Baseline Demographics and Disease Characteristics by Regions (Blinded)

Characteristic at First Dose	Mean (SD) or %		
	Region		
	Europe	US, CA, AU, IL	Asia
	N =110 (30.1%)	N = 189 (51.8%)	N = 66 (18.1%)
Years of age	51 ± 11.7	51 ± 13.5	49 ± 13.2
Female	75%	78%	71%
ILD	55%	40%	58%
Caucasian	101 (91.8%)	148 (78.3%)	0 (0.0%)
Asian	2 (1.8%)	10 (5.3%)	66 (100.0%)
Black	2 (1.8%)	16 (8.5%)	0 (0.0%)
Other	5 (4.6%)	15 (7.9%)	0 (0.0%)
Any immunosuppressive drug	80%	89%	79%
≥ 2 immunosuppressive drugs	43%	48%	38%
Mycophenolate	46%	70%	26%
Corticosteroids	31%	31%	53%
Methotrexate	30%	22%	23%
Other	31%	41%	26%
Modified Rodnan Skin Score	21.9 ± 7.75	23.8 ± 8.41	20.0 ± 7.72
Physician Global Assessment	5.9 ± 1.57	5.3 ± 1.56	5.0 ± 1.50
Patient Global Assessment	4.9 ± 2.02	5.0 ± 2.25	4.8 ± 1.89
HAQ-DI with aids/devices	1.0 ± 0.69	1.3 ± 0.76	0.7 ± 0.77
Forced vital capacity % predicted	83.2 ± 18.92	77.5 ± 16.41	82.5 ± 14.73

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