Figure 1. Mean change from baseline in mRSS by time point from baseline to the last visit (long-term safety analysis set)

BL, baseline; mRSS, modified Rodnan skin score

Figure 2. Changes in mRSS from Week 52 to last visit

^aDecrease by ≥5 units and ≥25% from Week 52 to last visit
mRSS, modified Rodnan skin score

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OP0250

EFFICACY AND SAFETY OF ROMILKIMAB IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC): RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 24-WEEK, PROOF OF CONCEPT STUDY

Y. Allanore¹, P. Wung², C. Soubrane³, C. Esperet³, M. Frederic³, R. Bejuit³, A. Lahmar², D. Khanna⁴, C. Denton⁵, ¹Cochin Hospital, Rheumatology, Paris, France; ²Sanofi R&D, Bridgewater, United States of America; ³Sanofi R&D, Chilly Mazarin, France; ⁴University of Michigan, Ann Arbor, United States of America; ⁵University College London, London, United Kingdom

Background: Systemic sclerosis (SSc) is a progressive, multi-organ disease with limited treatment options. Interleukin-4 (IL-4) and IL-13 have been implicated in the fibrotic pathway and pathogenesis of SSc and are promising targets. Romilkimab (RKB) is an engineered humanized bispecific Ig-G4 antibody that binds and neutralizes both IL-4/IL-13. We report a Phase IIa randomized, double-blind, placebo-controlled trial (NCT02921971, Sanofi funded) employing RKB in SSc.

Objectives: To evaluate the efficacy and safety of RKB in dcSSc.

Methods: Patients with dcSSc duration ≤36 months, mRSS 10-35, with or without immunosuppressive background therapy were randomized (1:1) to subcutaneous RKB 200mg or placebo (PBO) for 24 weeks and stratified on history of SSc-ILD. Primary endpoint was mean change in mRSS at Week 24 and FVC/DLCO and HAQ-DI were secondary endpoints. All analyses used a 1-sided p-value <0.05 as reaching statistical significance.

Results: Ninety-seven patients with similar baseline characteristics between arms, including use of background therapy (RKB 59.2% vs. PBO 52.1%) were randomized. Six (12.2%) and 4 (8.3%) patients discontinued study treatment early in the PBO and RKB arms, respectively. Primary endpoint showed an absolute change in mRSS of -2.45 (0.85) and -4.76 (0.86) for PBO and RKB groups, respectively with a difference of -2.31 (1.21) favoring RKB (p=0.029). Subgroup analysis based on background therapy showed a similar treatment effect with a PBO subtracted difference in mRSS of -2.69 (1.83) and -2.38 (1.59), suggesting an additive effect between background therapy and RKB. Secondary endpoints did not show a statistically significant difference between RKB vs. PBO arms, although there was numerically less decline in FVC with RKB with a PBO subtracted difference of 70ml (p=0.06). Exploratory endpoints suggested possible effect of RKB on overall pain, Raynaud's, digital ulcers, and EQ-5D-5L. Post-hoc analysis was undertaken to determine time to progression (first event defined as death, ≥10% relative decline in % predicted FVC, ≥15% relative decline in % predicted DLCO, ≥20% increase or +5 in mRSS, or other events: cardiac, SRC, PAH development) and showed a benefit for RKB (HR: 0.47 p=0.04). Adverse events were balanced between the two groups (RKB 83.3% vs. PBO 83.7%). There were 5 and 4 SAEs in the PBO and RKB arms, respectively. One death occurred in each arm (SRC – RKB, cardiomyopathy – PBO).

Conclusion: Patients with dcSSc who were treated with RKB showed a statistically significant reduction in mRSS compared to those receiving PBO. Secondary outcomes were not met, although RKB was associated with a smaller decline in FVC than PBO. Post-hoc analysis showed a possible reduction on time to progression with RKB. RKB was well tolerated with no major safety concerns.

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OP0251

THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) SCORE – A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SYSTEMIC SCLEROSIS

M. O. Becker¹, R. Dobrota¹, K. Fligelstone², A. Roennow³, Y. Allano⁴, P. Carreira⁵, L. Czirják⁶, C. Denton⁷, R. Hesselstrand⁸, G. Sandqvist⁹, O. Kowal-Bielecka⁹, C. Bruni¹⁰, M. Matucci Cerinic¹⁰, C. Mihai¹, A. M. Gheorghiu¹¹, U. Müller-Ladner¹², J. Sexton¹³, T. Heiberg¹⁴, O. Distler¹.

¹Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; ²FESCA, London, United Kingdom; ³FESCA, Aalborg, Denmark; ⁴Department of Rheumatology, University Paris Descartes and Cochin Hospital, Paris, France; ⁵Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain; ⁶Department of Immunology and Rheumatology, Faculty of Medicine, University of Pécs, Pécs, Hungary; ⁷Centre for Rheumatology, Royal Free and University College London Medical School, Royal Free Campus, London, United Kingdom; ⁸Department of Rheumatology, Lund University, Lund, Sweden; ⁹Department of Rheumatology and Internal Medicine, Medical University of Białystok, Białystok, Poland; ¹⁰Department of Rheumatology, University of Florence, Florence, Italy; ¹¹Department of Internal Medicine and Rheumatology, Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; ¹²Department of Rheumatology and Clinical Immunology, Justus-Liebig University Giessen, Kerckhoff-Klinik Bad Nauheim, Bad Nauheim, Germany; ¹³Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; ¹⁴Department of Health and Social Sciences, Østfold University College, Oslo, Norway

Background: Patient reported outcome measures (PROM) are important for clinical practice and research. Given the unmet need for a comprehensive PROM for systemic sclerosis (SSc), the ScleroID questionnaire was developed by a joint team of patients with SSc and medical experts. This is intended as a brief, specific, patient-derived, disease impact score for research and clinical use in SSc.

Objectives: Here, we present the validation and final version of the ScleroID.

Methods: This EULAR-endorsed project involves 9 European expert SSc centers. Patients fulfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in a large observational cohort study. Patients completed the ScleroID and comparators SHAQ, EQ5D, SF36. They also weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation is based on the ranking of the weights. The validation study included a reliability arm and a longitudinal arm, looking at sensitivity to change at follow-up.

Results: Of the 472 patients included at baseline, 109 patients also had a reliability visit and 113 patients a follow-up visit. 84.5% of patients were female, 29.8% had diffuse SSc, mean age was 54.6 years, and mean disease duration 9.5 years. The highest weights were assigned by the patients to Raynaud's phenomenon, fatigue, hand function and pain, confirming our previous results. The total ScleroID score showed good Spearman correlation coefficients with the comparators (SHAQ, 0.73; EQ5D -0.48; Patient's global assessment, VAS 0.77; HAQ-DI 0.62; SF36 physical score -0.62; each p<0.001). The internal consistency was good: Cronbach's alpha 0.866, similar to SS-HAQ (0.88) and higher than EQ5D (0.77). The ScleroID had a very good reliability: intra-class correlation coefficient 0.839 (ranging 0.608 to 0.788 for the individual items), superior to all comparators. Twenty of 113 patients reported a change in their disease status at follow up. Sensitivity to change: the standardized response mean was 0.34 for the total ScleroID score and highest for lower GI (0.633) and life choices domains (0.521), superior to all other PROM. Figure 1 shows the final ScleroID.

The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:

Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:

Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:

No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):

Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:

Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:

Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):

Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):

Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:

Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:

Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:

Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:

Circle the number that best describes how much your digital ulcers affected you overall during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Figure 1.

Conclusion: The EULAR ScleroID is a novel PROM designed for use in clinical practice and clinical trials to reflect the disease impact of SSc, showing good performance in the validation study. Importantly, Raynaud syndrome, impaired hand function, pain and fatigue were the main patient reported drivers of disease impact.

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