Objectives: To evaluate utility of risk stratification strategy in predicting outcomes in CTD-PAH patients by post-hoc analysis of prospectively collected AMBITION data.

Methods: This study examined 216 patients with CTD (COMB; n=117; MONO n=99) enrolled in the AMBITION study mITT population. The most common underlying CTD etiology was SSc (n=137). Abbreviated average risk score⁵⁾ was determined at baseline and at 16 weeks based on 6-minute walking distance, NT-proBNP, and WHO-FC. Time to clinical failure (TiCF) was compared between groups stratified by the risk stratification and/or treatment assignment using the log-rank test.

Results: At baseline, CTD patients were divided into low (n=27, 12.5%), intermediate (n=179, 82.9%), and high risk (n=10, 4.6%) and at Week 16, subjects were classified as low (n=55, 27.9%), intermediate (n=135, 68.5%), and high risk (n=7, 3.6%). Risk of clinical failure was lowest for subjects in the baseline low risk group and highest in the baseline high risk group. When TiCF was compared between COMB and MONO arms of CTD-PAH patients in individual risk groups at baseline, risk of clinical failure event was lower in COMB than in MONO in the low and the intermediate risk groups (P=0.05, hazard ratio [HR] NA due to no event in COMB, and P= 0.02, HR 0.519, 95%CI 0.297-0.905, respectively), however, no difference in the high risk group was observed. The same analysis was conducted using risk stratification at week 16, resulting in a 93% risk reduction in TiCF after Week 16 in COMB, compared with MONO in the low risk group (P<0.001, HR 0.069, 95%CI 0.009-0.548), but no difference between COMB and MONO in the intermediate risk group (P=0.3). Risk of clinical failure event was comparable between patients with low and intermediate risk after 16 weeks of treatment with MONO.

Conclusion: A simplified risk stratification at baseline and week 16 may be useful in predicting PAH related outcomes in patients with CTD-PAH. Among those achieving a low risk status at week 16, which could be considered a treatment goal, COMBO was associated with an improved outcome, when compared to MONO.

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OP0068

ABATACEPT IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS— RESULTS OF A PHASE 2 INVESTIGATOR-INITIATED, MULTICENTER, DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Background: Abatacept (ABA) is a recombinant fusion protein including extracellular domain of human CTLA4 and hinge—CH2—CH3 of the Fc domain of human IgG.

Objectives: This phase 2 trial assessed the safety and efficacy of ABA 125 mg subcutaneous (SC) versus placebo SC given every week on skin fibrosis using the modified Rodnan skin score (mRSS) in diffuse cutaneous SSc (dcSSc; clinicaltrials.gov NCT02161406).

Methods: A 12-month, investigator-initiated, multicenter double-blind, randomized placebo-controlled trial was conducted between September 2014 and February 2018 at 27 US, Canadian and UK sites. Eligible subjects were randomized in a 1:1 ratio to either ABA or matching placebo, stratified by duration of dcSSc (≤ 18 vs > 18 to ≤ 36 months). Key inclusion criteria included dcSSc with disease duration of ≤ 36 months (defined as first non-Raynaud phenomenon) and mRSS ≥ 10 and ≤ 35 units for disease duration of ≤ 18 months and mRSS ≥ 15 and ≤ 45 units with evidence of active disease for disease duration of > 18 -36 months. Escape therapy was allowed at 6 months for worsening SSc. Primary outcomes include safety and change in mRSS over 12 months (Δ mRSS). Secondary endpoints include Δ FVC%, Δ HAQ-DI, Δ patient and Δ physician global assessment, and ACR CRISS¹ (composite measure in dcSSc). The primary endpoint of Δ mRSS was assessed using a linear mixed model (see Table) with primary end point data censored after initiation of escape therapy.

Results: 88 subjects were randomized (44/group) and formed the mITT group; 34 (77%) and 35 (80%) completed the 12-month double-blind treatment period in ABA and placebo groups, respectively. At baseline, the mean age was 49 years, 75% were female, mean disease duration was 1.59 years, 60% had disease duration ≤ 18 months, mRSS was 22.4, mean FVC% was 84.3%, and mean HAQ-DI was 1.0. Compliance with both drugs was $> 98\%$. ABA was well tolerated with comparable adverse events (AEs), serious AEs, and AEs of special interest (e.g., infections and malignancies) between treatments. There were 3 deaths during the treatment—2 in ABA (both scleroderma renal crisis—days 11 and 46) and 1 in placebo (sudden cardiac arrest—day 310). The primary endpoint showed an adjusted mean improvement of mRSS of -6.24 in ABA vs. -4.49 in placebo, p= 0.28 (Table). The secondary outcome measures were statistically significant and clinically meaningful (HAQ-DI and physician global assessment) or showed numerical results favoring ABA (Table). A larger proportion of placebo subjects required escape immunosuppressive therapy vs. ABA (36% vs. 16%, p=0.03).

Outcome at Month 12	Abatacept N=44	Placebo N=44	Difference (ABA - Placebo)	P- value
Δ mRSS, 0-51, mean	-6.24	-4.49	-1.75	0.28
Δ Patient Global Assessment, 0-10, mean	-0.31	-0.09	-0.22	0.73
Δ Physician Global Assessment, 0-10, mean	-1.30	-0.35	-0.95	0.03
Δ FVC% predicted, mean	-1.34	-4.13	2.79	0.11
Δ HAQ-DI, mean	-0.17	0.11	-0.28	0.005
ACR CRISS index, median (IQR)	0.68 (1.00)	0.01 (0.86)		0.03

Estimates are from a linear mixed model with treatment group, month (3, 6, and 12), treatment x month interaction, duration of dcSSc (≤ 18 vs > 18 to ≤ 36 months), and baseline outcome measure as fixed effects and participant as a random effect (except for ACR CRISS). For ACR CRISS, treatment differences were assessed by the non-parametric Van Elteren test. Multiple imputation was used for ACR CRISS analysis.

Conclusion: In patients with early dcSSc, ABA was well tolerated, but Δ mRSS was not statistically significant. Secondary outcome measures showed evidence in favor of ABA, including greater requirement of escape therapy in the placebo group. mRSS showed large variability, despite recruiting an early dcSSc population.

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OP0069

PERFORMANCE OF AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) COMBINED RESPONSE INDEX IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (CRISS) SCORE IN PHASE 2 TRIAL OF LENABASUM IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSS)

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Background: Change in modified Rodnan skin score (mRSS) has been used as primary efficacy outcome in at least 13 failed controlled studies in dcSSc. In 2016, the CRISS score was provisionally accepted by ACR as a primary efficacy outcome for clinical trials in dcSSc. Its performance as a primary efficacy outcome has not been tested in a clinical trial.

Objectives: To evaluate performance of ACR CRISS outcome measure in the lenabasum Phase 2 study in dcSSc, the first study in which it was used prospectively as the primary efficacy outcome.

Methods: The Phase 2 study JBT101-SSc-001 (NCT02465437) included a 16-week, double-blinded, randomized, placebo-controlled Part A followed by an open-label extension (OLE). ACR CRISS score is calculated from a weighted exponential formula that includes change in mRSS, Patient Global Assessment (PtGA), HAQ-DI, Physician Global Assessment (MDGA), and FVC% predicted. Spearman correlations were determined for: pairs of core items at Baseline; change in pairs of core items; and change in a given core item and calculated ACR CRISS score. Median ACR CRISS scores were determined in subjects with different levels of improvement in patient-reported outcomes (PROs).

Results: Correlations among pairs of CRISS core items at baseline and change in core items were all < 0.80 at 4 and 12 months. The strongest correlations ($r \geq 0.60$, $P \leq 0.0001$) for core items at baseline were between PtGA and HAQ-DI, HAQ-DI and MDGA, and PtGA and MDGA. The strongest correlations ($r \geq 0.50$, $P \leq 0.001$) for changes in pairs of core items were between PtGA and HAQ-DI, HAQ-DI and MDGA, and MDGA and mRSS, all others were ≤ 0.30 (Table 1). Correlations between change in each core item and ACR CRISS score were all statistically significant, $p \leq 0.05$ at both 4 and 12 months and very strong for change in mRSS and ACR CRISS (Table 1).

Median ACR CRISS scores increased with increasing levels of improvement in PROs that were core items (HAQ-DI and PtGA) and even PROs (PROMIS-29 domains) that were not core items. Median ACR CRISS score associated with improvement in HAQ-DI at least -0.250 points was 0.82 and associated with at least 1-point improvement in PtGA was 0.53 at 12 months.

Table 1. Correlation of ACR CRISS with Change in Core Item, r

Time	Correlation of ACR CRISS with Change in Core Item, r				
	mRSS	PtGA	HAQ-DI	MDGA	FVC% predicted
4 months	-0.91	-0.37	-0.45	-0.66	0.38
12 months	-0.76	-0.38	-0.39	-0.38	0.54

Conclusion: In the context of the lenabasum Phase 2 clinical trial, ACR CRISS core items at baseline and change in ACR core items were not redundant ($r < 0.80$). Change in each core item correlated with ACR CRISS score, indicating each contributed to the score at both 4 and 12 months. The 12-month median ACR CRISS score was higher in subjects with greater levels of improvement in PROs, even PRO that were not core items, showing that ACR CRISS score reflects long-term clinical benefit in how the patient feels and functions. These data provide preliminary evaluation of the ACR CRISS score as a clinical trial endpoint in dcSSc.

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Bringing digital health care solutions to patients

OP0070-PARE

GEOCACHING AS AN ENCOURAGEMENT FOR BEING ACTIVE

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Background: The Finnish Rheumatism Association and Novartis started a project in 2017 to energise our local associations, members and their families by adapting an active lifestyle. Geocaching is a fun, family-friendly way to exercise both mind and body. It is for everybody to enjoy.

Geocaching is an outdoor recreational activity, in which participants use a Global Positioning System (GPS) receiver or mobile device and other navigational techniques to hide and seek containers, called "geocaches" or "caches", at specific locations marked by coordinates all over the world.

There are about three million geocaches hidden around the world. A typical cache is a small waterproof container containing a logbook and sometimes a pen or pencil. The geocacher signs the log with their established code name and dates it to prove that they found the cache. After signing the log, the cache must be placed back exactly where it was found.

Objectives: The main goal of the project was to hide 70 new caches all over Finland to create an enjoyable experience for other geocachers. Those caches were named "Reumageo" at the beginning of the cachename. For all the associations that were involved in this project received money allocated to sport and physical activity out of the 15,000 euro project budget. The project ended on 12 October 2018, and all logged caches were included in the game.

Methods: We started our project by training association representatives. The training included the basics of geocaching: how to find caches, how to hide your cache and create your cache page, different geocachetypes and everything you should know geocaching. The trained representatives told about geocaching in their own associations, and they were responsible for creating at least 2-3 new caches and handling the new caches. The main idea was that when you have found about 15-20 caches you would start to hide your own caches. Together with local associations our aim was to create 70 caches all over Finland to celebrate the 70-year-old Finnish Rheumatism Association.

Outdoor geocaching adventure starts indoors with preparation and online research. You need a Global Positioning System (GPS) receiver or a mobile device, your own account at the site geocaching.com. The site offers a completely free access to the caching data and all the site features. The site offers also a "premium" member status to access certain features. You can also download the Geocaching intro app onto your smartphone, like Geocaching.