identified PF and SSc auto-antibodies at first visit as independent parameters predicting the development of definite SSc. These data are of key importance for the risk stratification of patients with very early SSc in clinical practice and clinical studies.

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OP0066

EFFECTIVENESS OF SPECIALIZED HAND/FACE PHYSICAL-OCCUPATIONAL THERAPY IN PATIENTS WITH SYSTEMIC SCLEROSIS – PRELIMINARY RESULTS OF A ONE-YEAR CONTROLLED STUDY

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Background: Systemic sclerosis (SSc) is characterized by stiffness and contraction of tissues, which leads to a limitation in the execution of day-to-day activities. The aim of our study was to investigate the impact of specialized physical-occupational therapy (POT) focused on the hands/face and QoL of SSc patients.

Objectives: Fifty five patients fulfilled the EULAR/ACR criteria for SSc and had skin involvement leading to hand/face function impairment. 25 patients were recruited into the intervention group (IG) and 30 patients into the control group (CG). Both groups received an educational material for home exercise, but only the IG underwent a 6-month intervention with a subsequent 6-month follow-up period.

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedman+Dunn) Intervention gr. Control group		Inter-group analysis (2WA)
dFTP, dominant hand (cm)	m0: 5.7 ± 0.5 m3: 6.2 ± 0.5 m6: 6.8 ± 0.6 m12: 6.0 ± 0.6	m0: 6.8 ± 0.5 m3: 6.2 ± 0.4 m6: 5.9 ± 0.4 m12: 5.6 ± 0.4	m0-3: p<0.01 m3-6: p<0.05 m0-6: p<0.0001 m6-12: p<0.0001	m0-3: NS m3-6: NS m0-6: p<0.0001 m6-12: NS	p<0.0001
Hand grip strength, dominant hand (kg)	m0: 17.2 ± 1.8 m3: 19.2 ± 1.9 m6: 19.7 ± 1.9 m12: 17.5 ± 2.0	m0: 16.5 ± 1.2 m3: 14.9 ± 1.3 m6: 13.8 ± 1.2 m12: 14.2 ± 1.3	m0-3: p<0.05 m3-6: NS m0-6: p<0.001 m6-12: p<0.05	m0-3: NS m3-6: NS m0-6: p<0.01 m6-12: NS	p<0.0001
HAMIS, dominant hand	m0: 9.8 ± 1.3 m3: 7.1 ± 1.3 m6: 4.1 ± 0.9 m12: 7.2 ± 1.2	m0: 3.9 ± 1.1 m3: 6.3 ± 1.2 m6: 8.9 ± 1.1 m12: 9.8 ± 1.2	m0-3: p<0.01 m3-6: p<0.001 m0-6: p<0.0001 m6-12: p<0.001	m0-3: NS m3-6: p<0.001 m0-6: p<0.0001 m6-12: NS	p<0.0001
Inter-incisor distance (cm)	m0: 2.9 ± 0.2 m3: 3.2 ± 0.2 m6: 3.5 ± 0.2 m12: 3.2 ± 0.2	m0: 3.3 ± 0.1 m3: 3.1 ± 0.1 m6: 3.0 ± 0.1 m12: 3.0 ± 0.1	m0-3: p<0.01 m3-6: NS m0-6: p<0.0001 m6-12: p<0.01	m0-3: p<0.01 m3-6: NS m0-6: p<0.001 m6-12: NS	p<0.0001
SHAQ (mm)	m0: 28.8 ± 3.9 m3: 21.5 ± 3.4 m6: 22.0 ± 3.5 m12: 23.4 ± 3.7	m0: 21.5 ± 2.1 m3: 24.6 ± 2.6 m6: 24.9 ± 2.9 m12: 27.5 ± 3.3	m0-3: NS m3-6: NS m0-6: p<0.05 m6-12: NS	m0-3: NS m3-6: NS m0-6: NS m6-12: NS	p=0.0015

Methods: Patients were assessed by a physician and a physiotherapist blinded to intervention at months 0, 3, 6, and 12. Patients also filled out patient reported outcomes questionnaires and provided blood for routine laboratory analysis and bio-banking. Data analysis was done between groups and within the group.

Results: Compared to the observed statistically significant deterioration in the CG, we found a statistically significant improvement in the IG in objectively assessed function and strength of hand, distance between incisors and functional ability (SHAQ) (Table). Only numerical improvements in the IG during the intervention compared to numerical deterioration in CG that did not reach statistical significance were observed in subjectively assessed hand function and mouth handicap, functional ability (HAQ) and in some domains of QoL (SF-36) and fatigue (FIS – cognitive function). During the follow-up period, there was a significant deterioration or stagnation of the achieved positive results in the IG.

Conclusion: Our program led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and prevention of the expected worsening of hand/face handicap and QoL.

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OP0067

UTILITY OF RISK STRATIFICATION IN PREDICTING OUTCOMES OF INITIAL MONOTHERAPY VERSUS COMBINATION THERAPY IN PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONNECTIVE TISSUE DISEASE: A POST-HOC ANALYSIS OF THE AMBITION STUDY

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Background: The AMBITION study (NCT01178073, sponsored by GSK and Gilead) demonstrated a reduced risk of clinical failure event in patients receiving initial combination therapy of ambrisentan and tadalafil (COMB) compared with initial monotherapy of either agent (MONO) in treatment-naïve patients with pulmonary arterial hypertension (PAH)¹. A similar treatment outcome was observed in connective tissue disease (CTD)-PAH or systemic sclerosis (SSc)-PAH subgroups in both the primary analysis set and modified intention to treat (mITT) population^{2,3}. The 2015 ESC/ERS guidelines⁴ and 2018 WSPH consensus recommended the use of risk assessment (classified as low, intermediate, and high risk) based on the variables to predict prognosis, but the clinical utility of risk stratification in patients with CTD- or SSc-PAH has not been established.

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, COMB 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 CRISP¹ (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 CRISP 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 CRISP). For ACR CRISP, treatment differences were assessed by the non-parametric Van Elteren test. Multiple imputation was used for ACR CRISP 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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