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SAT0329

IS THE RATE OF LUNG FUNCTION DECLINE THE SAME IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED ILD (SSc-ILD) WHO EXPERIENCE WEIGHT LOSS? DATA FROM THE SENSICIS TRIAL

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Background: In the SENSICIS trial, nintedanib reduced the progression of SSc-ILD vs placebo, as shown by a lower rate of decline in forced vital capacity (FVC). The adverse event (AE) profile of nintedanib was characterised mainly by gastrointestinal (GI) events, including weight loss.

Objectives: Assess FVC decline and AEs in subgroups by weight loss $\leq 5\%$ vs $>5\%$ over 52 weeks in the SENSICIS trial.

Methods: Patients with SSc-ILD with first non-Raynaud symptom <7 years before screening and $\geq 10\%$ fibrosis of the lungs on an HRCT scan were randomised to nintedanib or placebo. In a non-randomised comparison, we analysed the rate of decline in FVC (mL/year) and AEs over 52 weeks in subgroups by weight loss ($\leq 5\%$ vs $>5\%$) over 52 weeks.

Results: In the nintedanib (n=288) and placebo (n=288) groups, respectively, 112 (38.9%) and 43 (14.9%) patients had weight loss $>5\%$ over 52 weeks. At baseline, patients with weight loss $>5\%$ over 52 weeks had a higher mean age (57.0 vs 52.9 years), greater proportion of females (81.3% vs 72.9%), and similar mean BMI (26.5 vs 25.7 kg/m², respectively) and FVC % predicted (71.0% vs 73.1%, respectively) vs patients with weight loss $\leq 5\%$. In the placebo group, the mean (SE) annual rate of decline in FVC was similar between patients who had weight loss $\leq 5\%$ and $>5\%$ over 52 weeks (-92.7 [14.7] mL/year and -96.4 [34.9] mL/year, respectively). The estimated annual rate of decline in FVC was lower in patients treated with nintedanib than placebo, with between-group differences in patients who had weight loss $\leq 5\%$ and $>5\%$ of 49.9 mL/year [95% CI 4.2, 95.6]) and 30.2 mL/year [95% CI -50.5, 110.9]), respectively, with no evidence of heterogeneity between subgroups by weight loss (p=0.68 for interaction). Standardised differences in baseline values of potential confounders were <0.2 (indicating negligible differences). The most frequent AEs in patients treated with nintedanib were diarrhoea (74.4% and 77.7% of patients with weight loss $\leq 5\%$ and $>5\%$,

respectively), nausea (30.1% and 33.9%, respectively) and vomiting (19.3% and 33.3%, respectively). In the nintedanib and placebo groups, respectively, AEs leading to discontinuation of study drug occurred in 17.0% and 8.6% of patients with weight loss $\leq 5\%$, and 14.3% and 9.3% of patients with weight loss $>5\%$ over 52 weeks.

Conclusion: In the SENSICIS trial in patients with SSc-ILD, a greater proportion of patients treated with nintedanib than placebo had weight loss $>5\%$ over 52 weeks. The rate of decline in FVC was numerically lower in the nintedanib group than in the placebo group both in patients with weight loss $\leq 5\%$ and $>5\%$ over 52 weeks. AEs leading to discontinuation of nintedanib were not more frequent in patients with weight loss $>5\%$ vs $\leq 5\%$.

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Figure. Rate of decline in FVC in subgroups by weight loss over 52 weeks in the SENSICIS trial

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SAT0330

NEW IMMUNOMODULATORY COMBINATION THERAPIES IN PATIENTS WITH SYSTEMIC SCLEROSIS: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background: Systemic sclerosis (scleroderma, SSc) is a rare complex connective tissue disease associated with high mortality and high morbidity¹. Active SSc

are typically treated with immunosuppressants, which may create a variety of severe side-effects, especially for long-term treatment². As the pathogenesis of SSc is still a matter of debate, growing evidences have focused on the immune disorders³. However, the quantitative status of lymphocyte subsets in SSc patients are unclear and effects of immunomodulatory combination therapies (avoiding side-effects of conventional therapy) on the lymphocyte subsets are unknown.

Objectives: To investigate the quantitative status of peripheral lymphocyte subpopulations and CD4+T subsets in SSc patients for the exploration of SSc pathogenesis and evaluate the effects of new immunomodulatory combination therapies on those cells.

Methods: From July 2014 to December 2019, total 166 patients with SSc and 206 healthy controls (HCs) were enrolled in this study, in which, 79 follow-up patients received immunomodulatory drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10. The absolute numbers of T, B, NK, CD4+T, CD8+T, Th1, Th2, Th17 and Tregs in peripheral blood of these subjects were detected by flow cytometry combined with standard absolute counting beads.

Results: Patients with SSc had lower absolute counts of total T, NK, Th2, Th17 and Tregs as compared with those of HCs ($P < 0.05$) (Figure 1). After immunomodulatory combination treatments, there were increases in a various of peripheral lymphocyte subsets such as T, B and CD8+T ($P < 0.05$). Moreover, the increased level of Tregs was much more dramatical than those of other lymphocyte subsets, resulting in the decrease ratios of Tefs/Tregs such as Th1/Tregs and Th2/Tregs and rebuilding immunologic equilibrium (Figure 2).

Conclusion: This cross-sectional study clarified the abnormal status of lymphocyte subsets in SSc patients, suggesting lymphocyte subsets, especially Tregs, might be relevant and play a crucial role in the pathogenesis of SSc, thus providing a potential therapeutic target for SSc patients. Immunomodulatory combination therapies effectively increase the level of Tregs as well as other lymphocytes to some degree and maintain the immunologic equilibrium, which may help for SSc patients' symptom remission.

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Figure 1: Comparison of absolute numbers of peripheral lymphocyte subsets between patients with SSc (n=166) and healthy controls (n=206). All the lymphocyte subpopulations were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. Patients had lower levels of T, NK, Th2, Th17 and Tregs compared with those of healthy controls. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Figure 2: Changes of peripheral lymphocyte subsets after immunomodulatory combination treatments (n=79). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. Absolute numbers of T, B, CD8+T, Th1, Th17 and Tregs in SSc patients were significantly increased after immunomodulatory combination treatments. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

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SAT0331

CHIPPING AWAY AT POLYMYOSITIS: A RETROSPECTIVE REVIEW AT A TERTIARY MYOSITIS CENTRE

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Background: Since first described, our understanding of polymyositis (PM) has evolved substantially. Patients previously diagnosed with PM may now be better described as having an alternative diagnosis, including immune-mediated necrotizing myopathy (IMNM), connective tissue disease overlap myositis (CTD-OM), anti-synthetase syndrome (ASS) or inclusion body myositis (IBM).

Objectives: To apply the current understanding of IIM subtypes to retrospectively review the diagnosis of patients classified as PM at our centre.

Methods: We reviewed a cohort of 255 patients from a UK tertiary myositis clinic, with 37 patients classified as PM according to the EULAR/ACR IIM criteria and expert opinion (1). Consensus decisions made as to whether reclassification as an alternative IIM subtype would be appropriate in each case.

Results: Thirty-seven patients with PM diagnosis according to EULAR/ACR IIM criteria and expert opinion were included in the analysis. Twenty-six patients (26/37, 68.4%) were female. The mean age at diagnosis was 57 years (SD 16.25) and mean follow up was 5.2 years (SD 4.8).

After consensus discussions, ten patients (27%) retained classification as PM, representing 3.9% (10/255) of the original cohort of 255 patients. The remaining 27 were reclassified as follows: 7 CTD-OM (18.9%), 6 IMNM (16.2%), 6 unspecified myopathy (16.2%), 2 DM (5.4%), 1 IBM (2.7%), and 1 non-inflammatory myopathy (2.7%, myofibrillar myopathy). Four patients (10%) had insufficient data available to allow for a defined diagnosis.

Of the 10 patients retaining classification as PM, 7 (70%) were female and mean age at diagnosis was 58.9 years. Clinical characteristics are represented in table 1. Mean CK at diagnosis was 2321 IU/L. Four patients (40%) were ANA positive, 8 patients (80%) were tested for the complete myositis antibody panel and 8 (80%) were specifically tested for the presence of HMGR antibodies (figure 1). EMG revealed a myopathic pattern in 6/7 patients tested, while MRI demonstrated muscle oedema compatible with myositis in 3/5 of the patients that were tested. A complete muscle biopsy report was available in 8/10 PM-classified patients (80%), diffuse HLA-1 upregulation was present in 5 patients (50%), endomysial inflammatory infiltrates in 5 (50%) and perimysial infiltrates (in conjunction with endomysial infiltrates) in 3 (30%). No other specific features were found.

Table 1. Clinical features.

	PM (n=10)	CTD-OM (n=7)	IMNM (n=6)	All (n=37)
Pyrexia	0	0	0	1 (2.7 %)
Weight loss	2 (20%)	2 (28.6%)	2 (33.3%)	6 (16.2 %)
Cutaneous rash	0	1 (14.3%)	0	2 (5.4 %)
Mechanic's hands	1 (10%)	2 (28.6%)	0	4 (10.8 %)
Sclerodactyly	0	1 (14.3%)	0	1 (2.7 %)
Periungual erythema	0	1 (14.3%)	0	2 (5.3 %)
Raynaud's	0	5 (71.4%)	0	8 (21.6 %)
Arthralgia	0	5 (71.4%)	0	8 (21.6 %)
Arthritis	0	2 (28.6%)	0	5 (13.5 %)
Muscle weakness	10 (100%)	7 (100%)	6 (100%)	36 (97.2 %)
Myalgia	3 (30%)	5 (71.4%)	3 (50%)	20 (54 %)
Dysphagia	3 (30%)	5 (71.4%)	1 (16.7%)	13 (35.1 %)
Interstitial lung disease (ILD)	0	3 (42.9%)	0	4 (10.5 %)
Malignancy	1 (9.1%)	0	2 (33.3%)	3 (8.1 %)

Figure 1. Antibody status according to consensus diagnosis.

* CTD-OM: Additionally 3 patients were anti-Ro52 positive and 1 patient was anti-Ro60 positive.

** Unspecified myositis. Additionally 2 patients were anti-Ro52 positive