Background: Deficiency of adenosine deaminase 2 (DADA2) is a monogenic autoinflammatory disease whose pathogenesis has not been clearly elucidated. **Objectives:** To investigate the role of vascular inflammatory factors in the pathogenesis of DADA2, to compare the vascular inflammation profiles of DADA2 patients with different phenotypes, and to compare DADA2 patients with classic polyarteritis nodosa (PAN).

Methods: The study included eighteen DADA2 patients, ten PAN patients, and eight healthy controls. Plasma levels of sST2, sRAGE, Tie-2, sCD40L, Tie-1, sFlt-1, LIGHT, TNF- α , PIGF, IL-6, IL-18, IL-10, MCP-1 were studied by cytometric bead-based multiplex assay panel.

Results: Among the DADA2 patients, five had hematological manifestations, 13 had vasculitic findings, and accompanying immunological findings were present in seven patients. Nine patients had neurological findings, five of whom had neuropathy. Hematological findings were Diamond-Blackfan anemia-like phenotype in four patients and bicytopenia (anemia and thrombocytopenia) in one patient. Disease characteristics of DADA2 and PAN patients revealed that neurological involvement and livedo reticularis were more frequent in DADA2 patients ($p=0.034$ and $p=0.009$, respectively), while myalgia was more common in PAN patients ($p=0.001$).

Plasma levels of Tie-1 and sFlt-1 were higher in the overall DADA2 patients compared to healthy controls and PAN patients ($p<0.001$ and $p=0.004$, respectively). DADA2 patients with PAN-like features had higher sRAGE, Tie-2, and TNF- α levels compared to PAN patients ($p=0.013$, $p=0.003$, and $p=0.001$, respectively). There was no significant difference in the levels of vascular inflammation markers between DADA2 patients with vasculitis and hematological involvement except IL-18. The plasma IL-18 levels were higher in the DADA2 patients with hematological findings compared to vasculitic phenotype ($p=0.001$). Finally DADA2 patients with neuropathy had higher sRAGE concentrations than patients without neuropathy and healthy controls ($p=0.03$ and $p=0.008$, respectively).

Conclusion: We suggest that the high plasma IL-18 levels may be associated with an activated IFN pathway, the pathogenesis of hematologic manifestations, and unresponsive to anti-TNF treatment. Higher concentrations of Tie-1, Tie-2, sFlt-1, sRAGE, and TNF- α distinguished DADA2 patients with PAN-like features from PAN patients. We identified sRAGE as a potential biomarker of neuropathy in DADA2 patients.

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Challenges for working people with RMDs in pandemic times

OP0169-PARE

DEVELOPMENT OF POINTS TO CONSIDER WHEN SUPPORTING PERSONS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES TO PARTICIPATE IN HEALTHY AND SUSTAINABLE PAID WORK

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Background: Despite earlier diagnosis and improved management of rheumatic and musculoskeletal diseases (RMDs), a work participation gap remains when compared to the general population. To bridge this work participation gap, EULAR's current strategy states that 'by 2023, EULAR's activities and related advocacy will have increased participation in work by people with RMDs'. To achieve this goal, guidance is needed how to support people with RMDs to remain in paid work or (re)-enter the labour force.

Objectives: To develop Points to Consider (PtC) when supporting people with RMD to participate in healthy and sustainable paid work.

Methods: An international expert group, established by Eular in 2019, convened twice to agree on a protocol for the development of PtC. EULAR's standard

operating procedures were followed. The group (a) defined the target audience, (b) identified areas from which knowledge should be derived to enable formulation of the PtC, (c) agreed on a strategy to collect evidence, (d) established an international taskforce to formulate and agree on the PtC, and (e) proposed an implementation plan.

Results: The target audience are professionals involved in clinical care for patients with RMDs as well as their organisations, persons with RMDs and their organisations, and administrators responsible for healthcare and work policies. Six knowledge areas are identified (Table). Depending on the specific knowledge area, strategies for collecting evidence comprise synthesis of published and grey literature, surveys among various organisations and collection of case studies from employers. Whenever evidence in RMDs is limited, evidence from other chronic diseases will be sought. The international taskforce includes experts from different disciplines in rheumatology (one in other chronic diseases), EU policy makers, and representatives of PARE, HCP, EULAR Public Affairs and EMEUNET. As part of the implementation, close cooperation with national professional and patients societies is planned. Additionally, results will be included in EULAR's activities at the EU policy level.

Table 1. Knowledge areas and strategy to retrieve evidence

	In persons with RMDs:	Sources of evidence
1	Is work relevant for the clinical outcome of disease	LR; Review of management recommendations and Care Standards
2	What are barriers and facilitators to enter or stay in the labor force	SLR
3	What is the effectiveness of interventions to enter or stay in the labor force	SLR; Survey among professional and patient organisations
4	Which social security systems are more effective when entering or staying in the labor force	LR
5	How does disease influence the cycle of work	SLR; Grey literature
6	What (not) to do by employers to let patients enter or stay in the work force	SLR; Survey among large companies; case studies

LR: Literature review; SLR: Systematic literature review

Conclusion: The proposed initiative to develop PtC should ultimately result in improvement of healthy and sustainable labor force participation of people with RMDs.

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Progress in myositis and scleroderma research - I

OP0170

DECLINE IN FORCED VITAL CAPACITY (FVC) IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) WITH AND WITHOUT DYSPNOEA: DATA FROM THE SENSICIS TRIAL

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Background: Some patients with SSC-ILD develop dyspnoea secondary to parenchymal lung disease, while others do not report dyspnoea even when their

lung function is impaired. It is unclear whether the presence of dyspnoea is associated with a worse course of SSc-ILD or with response to therapy.

Objectives: To investigate the rate of decline in FVC in patients with SSc-ILD in the SENSICIS trial in subgroups by patient-reported dyspnoea at baseline.

Methods: The SENSICIS trial enrolled patients with SSc-ILD with first non-Raynaud symptom within ≤ 7 years before screening, extent of fibrotic ILD $\geq 10\%$ on HRCT and FVC $\geq 40\%$ predicted. Patients were randomised to receive nintedanib or placebo until the last patient reached week 52. In post-hoc analyses, we analysed the rate of decline in FVC (mL/year) over 52 weeks in patients with and without dyspnoea at baseline based on the question about dyspnoea in the St. George's Respiratory Questionnaire (SGRQ). Patients who reported having shortness of breath "most days a week," "several days a week" or "a few days a month" (rather than "only with chest infection" or "not at all") over the last month were considered to have dyspnoea at baseline. A random slope and intercept model was used to assess the rate of decline in FVC (mL/year) and an interaction test was applied to assess potential heterogeneity in the treatment effect of nintedanib between the subgroups.

Results: Of 576 patients, 69.8% had dyspnoea at baseline. At baseline, in patients with and without dyspnoea, respectively, mean (SD) extent of fibrotic ILD on HRCT was 37.7 (21.7)% and 31.6 (19.4)%; mean (SD) FVC was 71.0 (16.3) and 76.5 (16.8) % predicted; 50.7% and 44.8% were taking mycophenolate; 53.5% and 41.9% were taking corticosteroids. In the placebo group, the rate of decline in FVC (mL/year) was similar in patients with and without dyspnoea at baseline (Figure). The effect of nintedanib versus placebo on reducing the rate of decline in FVC (mL/year) was numerically more pronounced in patients without dyspnoea (difference: 79.8 [95% CI: 9.8, 149.7]) than with dyspnoea (difference: 25.7 [-19.9, 71.3]), but the exploratory interaction p-value did not indicate heterogeneity in the treatment effect between subgroups ($p=0.20$).

Conclusion: In the SENSICIS trial, patients with SSc-ILD who had dyspnoea at baseline had a numerically greater extent of fibrotic ILD on HRCT and numerically lower FVC % predicted at baseline. The rate of decline in FVC in the placebo group was similar in patients with and without dyspnoea. Nintedanib had a numerically greater treatment effect in patients without dyspnoea. These data suggest that the presence of dyspnoea should not be used as a criterion for starting nintedanib in patients with SSc-ILD.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by dyspnoea at baseline in the SENSICIS trial.

Treatment-by-time-by-subgroup interaction $p=0.20$.

The presence of dyspnoea was based on this question from the St George's Respiratory Questionnaire: "Over the last month, I have had shortness of breath." Patients who ticked boxes for "most days a week," "several days a week" or "a few days a month" were considered to have dyspnoea.

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OP0171

PHASE 3 TRIAL OF LENABASUM, A CB2 AGONIST, FOR THE TREATMENT OF DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (dcSSc)

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Background: Lenabasum is an oral CB2 agonist that attenuates inflammation and fibrosis in SSc animal models and showed clinical benefit with acceptable safety in a Phase 2 trial in dcSSc.

Objectives: Test efficacy and safety of lenabasum in a Phase 3 trial in dcSSc.

Methods: Subjects ≥ 18 years old with disease duration ≤ 6 years were randomized 1:1:1 to lenabasum 5mg, 20mg, or placebo (PBO), all BID, with stable background immunosuppressant therapy (IST) allowed. The primary efficacy endpoint was ACR CRIS score, and secondary endpoints were Δ mRSS, Δ HAQ-DI, and Δ FVC, all at Week 52 for lenabasum 20mg vs PBO.

Results: 363 adults were dosed; 37 (10%) stopped study drug early, with only 1 subject (PBO cohort) stopping due to adverse event (AE). Baseline demographics were similar among groups. Disease duration was ≤ 3 years in 60% and 66%, mean mRSS score was 22.0 and 23.3, and background IST was used by 89% and 84% of lenabasum 20mg and PBO groups, respectively.

Safety results showed serious AEs and severe AEs occurred in 9.2% and 5.8% vs 14.6% and 13.0%, respectively, of lenabasum 20mg and PBO groups.

Efficacy results (Table) demonstrated:

- No significant differences were seen in primary and secondary efficacy endpoints. Primary MMRM analyses with treatment-by-time-by-subgroup interactions showed that background mycophenolate (MMF) significantly influenced the outcome
- oSubjects on no IST with disease duration ≤ 3 years were only 7% of PBO subjects and showed little improvement on PBO, in line with other dcSSc trials in which IST was restricted. Post-hoc subgroup analyses of these subjects on no IST suggested improvement in Δ mRSS and Δ HAQ-DI, for lenabasum 20mg vs PBO
- uUnexpectedly high improvement occurred in PBO subjects receiving IST, notably those on MMF started within 2 years of baseline
- nPost-hoc analyses of subjects on established IST (MMF or, if no MMF, ≥ 1 non-MMF IST started > 2 years before baseline)