Background: Rheumatoid arthritis (RA) is categorized as seropositive or seronegative referring to the presence or absence of IgM rheumatoid factor (IgM-RF) and/or anti-citrullinated protein antibodies (ACPA).

Patients with an autoimmune disease are more likely to develop additional autoimmune conditions than individuals without pre-existing autoimmune disease.

Objectives: The aims of this study were to examine patterns of polyautoimmunity in seropositive compared with seronegative patients with recent-onset RA.

Methods: The study was register-based and used the nationwide DANBIO register (identification of recent-onset (<1 year) seropositive, ICD-10 M05, and seronegative, M06, RA patients) linked to the Danish National Patient Registry and the Danish National Prescription Registry to obtain information on additional autoimmune diseases (see Table 1 for autoimmune conditions). Using age and sex adjusted logistic regression analysis, the odds ratio (OR) of prevalent polyautoimmunity in seropositive compared with seronegative patients at the time of RA diagnosis was calculated.

To estimate the hazard ratio (HR) for developing yet another autoimmune disease in the 5 years after RA diagnosis, adjusted cause-specific Cox regression models were performed. Several sensitivity analyses were carried out including alternative exposure and outcome definitions.

Results: In total, 12,517 patients with recent-onset RA were included. The groups were similar in terms of disease characteristics and DMARD treatment, but seropositive patients were younger and included more women, see Table 1. Patients with seropositive RA had an OR of 0.79 (95% CI 0.71-0.89) for baseline presence of polyautoimmunity compared with seronegative patients, whereas the 5-year HR was 0.86 (95% CI 0.71-1.05) for incident polyautoimmunity. The results remained similar in all sensitivity analyses.

Conclusion: Patients with seropositive RA had a slightly lower prevalence and incidence of polyautoimmunity compared to seropositive patients. The results were somewhat surprising, yet very robust, and thus raises the question if seronegative RA is in fact "more autoimmune" despite the absence of (identified) autoantibodies.

Table 1. Characteristics, prevalence, and incidence of polyautoimmunity in incident RA patients.

	Seropositive	Seronegative
N	7983	4534
Age in years	59.4 (48.6 to 69.1)	63.0 (51.5 to 72.3)
Women	5476 (69 %)	2856 (63 %)
HAQ-DI	0.857	0.875
	(0.375 to 1.375)	(0.375 to 1.375)
DAS28-CRP	4.3 (3.3 to 5.2)	4.6 (3.6 to 5.5)
CRP, mg/mL	10 (4 to 23)	10 (3 to 26)
VAS physician, 0-100mm	27 (15 to 45)	30 (16 to 47)
Treated with methotrexate	86 %	84 %
-other csDMARD, %	24 %	24 %
-Biological DMARD, %	5 %	6 %
Smoking status:	13 / 11 / 17 / 59 %	9 / 9 / 23 / 59 %
Current / previous / never / unknown, %		
Prevalence of polyautoimmunity /	549 (10.6 %)	349 (12.8 %)
diabetes mellitus type 1 / autoimmune	1.4 % / 6.7 %	1.4 % / 7.8 %
thyroid disease / inflammatory bowel disease		
Age and sex adjusted odds ratio	0.79 (0.71 to 0.89)	1 (ref.)
Incident cases of polyautoimmunity	373 (4.7 %)	242 (5.3 %)
Adjusted hazard ratio	0.86 (0.71 to 1.05)	1 (ref.)

Continuous variables shown as median with interquartile ranges. Autoimmune conditions included: autoimmune thyroid disease (redeemed prescriptions of ATC=H03A); diabetes mellitus type 1 (ICD-10 diagnosis E10 combined with redeemed prescriptions of insulin, ATC=A10A); pernicious anaemia (D51.0); autoimmune haemolytic anaemia (D59.1); idiopathic thrombocytopenic purpura (D69.3); Autoimmune adrenalitis (E27.1B); multiple sclerosis (G35); neuromyelitis optica (G36.0); Guillain-Barré syndrome (G61.0); myasthenia gravis (G70); inflammatory bowel disease (K50-1); primary biliary cirrhosis (K74.3); primary sclerosing cholangitis (K83.0); autoimmune hepatitis (K75.4); celiac disease (K90.0); pemphigus vulgaris (L10.0); bullous pemphigoid (L12.0); dermatitis herpetiformis (L13.0); alopecia areata (L63); vitiligo (L80); lichen sclerosis (L90.0); chronic interstitial cystitis (N30.1).

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POS0314

PROSPECTIVE EVALUATION OF A DEDICATED, SERIAL OCCUPATIONAL THERAPY EXERCISE PROGRAM ON HAND FUNCTION IN RHEUMATOID ARTHRITIS (RA)

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Background: Rheumatoid arthritis (RA) frequently affects the joints of the hands causing severe pain and significant functional impairment affecting all activities of daily living. At early stages, functional impairment is primarily caused by reversible joint and tendon sheath effusions while at later stages synovial thickening, muscular atrophy and irreversible damage to cartilage, bone, tendons and ligaments cause a reduced range of motion and deformities. Occupational therapy aims to maintain and improve joint mobility and function. However, there is limited data on the effectiveness of serial exercise programs specifically aiming at maintaining and improving hand function in RA.

Objectives: To prospectively evaluate the effects of a dedicated exercise program on hand function, grip strength, joint mobility and pain compared with conventional outpatient physiotherapy not specifically targeting hand function.

Methods: A total of 51 RA patients receiving outpatient physiotherapy once a week were enrolled and randomized to either continue their usual therapy (control group) or to participate in a dedicated hand function training (HFT) twice a week in addition to their usual therapy (HFT group). The HFT program was supervised by an occupational therapist who conducted once weekly HFT sessions and instructed the participants to perform an additional self-administered HFT session at home once a week. Study duration was six months with an option to continue HFT for additional 6 months. Study participants were evaluated at baseline and every 3 months.

The primary outcomes hand function and grip strength were assessed using standardized questionnaires (Cochin hand function scale (CHFS), Australian/Canadian Osteoarthritis Hand Index (AUSCAN), Michigan Hand Outcomes Questionnaire (MHOQ)) and dynamometer/pinch gauge readings for different types of grip (cylindrical grasp, spherical grasp, hook grasp, tip to tip pinch and key pinch), respectively. The secondary outcomes joint mobility and pain were assessed using a digital goniometer and visual analogue scales (VAS), respectively. Statistical analysis used the Wilcoxon test for evaluating changes of parameters over time within the groups and the Kruskal Wallis test for group comparisons and Bonferroni-Holm correction.

Results: 41 of the 51 patients (HFT group: n = 20, mean age 60.3 ± 8.4 years; control group: n = 21, mean age 60.5 ± 11.5 years) completed the 6-month study period, 14 patients extended their HFT to 12 months. Within the 6-month study period there were no significant improvements of the primary outcome parameters and of pain within the groups vs. baseline and no significant differences between the groups. Only the CHFS improved significantly in the HFT group as of month 9. A significant improvement of the range of motion vs. baseline was achieved by HFT as early as 3 months after baseline which persisted up to month 12. As some improvement was also seen in the control group, there was no significant difference between the groups. Hand mobility improved particularly in the subgroup of patients >60 years of age. There was no influence by pain intensity at baseline (VAS ≤50 mm vs. VAS >50 mm).

Conclusion: Serial dedicated HFT for 6 months resulted in improved joint mobility but did not improve global hand function, grip strength and pain in RA patients. A longer treatment duration (≥12 months), a higher treatment frequency (>2 times/week) and a larger cohort of patients may be required.

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Scleroderma, myositis and related syndromes

POS0315

LONG-TERM SAFETY AND EFFICACY OF LENABASUM DURING 3 YEARS IN AN OPEN-LABEL EXTENSION (OLE) OF A PHASE 2 STUDY OF LENABASUM IN REFRACTORY SKIN DISEASE IN DERMATOMYOSITIS (DM)

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Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of inflammation. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in DM subjects with refractory skin involvement. In that study, lenabasum or placebo was added to stable background treatment, with immunosuppressive therapies allowed.

Objectives: To assess long-term safety and efficacy in DM subjects in this study.

Methods: Subjects who completed Part A of the Phase 2 study (n = 22) were eligible to receive oral lenabasum 20mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 20/22 (91%) eligible subjects enrolled in the OLE, following a mean interval of 31 weeks from the end of Part A, during which they continued to receive standard-of care treatments, to the start of the OLE during which lenabasum 20mg BID was added. 17/20 (85%) subjects were on stable baseline immunosuppressive drugs. At the time of this data cut-off, 17 subjects were still enrolled, 17 had completed 140 months (2.7 years), and 15 had completed 156 months (3 years) of OLE dosing. All OLE subjects experienced at least 1 adverse event (AE), with 118 AEs during the OLE through Dec 2020. Most AEs were mild ($n = 111$, 94%), with 2 severe AEs (fatigue and metastatic prostate cancer) considered unrelated to lenabasum. AEs occurring in $\geq 3/20$ OLE subjects were: URI ($n = 5$); fatigue ($n = 4$); nausea ($n = 3$); common cold ($n = 3$); UTI ($n = 3$); and DM flare ($n = 3$). No serious AEs related to lenabasum have been reported in this OLE to date. No subject discontinued the OLE because of an AE related to lenabasum. Improvement was seen in multiple physician- and patient-reported efficacy outcomes. CDASI activity score improved through the first 15 months of lenabasum treatment in the OLE and remained stable thereafter, with an improvement of ~ 20 points from the beginning of the study maintained from Month 15 through Year 3 in the OLE. CDASI damage score increased through the first year of the OLE, even though skin activity was decreasing, but lessened thereafter, returning after 3 years to about the same level it was at the beginning of the OLE. Other outcomes shown in Figure 1 followed the same general pattern as CDASI activity score, with improvement through the first 12-16 months of the OLE, then stability thereafter. Of note, 2 subjects had disease flares shortly after stopping lenabasum for conclusion of the OLE.

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 JBT101-DM-001 with no serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved and have remained stable, showing durability of improvement in these patients with refractory skin disease. Skin damage was reversible and began to improve once skin activity stabilized. The limitations of attributing this improvement to lenabasum in the setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM is ongoing.

Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-DM-001

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POS0316

MODELLING SHORT-TERM FVC CHANGES FROM SENSICIS TO LONG-TERM FVC COURSE IN SSC-ILD DEMONSTRATES CLINICALLY MEANINGFUL REDUCTION OF FVC DECLINE AND SURVIVAL BENEFITS

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Background: Nintedanib has shown to slow FVC decline by 41ml over 52 weeks in systemic sclerosis-associated interstitial lung disease (SSc-ILD). However, the long-term effect of nintedanib treatment on ILD progression and mortality in SSc patients is so far unknown.

Objectives: Here, the 52-week treatment efficacy of nintedanib was modeled and extrapolated on the long-term FVC course and survival in SSc-ILD patients from the European Scleroderma Trial and Research (EUSTAR) database.

Methods: SSc patients from the EUSTAR database fulfilling the inclusion criteria of the SENSICIS trial (SSc classification criteria, ILD confirmed by imaging, disease duration of <7 years, FVC $\geq$ 40%pred, diffusion capacity of the lung for carbon monoxide (DLCO) 30-89%pred) and matched for baseline characteristics as well as matched for the 52-week FVC change of SENSICIS patients were included ($n=236$). Linear mixed models including time, risk factors at baseline (sex, age, dyspnea class, DLCO%, CRP, modified Rodnan skin score, SSc subtype, SSc auto-antibodies, disease duration, synovitis and muscle weakness) were used to estimate the natural FVC course over time. On this natural course of FVC, the observed effect from the SENSICIS trial representing the absolute 52-week difference of FVC decline between the nintedanib and the placebo group was applied as continuous annual effect (SENSICIS effect model). Survival was estimated for both the natural course as well as the SENSICIS effect model using Cox regression.

Results: Of the 236 included patients, 75% were females, 65% had diffuse cutaneous SSc. Mean age was 50.6 years, mean FVC 78.2%pred and DLCO 56.3%pred at time of inclusion. Mean FVC change after 12 $\pm$ 3 months was -2.3 $\pm$ 6.9%pred. These parameters were largely similar to the characteristics of the SENSICIS population.

In the longitudinal follow up of this population, the natural course of FVC showed a total FVC decline of -16.3%pred over 5 years. With assumed SENSICIS effects (effects of nintedanib treatment reported in SENSICIS), the 5-year FVC decline was reduced to -10.3%pred (Figure 1).

The reduced FVC progression translated into an improved survival. The natural 5-year survival of this SSc-ILD population was 88.2%. When extrapolating also a severe FVC decline early in the course, frequently terminated by early mortality of SSc patients excluding them from long-term outcome assessment, the estimated 5-year survival was reduced to 81.6%. When the SENSICIS effects on