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POS0853

DECREASE IN ANTI-TOPOISOMERASE-1 ANTIBODY TITER IN PATIENTS WITH SYSTEMIC SCLEROSIS DURING LONG-TERM RITUXIMAB THERAPY

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Background: Rituximab (RTX) is a new option in the treatment of systemic sclerosis (SSc) [1]. There is not enough data on changes in the level of autoantibodies and their clinical significance during RTM therapy. There are only a few reports on the higher efficiency of RTX in patients (pts) with SSc positive for anti-topoisomerase-1 antibodies (a-Topo-1), therefore the study of this issue might be interested.

Objectives: To compare clinical parameters and B-lymphocytes (B-lymph) level in SSc pts depending on the presence or absence of a-Topo-1 during RTX therapy with prospective long-term follow-up.

Methods: This study included 88 pts with SSc. The mean follow-up period was 26,3±10,7 months. The mean age was 47years (17-71), female-73 pts (83%), the diffuse cutaneous subset of the disease had 50 pts (57%). Symptoms of the interstitial lung disease (ILD) were observed in 70 pts (80%). The mean disease duration was 5,9±4,8 years. The cumulative mean dose of RTX was 2,9±1,1 grams. All patients received prednisone at a dose of 11,7±4,4 mg, immunosuppressants received 42% of them. There were 63 pts positive for a-Topo-1 and 25 pts - negative. The pts of the compared groups did not differ in the main demographic and clinical parameters, excepting lung involvement. In a-Topo-1 positive group 55 (87%) pts had ILD and only 15 (60%) – in a-Topo-1-negative group (p=0,02). The results at baseline and at the end of the follow up are presented in the form of mean values and changes in parameters (delta).

Results: Considering the entire cohort, an improvement of almost all outcome parameters was found. When a-Topo-1 positive and a-Topo-1-negative pts were analyzed separately, we observed a significantly higher decrease in the activity score, depletion of B-lymph, an increase in forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO) in a-Topo-1 positive group of pts (table 1).

Table 1. Changes of the main outcome parameters depending on the presence of a-Topo-1 on RTX therapy.

Parameters	a-Topo-1 positive pts	a-Topo-1 negative pts	P
Delta Activity score (EScSG-AI)	1,79	0,9	0,001
Delta Rodnan skin score (mRSS)	4,9	5,2	NS
Delta B-lymphocytes (absolute count)	0,212	0,193	0,001
Delta FVC*, %	8,64	6,46	0,001
Delta DLCO**, %	2,86	0,032	0,001

*FVC - forced vital capacity % predicted, **DLCO - diffusion capacity for carbon monoxide % predicted

The a-Topo-1 level decreased from 174,2±50,1 to 148,1±66,1 units/ml (p=0,0009). In this group, a-Topo-1 became negative in 5 pts (7,9%). The disappearance of a-Topo-1 positivity was accompanied by a more pronounced decrease in mRSS (delta mRSS=7,4) and a higher depletion of B-lymph. There was a higher cumulative dose of RTX (4±1,4grams) in this 5 pts compared with the pts who sustained a-Topo-1 positivity. There was a moderate negative statistically significant correlation between the a-Topo-1 and the total dose of RTX (r=-0,298, p=0,017). A moderate negative statistically significant correlation was found between the a-Topo-1 and FVC (r=-0,322, p=0,009).

Conclusion: In our study, the a-Topo-1 level significantly decreased during RTX therapy in Russian pts. The decrease in a-Topo-1 titers correlated with the total dose of RTX and was accompanied by a decrease in mRSS, disease activity index and an increase in FVC and DLCO. A higher efficacy of RTX in the a-Topo-1 positive group with prevalence of ILD was revealed, therefore a-Topo-1 positivity could be considered as a predictor of a better response to RTX therapy.

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POS0854

SEX DIFFERENCES IN SYSTEMIC SCLEROSIS PATIENTS IN A SINGLE CENTER IN EASTERN EUROPE

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Background: The low overall prevalence of systemic sclerosis (SSc) and the low proportion of male patients have resulted in a scarcity of studies assessing sex differences in SSc patients, and contradictory results have often been observed. **Objectives:** The aim of the study was to assess differences in disease manifestations in a cohort of SSc patients according to gender.

Methods: We performed a retrospective observational study using data extract from the EULAR scleroderma trials and research (EUSTAR) cohort 096. We looked at sex influence on disease characteristics at baseline and then focused on patients with at least 2 years of follow-up to estimate the effects of sex on disease progression and survival.

Results: 173 patients with SSc were available for the baseline analyses. Males were older (52,96 vs 45,88, p=0.009), were more likely to smoke (73% vs 7%, p<0.001), had more frequent diffuse skin involvement (73,1% vs 56,5%, p<0.01), higher modified Rodnan skin score (34,61% vs 17%, p=0.01) and activity score (84,62% vs 46,26%, p<0.001) and were more often associated with positive acute phase reactants (65,38% vs 38,77%, p=0.01). Severe interstitial lung disease was more common in males (59,09% vs 27,53%, p=0.003), also the presence of tendon friction rubs was more frequent in this sex group (23,07% vs 8,84%, p=0.032).

In the longitudinal analysis after a mean follow-up of 3,5(±0,65) years, male sex was associated with a higher risk of scleroderma renal crisis (OR:9.45 (1.49 to 59.69); p=0.004), digital contractures (OR:8,2 (3,1 to 21,9); p<0,001), arrhythmias (OR:3,37 (1,36 to 8,34); p=0.006), pulmonary fibrosis (OR: 3.56, (1.51 to 8.41); p=0.003), pulmonary hypertension (OR: 3.01 (1.19 to 7,59); p=0.016), severe vascular involvement (OR:2,86, (1,22 to 6,73); p=0.013) and low ventricular ejection fraction (OR: 2,84, (1,2 to 6,73); p=0.014). Males had significantly reduced survival time after diagnosis (p=0,004). The most frequent causes of death were scleroderma renal crisis in males and pulmonary hypertension in females.

Conclusion: Although more common in women, SSc appears as strikingly more severe in men. Our results demonstrate a higher risk of severe organ involvement and poor prognosis in men. These results raise the point of including sex in the management and the decision-making process.

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POS0855

PATIENT PREFERENCES, TRADE-OFFS AND ACCEPTABLE RISKS IN THE TREATMENT OF SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: A STEP TOWARDS SHARED DECISION-MAKING

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Background: Current treatments for systemic sclerosis-associated interstitial lung disease (SSc-ILD) are characterised by different attributes such as mode of administration, adverse events (AE) and efficacy. Physicians and patients often have different perspectives on treatments, thus shared decision-making between patients and physicians is essential. An understanding of patients' decision processes when weighing treatment attributes and the trade-offs they are willing to make is important for shared decision-making.

Objectives: The study aimed to 1) identify relevant treatment attributes, 2) elicit patient preferences for these attributes and 3) quantify preference as relative attribute importance (RAI); a higher RAI indicates that more of the variability in patients' responses may be explained by changes in the attribute; and maximum acceptable risk (MAR) of diarrhoea, nausea and/or vomiting (MAR is a trade-off measure that evaluates attributes in risk-equivalences as a unit of measurement).

Methods: A discrete choice experiment (DCE) was created, based on a literature review, a patient advisory board, qualitative patient interviews, and a workshop involving SSc-ILD expert physicians. Seven SSc-ILD treatment attributes were identified: 1) mode of administration; 2) shortness of breath; 3) skin tightness; 4) cough; 5) tiredness; 6) risk of gastrointestinal tract (GIT) AEs; and 7) risk of serious and non-serious infections. The levels of AE risk were informed by frequencies observed in clinical trials and patient input during the interviews. The DCE was integrated into an online survey, which asked patients to make repeated choices between two alternatives described by varying levels of included attributes. Patients with SSc-ILD were recruited by physician referral from Switzerland, Norway, France, Germany and the USA. DCE data were analysed using a logit model, and RAI and MAR measures were calculated.

Results: A total of 231 patients with physician-confirmed SSc-ILD (mean age 52.6±13.2 years; 54% diagnosed for >5 years) completed the survey. Patients with SSc-ILD mostly preferred twice-daily oral treatments ($p<0.001$) and infusion every 6–12 months ($p<0.001$) over monthly infusions. Patients' choices were mostly affected by the risk of GIT AEs (RAI=25%; 95% CI 22–28%) and risk of infections (RAI=20%; 95% CI 16–24%). Improvements in shortness of breath and type and severity of cough were jointly more important than improvement in skin tightness ($p<0.001$).

Patients accepted an additional 21% risk (95% CI 13–29%) of GIT AEs if they could reduce the frequency of infusions from monthly to 6–12 monthly, or accepted an extra 15% (95% CI 7–23%) increase in risk if changing to an oral treatment twice daily. Among symptoms, an additional 28% (95% CI 20–36%) risk of GIT AEs was considered acceptable if the severity of patients' persistent cough was reduced to a level that was easier to tolerate, even if it remained persistent. Similarly, a 37% (95% CI 28–46%) increase in the risk of GIT AEs was acceptable if it resulted in breathlessness during routine activities rather than breathlessness at rest. Finally, patients were willing to accept an additional 36% risk (95% CI 27–45%) of GIT AEs if it reduced their risk of non-serious infections from 30% to 15% and of serious infections from 10% to 5%.

Conclusion: This is the first study to quantitatively elicit patients' preferences for attributes of SSc-ILD treatments. Preferences were driven by safety, efficacy and technical considerations. Patients showed willingness to make trade-offs, providing a firm basis for shared decision-making in routine clinical practice.

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Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: JHWD has received research funding from Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB, Eric Hachulla: None declared, Vivian Hsu Speakers bureau: I am a speaker for Boehringer Ingelheim Pharmaceuticals, Consultant of: with Boehringer Ingelheim Pharmaceuticals, Grant/research support from: Principal Investigator for several clinical trials, currently with Genentech, Corbus Pharmaceutical, and EICOS, Nicolas Hunzelmann Speakers bureau: Boehringer, Roche, Sanofi, Dinesh Khanna Shareholder of: Eicos Sciences, Inc (less than 5%), Consultant of: Paid Consultant for: Acceleron, Actelion, Abbvie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead, Galapagos, Genentech/Roche, GSK, Horizon, Merck, Mitsubishi Tanabe Pharma, Sanofi-Aventis, and United Therapeutics, Grant/research support from: Research Grant support from: Immune Tolerance Network, Bayer, BMS, Horizon, Pfizer, Employee of: Leadership/Equity position – Chief Medical Officer, CiviBioPharma/Eicos Sciences, Inc – receives a stipend for role as Chief Medical Officer, which would technically qualify as employment., Marie-Elise Truchetet Speakers bureau: Abbvie, Lilly, Sobi, Boehringer, Paid instructor for: Lilly, Consultant of: UCB, Sobi, Abbvie, Grant/research support from: UCB, Gilead, Ulrich Walker Shareholder of: Bayer, NASDAQ, MSCI-World ETF's, Speakers bureau: All companies producing pharmaceuticals used in AIDS, Paid instructor for: Roche, Abbvie, Novartis, Consultant of: All companies producing pharmaceuticals used in AIDS, Grant/research support from: Gilead, Abbvie, (in the last two years). Other companies in previous years., Margarida Alves Employee of: Boehringer Ingelheim, Nils Schoof Employee of: Employee of Boehringer Ingelheim International GmbH, Lesley Ann Saketkoo Speakers bureau: Boehringer Ingelheim, Actelion, Janssen, Mallinckrodt, United Therapeutics, Consultant of: Actelion, Boehringer Ingelheim, Bayer, Bristol Meyer Squibb, Corbus, EICOS, Janssen, Horizon, United Therapeutics, Inc, Grant/research support from: Mallinckrodt, United Therapeutics, Oliver Distler Speakers bureau: Boehringer Ingelheim, Medscape, IQone, Roche, Consultant of: OD has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, IQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), Grant/research support from: Kymera Therapeutics, Mitsubishi Tanabe

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POS0856

CLINICAL UTILITY OF BREATH-HOLDING TEST FOR MEASURING CARDIOPULMONARY FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are major causes of death in systemic sclerosis (SSc). Six-minute-walk test (6MWT) is a standard outcome measure for exercise capacity in cardiopulmonary diseases. However, the results of 6MWT may not reflect real cardiopulmonary function of SSc patients in whom musculoskeletal system is frequently inflected.

Objectives: This study aimed to evaluate the clinical utility of breath-holding test (BHT) in evaluating cardiopulmonary function in SSc patients, as compared with 6MWT.

Methods: Seventy-two patients with SSc were prospectively enrolled and underwent BHT and 6MWT with measurement of Borg score and Scleroderma Health Assessment Questionnaire (SHAQ). Data on diffusing capacity for carbon monoxide (DLCO, %), forced vital capacity (FVC, % and liters), and ejection fraction and pulmonary arterial systolic pressure (PASP) measured by transthoracic echocardiography (TTE), were also collected. For BHT, participants were required to make a maximum expiration followed by a maximum inspiration and to hold the breath as long as possible at maximum inspiratory level. This procedure was repeated three times, with 5-minute intervals. 6MWT was performed according to the American Thoracic Society guidelines. Pearson's correlation test was applied to demonstrate the relationship between BHT results and each clinical parameter.