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 RTX therapy. There are only a few reports on the higher efficiency of RTX in patients (pts) with SSc positive for anti-topo-1-antibodies (a-Topo-1) and 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 47 years (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 mg. 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.

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.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>a-Topo-1 positive</th>
<th>a-Topo-1 negative</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta Activity score (EScSG-AI)</td>
<td>1.79</td>
<td>0.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Delta Rodnan skin score (mRSS)</td>
<td>4.9</td>
<td>5.2</td>
<td>NS</td>
</tr>
<tr>
<td>Delta B-lymphocytes (absolute count)</td>
<td>0.212</td>
<td>0.193</td>
<td>0.001</td>
</tr>
<tr>
<td>Delta FVC, %</td>
<td>8.64</td>
<td>6.46</td>
<td>0.001</td>
</tr>
<tr>
<td>Delta DLCO%, %</td>
<td>2.86</td>
<td>0.032</td>
<td>0.001</td>
</tr>
</tbody>
</table>

P - 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=0.009). In this group, a-Topo-1 became negative in 5 pts (7%). 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.

REFERENCES:

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.

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 65.5%, p<0.01), higher modified Rodnan skin score (34.61% vs 17%, p=0.001) and activity score (64.62% 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 27.33%, p=0.003), the presence of tendon friction rubs was more frequent in this sex group (23.77% vs 4.84%, 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:4.95 (1.49 to 59.69; p=0.004), digital contractures (OR:3.21 to 21.9; p<0.001), arrhythmias (OR:3.37 (1.66 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 venricular 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.

Disclosure of Interests: None declared

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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) breathlessness at rest; 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. The 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 extremely 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 infections (RAI=20%; 95% CI 16–24%) was considered acceptable if the severity of patients’ 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.

Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Consultant of: Eli Lilly, Grant/research support from: Group Italiano Lotta alla Sclerodermia GILS, Foundation for the Defence of Arterial Disease over la Ricerca Artite (FIRA), New Horizon Fellowship, European Scleroderma Trial and Research (EUSTAR), Foundation for Research in Rheumatology (FOREUM), Sebastian Heidenreich Consultant of: Sebastian Heidenreich, PhD is employed by Evidera Inc, a business unit of PPD. Evidera is a CRO that offers paid research services to pharmaceutical companies., Ashley Duenas Consultant of: Yes. I am an employee of Evidera, Shareholder of: Evidera Inc, a business unit of PPD. Evidera is a CRO that offers paid research services to pharmaceutical companies., Margarida Alves Employee of: Boehringer Ingelheim, Nils Schoof Employee of: Boehringer Ingelheim, Jörg H.W. Distler Consultant of: Jörg H.W. Distler is employed by University Hospital Basel, Department of Medicine, University Hospital, Division of Rheumatology, Department of Internal Medicine, University of Basel, Switzerland, Consultant of: Boehringer Ingelheim, CiviBioPharma, Eicos Sciences, Inc., JHSU HSU Speaker Bureau: I am a speaker for Boehringer Ingelheim Pharmaceuticals, Consultant of: of with Boehringer Ingelheim Pharmaceuticals, Consultant of: Chief Medical Officer, Nicu Huntau Speaker Bureau: I am a speaker for Boehringer Ingelheim Pharmaceuticals, Consultant of: Chief Medical Officer, JHSU HSU Speaker Bureau: I am a speaker for Boehringer Ingelheim Pharmaceuticals, Consultant of: Chief Medical Officer, Marie-Elise Truchetet Speaker Bureau: Boehringer Ingelheim, Consultant of: Lilly, Novartis, Consultant of: of with Boehringer Ingelheim Pharmaceuticals, Consultant of: Chief Medical Officer, Boehringer Ingelheim, Consultant of: Lilly, Novartis, Consultant of: Chief Medical Officer, Boehringer Ingelheim, Consultant of: Lilly, Novartis, Consultant of: Chief Medical Officer.

Clinical Utility of Breath-Holding Test for Measuring Cardiopulmonary Function in Patients with Systemic Sclerosis

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Background: Intestinal 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 sarcoidosis is a co-existing condition.

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 ejection fraction and pulmonary arterial systolic pressure (PASP) measured by transhast- racic 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 using a six-minute walking test protocol.

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