Background: Interstitial lung disease associated with systemic sclerosis (ILD-SSc) is a frequent manifestation of the disease, impairing the quality of life and the prognosis of the disease. The efficacy of rituximab (RTX) in patients (pts) with ILD-SSc have been shown [1]. The "biosimilar" versions of RTX might reduce the cost of therapy and increase pts accessibility to this treatment option. The RTX biosimilar Acellbia (ACB), "BIOCAD", has received approval in Russian Federation in 2014 for all indications held by reference RTX.

Objectives: to investigate the efficacy and safety of ACB in naive to biological therapy pts with ILD-SSc during at least 12 month of follow-up.

Methods: Twenty pts were included in prospective observational study. The pts were aged 49,7 (s.d.14) years, 14 (70%) were females, mean disease duration was 3,5±2,7 years, with diffuse subset in 11 (55%), 13 (65%) were anti-topoisomerase positive, all pts has NSIP-pattern by HRCT. All pts were naive to ACB, received glucocorticoids in low doses, 10 (50%) pts were previously treated with immunosuppressants and 4(20%) of them continued to take mycophenolate mofetil as a concomitant therapy. Pts received two courses of ABC with the same scheme: 1g repeated 1 week apart (4g ACB in total). An assessment of basic measurements was obtained at baseline (Point 0), before the second course (after 7,2±1,7 mo, Point 1) and at the end of follow-up (13,4±1,6 mo, Point 2). The results are presented in the form of mean values and standard deviations.

Results: We observed a gradual improvement in the main parameters from Point 0 to Point 2 (table). Importantly, that at Point 1 there were no differences in most parameters, except for Rodnan skin score (mRSS) and the absolute number of B-lymphocytes (B-lymph), but at Point 2 there were significant differences between most basic outcome measures.

Table 1. Follow-up data of ACB treatment in ILD-SSc pts

Parameters	Point 0 (n=20)	Point 1 (n=20)	Point 2 (n=18)#	P 1-2	P 1-3
mRSS	12,75±11,1	8,25±7,72	6,16±5,65	0,002	0,002
FVC*, % pred	89,1±18,2	92,31±19,21	98,26±16,13	NS	0,0002
DLCO**, % pred	56,67±15,7	58,11±17,71	61,86±17,16	NS	0,019
SHAQ	1,13±0,628	0,98±0,678	0,61±0,495	NS	0,00001
lgA, g/l	12,61±2,348	11,5±1,61	10,19±2,18	NS	0,002
a-Topo-1, unit/ml	109,68±86,92	96,46±81,72	72,46±69,46	NS	0,004
B-lymph, absolute count	0,329±0,34	0,0016±0,003	0,00189±0,003	0,0004	0,001
Glucocorticoids, mg/day	11,0±2,7	10,75±2,0	9,4±2,3	NS	0,03

*FVC - forced vital capacity % predicted, **DLCO - diffusion capacity for carbon monoxide % predicted. # Of the 20 patients who received the second course, 2 (10%) dropped out the follow-up due to pregnancy (1) and lung cancer (1).

The frequency and spectrum of adverse events (AE) corresponds to the known in the treatment of RTX, most AEs were classified as mild ones. There were 11 (55%) of AE in 9 (45 %) pts. Infections were observed in 7 (35%) pts: 4 cases of acute respiratory tract infections, 2 cases of positivity in interferon-gamma release assay and one case each of otitis, cystitis, cholecystitis (9 AE in total). One pts developed low limb vein thrombosis and one - lung cancer. There were no infusion-related reactions.

Conclusion: The data from this prospective pilot study showed the effectiveness of the ACB in ILD-SSc. The clinical effect of ACB arises gradually and the baseline outcome measures reliably improve by the end of the first year. Our study have demonstrated a well-tolerated safety profile. We believe that ACB can be prescribed at SSc-ILD as a first-line drug and/or in the form of monotherapy.

REFERENCES:

- [1] Erre G.L., et al. Efficacy, Safety, and Tolerability of Treatments for Systemic Sclerosis-Related Interstitial Lung Disease: A Systematic Review and Network Meta-Analysis. *J.Clin.Med.* 2020,9,2560;doi:10.3390/jcm90825-60.

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POS0861

EFFECTIVENESS AND SAFETY OF TOCILIZUMAB IN PATIENTS WITH SYSTEMIC SCLEROSIS: A PROPENSITY SCORE CONTROL MATCHED OBSERVATIONAL STUDY OF THE EUSTAR COHORT

S. Kuster¹, S. Jordan¹, M. D. Elhai², U. Held³, K. Steigmiller³, C. Bruni⁴, F. Iannone⁵, S. Vettori⁶, E. Siegert⁷, S. Rednic⁸, V. Codullo⁹, P. Airo¹⁰, Y. Braun-Moscovici¹¹, N. Hunzelmann¹², M. J. Salvador¹³, V. Ricciardi¹⁴, A. M. Gheorghiu¹⁵, J. J. Alegre Sancho¹⁶, K. Romanowska-Prochnicka¹⁷, I. Castellvi¹⁸, I. Koetter¹⁹, M. E. Truchet²⁰, F. J. López-Longo²¹, P. Novikov²², A. Giollo²³, Y. Shirai²⁴, L. Belloli²⁵, E. Zanatta²⁶, E. Hachulla²⁷, V. Smith²⁸, C. Denton²⁹, R. Ionescu³⁰, T. Schmeiser³¹, J. H. W. Distler³², A. Gabrielli³³, A. M. Hoffmann-Vold³⁴, M. Kuwana³⁵, Y. Allanore³⁵, O. Distler² on behalf of EUSTAR. ¹University of Zurich, University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland; ²University of Zurich, University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland; ³University of Zurich, Department of Biostatistics at Epidemiology, Biostatistics and

Prevention Institute, Zurich, Switzerland; ⁴University of Florence, Division of Rheumatology, Department of Experimental and Clinical Medicine, Florence, Italy; ⁵GISEA, University Hospital of Bari, Bari, Italy; ⁶University of Campania 'Luigi Vanvitelli', Department of Precision Medicine, Naples, Italy; ⁷Charité-Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany; ⁸University of Medicine & Pharmacy 'Iuliu Hatieganu' Cluj, Clinica Reumatologie, Cluj Napoca, Romania; ⁹University and IRCCS Policlinico S. Matteo Foundation, Division of Rheumatology, Pavia, Italy; ¹⁰University of Brescia, ASST Spedali Civili di Brescia, Rheumatology and Clinical Immunology, Brescia, Italy; ¹¹Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion, B. Shine Rheumatology Unit, Haifa, Israel; ¹²Universitätsklinikum Köln, Universitätsklinik Köln, Köln, Germany; ¹³University of Coimbra, University Hospitals, Department of Rheumatology, Coimbra, Portugal; ¹⁴Sapienza University, Department of Internal Medicine and Medical Specialties, Rome, Italy; ¹⁵Ion Cantacuzino Clinical Hospital, Department of Internal Medicine and Rheumatology Clinic, Bucharest, Romania; ¹⁶University of Valencia, University Hospital Dr. Peset, Department of Rheumatology, Valencia, Spain; ¹⁷Institute of Rheumatology, Department of Connective Tissue Disease, Warsaw, Switzerland; ¹⁸Hospital Universitari de La Santa Creu i Sant Pau, Department of Rheumatology, Barcelona, Spain; ¹⁹Asklepios Clinic Altona, Medical Department 4, Rheumatology, Immunology, Nephrology, Hamburg, Germany; ²⁰National Reference Center for Systemic Autoimmune Rare Diseases, Hôpital Pellegrin, Department of Rheumatology, Bordeaux, France; ²¹Hospital General Universitario Gregorio Marañón, Department of Rheumatology, Madrid, Spain; ²²Sechenov First Moscow State Medical University, Clinic of Nephrology, Internal and Occupational Diseases, Moscow, Russian Federation; ²³University of Verona, Rheumatology Section, Department of Medicine, Verona, Switzerland; ²⁴Nippon Medical School Hospital, Allergy and Rheumatology, Tokyo, Japan; ²⁵'Niguarda Ca' Granda Hospital, Rheumatology Unit, Milano, Italy; ²⁶University of Padova, Rheumatology Unit, Department of Clinical and Experimental Medicine, Padova, Italy; ²⁷Referral Centre for Rare Systemic Auto-immune Diseases for North and North-West of France, University of Lille, Department of Internal Medicine, Claude Huriez Hospital, Lille, France; ²⁸University of Ghent, Department of Rheumatology, Ghent, Belgium; ²⁹Royal Free and University College London Medical School, Royal Free Campus, Centre for Rheumatology, London, United Kingdom; ³⁰University of Medicine and Pharmacy, Department of Rheumatology - St. Maria Hospital, Carol Davila, Bucharest, Romania; ³¹Krankenhaus St. Josef, Innere Medizin und Rheumatologie, Wuppertal-Elberfeld, Germany; ³²Universitätsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany; ³³Istituto di Clinica Medica Generale, Università Politecnica delle Marche Polo Didattico, Ematologia ed Immunologia Clinica, Ancona, Italy; ³⁴Rikshospitalet University Hospital, Department of Rheumatology, Oslo, Norway; ³⁵Cochin Hospital, APHP, Paris Descartes University, Rheumatology A Department, Paris, France

Background: Tocilizumab (TCZ) showed trends for improving skin fibrosis and prevented progression of lung fibrosis in patients with systemic sclerosis (SSc) in placebo-controlled randomised clinical trials (RCTs). However, safety and effectiveness of TCZ beyond these selected and enriched clinical trial populations in SSc is still unknown.

Objectives: To assess safety and effectiveness of TCZ treatment compared to standard of care in SSc patients from the large, multicentre, observational, real-life EUSTAR network/database using propensity score matching.

Methods: SSc patients from the EUSTAR network/database, who fulfilled the ACR/EULAR 2013 classification criteria, with a baseline and a follow-up visit at 12±3 months, receiving TCZ or standard of care (controls), were selected. The following variables were used for the propensity score matching (1:1): age at diagnosis, gender, disease subtype, baseline modified Rodnan skin score (mRSS), forced vital capacity (FVC), and diffusing capacity for carbon monoxide (DLCO), co-therapy with immunosuppressives, disease duration, and year of treatment. Primary endpoints were mRSS and FVC at 12±3 months follow-up compared between the groups, using paired t-tests. Secondary endpoints were the percentage of progressive/regressive patients for skin and lung at 12±3 months follow-up according to standard definitions (1,2). Sensitivity analyses assessed pre-processing decisions (selection of most recent vs. random observation for control patients with multiple suitable time intervals), as well as the matching method (optimal vs. exact matching). Missing values were addressed with 100-fold multiple imputation using chained equations. Safety data were analysed in all patients. The study including the statistical analysis plan was pre-registered at www.drks.de (DRKS-ID: DRKS00015537).

Results: We identified 93 SSc patients treated with TCZ and 2370 SSc patients with standard of care who fulfilled the inclusion criteria. Forty nine (57.7%) of the TCZ treated patients were diffuse, eight patients were not classified, disease duration was (mean±SD) 6.35±5.40 years, their baseline mRSS was 15.05±10.85, and 76 (81.7%) received immunosuppressive therapy in addition to TCZ. Through multiple imputation and propensity score matching, 100 imputed

sets of 93 pairs of TCZ/controls were generated. Comparison between groups showed consistent effects of TCZ across all pre-defined primary and secondary endpoints: mRSS was lower in the TCZ group (mean difference (95% confidence interval (CI)) -1.8 (-4.79 to 1.19), $p=0.24$, Figure 1A). Similarly, FVC % predicted was higher in the TCZ group mean difference (2.25, 95% CI -4.57 to 9.06), $p=0.51$, Figure 1B). Considering secondary endpoints, the percentage of skin progressors as well as lung progressors at follow up was lower in the TCZ group (odds ratio OR 0.67 (95% CI 0.07 to 6.41), $p=0.74$ and OR 0.53 (95% CI 0.16 to 1.7); $p=0.2$, respectively. Consistently, the percentage of regressors for skin (OR 1.6 (95% CI 0.56 to 4.54), $p=0.38$) and for lung (OR 1.74 (95% CI 0.66 to 4.58), $p=0.26$) was higher in TCZ. These results were robust regarding the sensitivity analyses. Safety analysis confirmed previously reported adverse event profiles.

Conclusion: In this large, observational, controlled, real-life EUSTAR study, effectiveness of TCZ did not reach statistical significance compared to standard of care treatment but showed consistent positive effects of TCZ on skin and lung fibrosis across all pre-defined primary and secondary endpoints confirming data from recent RCTs.

REFERENCES:

- [1] Prediction of improvement in skin fibrosis in diffuse cutaneous systemic sclerosis: a EUSTAR analysis. *Ann Rheum Dis* 2016;17:43-8.
- [2] Progressive interstitial lung disease in patients with systemic sclerosis-associated interstitial lung disease in the EUSTAR database. *Ann Rheum Dis* 2021;219-227.

Figure 1. mRSS and FVC at follow up (123 months)

- A) Mean mRSS (95% CI) TCZ 10.68 (8.96 to 12.4) vs control 12.5 (10.5 to 14.5), between group mean difference -1.8 (-4.79 to 1.19), $p=0.24$
- B) Mean FVC, predicted (95% CI) TCZ 89.22 (84.77 to 93.67) vs control 86.97 (82.43 to 91.52), between group difference 2.25 (-4.57 to 9.06), $p=0.51$

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Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Consultant of: Oliver Distler 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, Baeon 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: The study was partially supported by a grant from Roche. Roche was not involved in analysis or interpretation of the results.

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POS0862 NAILFOLD CAPILLAROSCOPY IN UNDIFFERENTIATED AND MIXED CONNECTIVE TISSUE DISEASES

C. Pizzorni¹, G. Ferrari¹, C. Schenone¹, E. Gotelli¹, S. Paolino¹, A. Sulli¹, G. Pacini¹, E. Alessandri¹, V. Smith², M. Cutolo¹. ¹Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic, Genoa, Italy; ²Department of Rheumatology – Department of Internal Medicine – Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent University Hospital, Ghent, Belgium

Background: Microvascular damage is a frequent feature in connective tissue diseases (CTDs) and can be easily detected through nailfold videocapillaroscopy (NVC) (1,2). Mixed and Undifferentiated connective tissue diseases (MCTD and UCTD) do not show a specific and unique NVC pattern (3). However, a variety of microvascular abnormalities can occur in these two CTDs, both non-specific or specific for the scleroderma-like-pattern (3-5).

Objectives: To retrospectively assess and compare nailfold microangiopathy observed by NVC in MCTD and stable UCTD versus primary Raynaud's phenomenon (PRP) (6). In addition, the aim was to correlate NVC findings with serum levels of autoantibodies (Abs) against extractable nuclear antigen (ENA) detected in UCTD.

Methods: Files of forty-six MCTD patients (Kasukawa's criteria) (mean age 42.8±16 SD years), forty-seven UCTD patients (mean age 47.7±16.1 SD years), fifty-one PRP (mean age 45.9±17.3 SD years) were retrospectively evaluated in the study. Among UCTD and MCTD patients 95% of both showed Raynaud's phenomenon. Main NVC parameters (i.e. dilated capillaries, giant capillaries, microhemorrhages, abnormal shapes and number of capillaries) and related semiquantitative scale (score 0–3 for every parameter), were analyzed and compared between the two distinct CTD groups and PRP. Furthermore, ENA Abs (in particular, Ro/SSA, La/SSB, Scl70 and Jo1) were evaluated. The CTD patients were receiving different immunosuppressive treatments. Statistical analysis was performed by non-parametric tests.

Results: Among UCTD group, 36% of patients showed a normal NVC pattern, 53% had non-specific NVC abnormalities and 11% had a scleroderma-like-pattern. The latter was significantly more frequent in MCTD than in UCTD ($p<0.001$), in fact 22 out of 46 (48%) MCTD patients presented a scleroderma-like pattern. On the other hand, normal pattern or non-specific NVC abnormalities were respectively found in 9% and 43% MCTD patients. Therefore, CTD patients showing giant capillaries, abnormal shapes (i.e. angiogenesis) and lower capillary density were significantly more affected by MCTD than UCTD ($p<0.001$). Finally, the absolute number of capillaries was found significantly lower in MCTD versus UCTD patients (mean 7±1.7 SD vs mean 9.2±1 SD, respectively, $p<0.001$). Not any statistical correlation was observed between NVC parameters and specific Abs ENA in UCTD. PRP showed a normal NVC pattern in 2% and non-specific capillary abnormalities in 98%, (including dilated capillaries and microhemorrhages).

Conclusion: NVC features in UCTD patients seem very close to the pattern observed in PRP (mostly non-specific capillary abnormalities), conversely in MCTD the scleroderma-like pattern was found significantly prevalent together with a significant capillary number reduction. The transition from the scleroderma-like to the scleroderma pattern (mean systemic sclerosis) is matter of actual investigation.

REFERENCES:

- [1] Cutolo M. et al. *Best Pract Res Clin Rheumatol* 2008; 22:1093-108.
- [2] Sulli A, *Ann Rheum Dis*. 2008;67:885-7.
- [3] Smith V. et al. *Autoimmunity Reviews* 2020; 19:102458.
- [4] De Holanda Mafaldo DA, et al. *Lupus*. 2007; 16:254–8.
- [5] Smith V, et al. *Ann Rheum Dis* 2010; 69: 1092-96.
- [6] Antunes M, et al. *RMD Open*. 2019, 26;4.

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