Table 2 Clinical findings in patients of 2 groups

		Early-remission n=41		Long-therapy n=21		p
Demographic, clinical, and laboratory findings at diagnosis						
Woman	n (%)	20	(48.8)	12	(57.1)	0.5
Age: years	mean (SD)	74.2	(7.8)	73.7	(5.8)	0.8
Body weight, kg	mean (SD)	55.3	(11.18)	52.1	(9.23)	0.3
Body mass index, kg/m ²	mean (SD)	22.7	(4.03)	20.7	(3.10)	0.06
Fever	n (%)	10	(24.4)	7	(33.3)	0.5
Body weight loss	n (%)	13	(31.7)	10	(47.6)	0.2
Peripheral edema	n (%)	16	(39.0)	10	(47.6)	0.3
Serum C-reactive protein, mg/dL	mean (SD)	6.4	(4.17)	8.8	(4.06)	0.03
Serum albumin, mg/dL	mean (SD)	3.2	(0.47)	3.2	(0.57)	0.7
Treatment and clinical course						
Starting dose of PSL: mg/day	mean (SD)	12.6	(4.09)	14.5	(3.94)	0.1
mg/kg/day	mean (SD)	0.24	(0.084)	0.28	(0.079)	0.1
Mean duration of GC treatment	month (SD)	14.2	(4.59)	43.4	(21.98)	<0.01
Achieving remission	n (%)	41	(100)	9	(42.9)	
Relapse: times	mean (SD)	0.4	(0.70)	3.1	(2.06)	<0.01
Relapse till 6 months	n (%)	3	(7.3)	8	(38.1)	<0.01
PSL, prednisolone; GC, glucocorticoid; SD, standard deviation						

PSL, prednisolone; GC, glucocorticoid; SD, standard deviation

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THU0294

THE DIFFERENCES IN THE CLINICAL SPECTRUM OF CRYOGLOBULINEMIC VASCULITIS BETWEEN SJÖGREN'S SYNDROME AND HCV HEPATITIS

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Background: Cryoglobulinemic vasculitis (CV) is a serious complication of Sjögren's syndrome (SS) and is closely associated with type II IgMk cryoglobulins. CV has been well documented in HCV patients without SS, and shares common features with CV in SS. So far, few studies have described the clinical picture of CV in HCV negative SS, but the number of studied patients was rather small and CV was not well defined. To better describe the clinical spectrum of CV in SS and explore the differences compared to HCV-related CV, a large cohort of well characterized patients is required.

Objectives: To study the clinical phenotype of CV in HCV-negative SS patients, in a large cohort of well characterized patients, after applying stringent classification CV criteria and in comparison with the classical CV of HCV patients.

Methods: From a total cohort of 1997 consecutive SS patients who fulfill the 2016 EULAR/ACR criteria and are followed up in 5 clinical centers ([Universities of Udine, Pisa and Athens, Harokopio and Ioannina, (UPAH)], those who fulfill the 2011 classification criteria for CV were identified and compared with matched HCV-CV patients according to age and gender. Glandular, extra-glandular manifestations and serologic features were compared between the 2 CV groups. Statistical analysis for categorical variables was performed by Fisher exact or chi-square tests and for continuous variables with t test or Mann-Whitney accordingly.

Results: Among the 1083 SS patients who have been evaluated for cryoglobulins, 114 (9.8%) were found positive. Seventy-one (6.5%) SS patients met the 2011 CV criteria while 44 patients presented with type II IgMk cryoglobulinemia without CV. Sixty nine of 71 (97%) SS related CV patients were females and 2 of 71 (3%) males. Forty eight of 71 (68%) had SS disease onset >35 and <65 years old while 14/71 (19.7%) and 9/71 (12.7%) had SS disease onset <35 and >65 years old respectively. The most common clinical manifestations of CV among SS patients were purpura (90%) followed by arthralgias (70%), fatigue (59%), Raynaud's phenomenon (48%), lymphadenopathy (31%), peripheral neuropathy (22.3%), vasculitic ulcer (11.3%) and glomerulonephritis (11.3%). Interestingly, almost 50% of SS related CV patients developed lymphoma and displayed high frequency of strong predictors including purpura, low C4 complement (88.6%) and salivary gland enlargement (SGE). Compared to HCV-CV patients, SS-CV

patients had higher frequency of sicca manifestations, SGE, fatigue, arthritis, Raynaud's phenomenon, lymphadenopathy, type II IgMk cryoglobulins and lymphoma.

Conclusion: The prevalence of cryoglobulinemia and CV among SS patients is about 10% and 6-7% respectively. SS-CV patients are mainly middle-aged females with purpura as the main clinical manifestation, and up to one half of them may develop lymphoma, which is rarer in HCV-CV. Compared to HCV-CV patients, SS patients with CV have more frequently sicca symptoms, SGE and type II IgMk cryoglobulins.

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THU0295

LOW IMMUNOGENICITY IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB: 3-YEAR RESULTS FROM THE RANDOMIZED CONTROLLED PORTION AND OPEN-LABEL FOLLOW-UP OF A PHASE 3 TRIAL

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Background: Tocilizumab (TCZ) has low immunogenicity in patients with rheumatoid arthritis.¹ The risk for immunogenicity remains to be determined in patients with giant cell arteritis (GCA) treated with TCZ. TCZ administered subcutaneously every week (QW) or every other week (Q2W) with 26-week prednisone tapering was superior to placebo (PBO) plus 26-week (PBO+26) or 52-week (PBO+52) prednisone tapering for the achievement of sustained remission in patients with GCA in the 52-week, double-blind part 1 of the GiACTA trial.² Part 2 was a 2-year open-label, long-term follow-up in which patients were treated at the investigators' discretion; part 2 treatment could include initiation/termination of TCZ QW with or without glucocorticoids or methotrexate.

Objectives: To investigate immunogenicity of TCZ QW and Q2W regimens in patients with GCA in combination with a 26-week prednisone taper regimen versus PBO+26 or PBO+52 over the course of the GiACTA study in the randomized controlled part 1 and long-term follow-up part 2.

Methods: In parts 1 and 2 combined, anti-TCZ antibodies (ADA) and corresponding pharmacokinetic (PK) parameters were assessed in serum samples taken at scheduled times at weeks 0, 8, 24, 36, 52, 76, 100, 136, and 156 or at early withdrawal. Additional assessments were made for patients who interrupted blinded TCZ treatment for ≥4 weeks in part 1 and those who withdrew from the study because of anaphylaxis/hypersensitivity. All samples were tested by screening assay, and samples that were ADA positive were further analyzed by a confirmation assay to verify specificity. If the confirmation assay was positive, 2 additional tests were performed to characterize the detected ADA: a neutralizing assay to test the neutralizing potential of ADAs and an assay to determine whether the detected ADA were of the IgE isotype. Proportions of patients in whom ADA developed were summarized for the safety population.

Results: Among evaluable patients (had baseline and ≥1 postbaseline ADA assessments and received ≥1 dose of study treatment) in part 1, ADA developed in 1 of 95 (1.1%) and 3 of 46 (6.5%) patients after TCZ QW and Q2W dosing, respectively. One of 49 (2.0%) and 1 of 47 (2.1%) in the PBO+26 and PBO+52 groups, respectively, tested positive for ADA but had not received TCZ and were considered false positives. In parts 1 and 2 combined, among 199 patients who received ≥1 dose of TCZ, 193 (97%) were evaluable (Table); TCZ-induced ADA developed in 13 of these patients (6.7%) postbaseline (4 during part 1, 9 during part 2). Of these 13 patients, 8 (4.1%) had ADA with neutralizing potential and 1 (0.5%) had IgE ADA. Most TCZ-induced ADA were transient. There was no clear impact of TCZ-induced ADA on TCZ PK (Figure). No patients with TCZ-induced ADA experienced anaphylaxis, hypersensitivity reactions, or injection site reactions, and none withdrew because of lack of efficacy.

Conclusion: In patients with GCA, treatment-induced ADA developed in a minority of patients and had no impact on TCZ PK, efficacy, or safety. The

Table. Immunogenicity in Patients Who Received TCZ (part 1 + part 2)

	Patients Who Received TCZ N = 199
Baseline	
Evaluable patients	194 (97.5)
Positive screening assay	12 (6.0)
Positive confirmation assay	6 (3.0)
Postbaseline	
Evaluable patients	193 (97.0)
Treatment-induced ADA	13 (6.7)
Characterization of ADA	
Neutralizing potential	8 (4.1)
IgE	1 (0.5)

Data are number (%) of patients based on N at baseline and on number of evaluable patients postbaseline.

immunogenicity of subcutaneous TCZ treatment was low, consistent with that observed in patients with RA.

References:

- [1] Burmester GR et al. *Ann Rheum Dis* 2017;76:1078-85.
- [2] Stone JH et al. *N Engl J Med* 2017;377:317-28.

Figure. Time-Concentration Profiles of TCZ in Part 1 by TCZ Dosing Regimen: (A) QW (B) BQW

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THU0296 PROTEIN PROFILING IN INDIVIDUALS BEFORE ONSET OF ANCA-ASSOCIATED VASCULITIS

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Background: Etiology and pathogenesis of ANCA-associated vasculitis (AAV) is multifactorial and understanding of the processes leading from a healthy immune system to autoimmunity and on to debut of symptoms in AAV is rudimentary.

Objectives: To identify inflammatory proteins related to the early processes preceding AAV development, and potential novel biomarkers, using large-scale protein analyses

Methods: The Swedish National Patient Register of in-patient care and the Swedish Cause of Death Register with discharge diagnosis from ICD-9 and -10 for AAV were co-analysed with the registers of 4 different blood biobanks to identify AAV individuals with available samples predating onset of symptom. Of the pre-AAV cases 86 (36 male, 50 female; mean age (SD); 51.9 (16.9) years) were identified with at least one plasma or serum sample (28 plasma, and 100 serum) pre-dating symptom onset (mean (SD); -4.3 (3.1) years), and 14 had 2-3 samples. Serum and plasma control samples matched for sex, age and sampling date were identified (n=198; 82 male, 116 female; mean age (SD); 51.9±15.9 years). The samples were analysed for levels of 92 proteins using proximity extension assay (OLINK inflammation panel, SciLifeLab, Uppsala, Sweden). Data were analysed using routine statistical methods, random forest and Partial Least square-discriminant analysis (PLS-DA).

Results: As previously described for the assay significant difference between plasma and serum samples were observed both in pre-AAV individuals and controls. In pre-AAV plasma samples significantly increased concentrations of interleukin (IL)-2, chemokine ligand (CCL)-4, fibroblast growth factor (FGF)21, IL-4 and CCL20 were found closer to symptom onset, (<5 years) than later (> 5 years) and compared with controls. In serum tumor necrosis factor receptor superfamily member (TNFRSF)9, CXCL9, osteoprotegerin and vascular endothelial growth factor-A were significantly increased <5 years before onset vs. later (>5 years) and compared with controls. PLS-DA

score scattered plot separated the pre-AAV individuals from healthy controls ($R^2=0.26$), with significantly increased levels of CCL23, CXCL5, and matrix metalloproteinases-1 (MMP-1), transforming growth factor- β , orosomucoid, en-rage (S100A12) and IL-7 and decreased FGF-19 level in serum. Binary logistic regression analyses comparing tertiles for these proteins confirmed significantly increased odds ratios for disease development of CCL23, CXCL5 and MMP-1. The findings were confirmed in random forest analysis where these factors were among the 20 most discriminatory factors between pre-symptomatic AAV and controls.

Conclusion: In serum samples collected years before symptom onset of AAV, proteins involved in immune system activation were increased, suggesting that the inflammatory process is initiated long before clinical manifestations of the disease appear. These findings propose the elevated proteins as novel biomarkers for disease progression.

References:

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THU0297 SERIOUS INFECTIONS IN 134 PATIENTS WITH GIANT CELL ARTERITIS WITH TOCILIZUMAB IN CLINICAL PRACTICE. FREQUENCY, TYPE AND CLINICAL ASSOCIATIONS

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Background: Infections are the most common adverse event of Tocilizumab (TCZ) in Giant Cell Arteritis (GCA). In GiACTA study (1), serious infections were observed in 7% (9.6/100 patient-years) of patients who received TCZ weekly. Randomized clinical trials (RCTs) are conducted under highly standardized design excluding some real-world patients. Therefore, adverse events may be underestimated in RCTs. In our series of real-life, serious infections occurred in 11.9% (10.6/100 patient-years) (2).

Objectives: In a wide series of GCA of clinical practice treated with TCZ, we assess the frequency, type and predisposing factors of serious infections.

Methods: Multicenter study of 134 patients diagnosed with GCA, all of them refractory to conventional therapy, treated with TCZ. Serious infection was considered when a life-threatening infection, fatal, or requiring hospitalization occurred, intravenous antibiotics were required, or the infectious process led to persistent or significant disability.

Results: 16 of 134 (11.9%, 10.6/100 patient-years) patients developed serious infections during follow-up. The most frequent infections were pneumonia (n=4), urinary tract infection (n=4), and facial herpes zoster (n=2). At TCZ onset, serious infections were more frequent in older patients (74.3±9.6 vs 72.9±8.7 years), with a longer GCA evolution (20 [4.3-45.6] vs 13 [5-29.3] months), with visual manifestations (43.75% vs 17.8%) and a higher dose of prednisone at TCZ onset (30.4±15.5 vs 21.1±16.1 mg/day) (TABLE). Presence of comorbidities were similar in both groups. 13 of the 16 patients who had infections received a dose of prednisone greater than 15mg/day (16.3/100 patient-years) compared to 3 patients under treatment with less than 15mg/day of prednisone (4.2/100 patient-years).

Conclusion: The age, GCA duration, ocular involvement and the dose of glucocorticoids, at TCZ onset, seem to be predisposing factors related to an increased risk of developing serious infections in GCA patients.