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

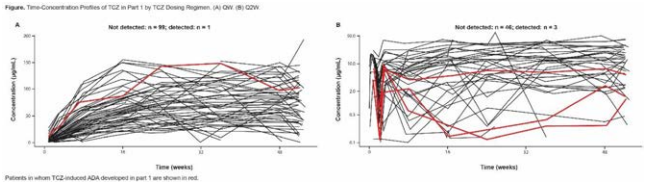
	Patients Who Received TCZ N = 199
Baseline	
Evaluable patients	194 (97.5)
Positive screening assay	12 (6.0)
Positive confirmation assay	6 (3.0)
Postbaseline	
Evaluable patients	193 (97.0)
Treatment-induced ADA	13 (6.7)
Characterizaton of ADA	
Neutralizing potential	8 (4.1)
IgE	1 (0.5)

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.



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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 carevand 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*-ß, 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:

[1] Watts et al. Ann Rheum Dis 2007;66:222-22

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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 15 mg/day (16.3/100 patient-years) compared to 3 patients under treatment with less than 15 mg/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.