center (1) and other university outpatient clinics (2). Possibly DMARD-therapy may protect against the occurrence of cytokine storm and vasculitic complications, which lead to severe courses and lethal outcomes in some of the patients. The data support the recommendation not to discontinue DMARDs for fear of COVID-19.

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POS1255 REACTOGENICITY OF SARS-COV-2 VACCINES IN PATIENTS WITH AUTOIMMUNE AND INFLAMMATORY DISEASE

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Background: Patients with autoimmune disease often require immunosuppressive medications that may increase their risk of developing severe illness from COVID-19. The importance of immunization in this population is particularly high. While the studied vaccines show efficacy in the general population, nothing is known regarding the immune response or safety profile in patients with autoimmune disease and those taking immunomodulatory medications.

Objectives: To assess the safety profile and degree of adverse events from SARS-CoV-2 vaccines in patients with autoimmune and inflammatory disease.

Methods: This study is part of a larger prospective observational study examining the immunogenicity and safety profile of the SARS-CoV-2 vaccine in patients with immune-mediated diseases taking immunomodulatory medications. Adults with an immune-mediated disease scheduled to receive either a Pfizer or Moderna SARS-COV-2 vaccine were enrolled in this study. Subjects participated in 3 study visits (pre-vaccine, dose 1 (D1) and dose 2 (D2)) where blood, for immunologic assays, and clinical data were collected. Assessments of adverse events (AE), including local and systemic symptoms and validated degree of AE severity were solicited within 7 days of receiving each vaccine dose.

Results: To date, 70 patients with autoimmune and inflammatory disease have been enrolled. Demographic and clinical characteristics are shown in Table 1. Distribution of current immunomodulatory medications included prednisone 18.6%, conventional synthetic DMARD 55.7%, targeted synthetic DMARD 4.3%, and biologic DMARD 68.5%. Almost all participants experienced an adverse event following vaccination (D1 96%, D2 100%). Following D1 AEs were generally mild (76.5%) whereas following D2 a large portion of patients experienced AEs that were moderate (47.8%) and severe (30.5%). Injection site pain was the most common AE following both doses followed by arthralgias (D1 21.6%, D2 78.2%), fever (D1 21.6%, D2 70%) and fatigue (D1 21.6%, D2 65.2%) (Figure 1).

Table 1. Demographic and Clinical Characteristics of Participants

Parameter N (%)	N=70
Age [years], mean (SD)	
Age group	48.3 ± 16.4
< 65	53 (75.7)
65+	17 (24.3)
Gender	
Female	48 (68.6)
Male	20 (38.5)
Other	2 (2.9)
Race	
White	47 (67.1)
Asian	14 (20.0)
Hispanic	8 (11.4)
Black	1 (1.4)
BMI [kg/m2], mean (SD)	25.0 ± 5.4
Immunologic Diagnosis	
Rheumatoid Arthritis	21 (30.0)
Spondyloarthritis*	21 (30.0)
Systemic Lupus Erythematous	8 (11.4)
Connective Tissue Disease, Other‡	12 (17.1)
Vasculitis	3 (4.2)
Inflammatory Bowel Disease	7 (10.0)
Autoinflammatory Syndrome	5 (7.1)
Multiple Sclerosis	2 (2.9)
IgG4 Related Disease	2 (2.9)
Disease Duration [years], mean (SD)	9.0 ± 5
Medications	
Prednisone	13 (18.6)
DMARDs	
Hydroxychloroquine	16 (22.9)
Methotrexate	15 (21.4)
Sulfasalazine	6 (8.6)
Tofacitinib	3 (4.3)
Azathioprine	2 (2.9)
Biologics	
TNF inhibitor	33 (47.1)
Rituximab	7 (10)
Abatacept	6 (8.6)
IL-23 inhibitor	2 (2.9)

* Spondyloarthritis includes Axial Spondyloarthritis and Psoriatic Arthritis. ‡ Other Connective Tissue Disease includes scleroderma, Sjogren's syndrome, polymyositis, and UCTD.

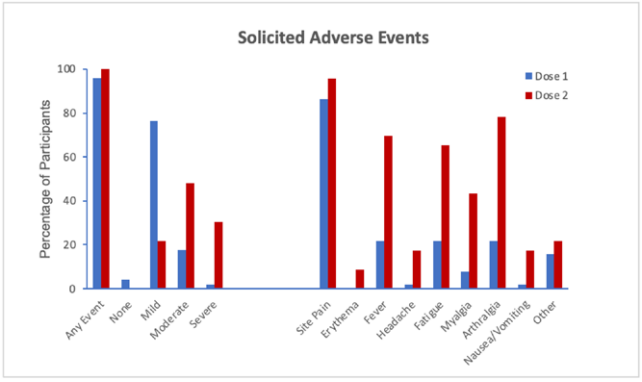

Figure 1. Solicited Local and Systemic Adverse Events. Percentage of participants who had endorsed an adverse event within 7 days of first or second dose of SARS-CoV-2 Vaccine. 'Other' symptoms included chills, blurry vision, brain fog and dizziness.

Conclusion: Patients with autoimmune and inflammatory disease experience a significant burden of adverse events following SARS-CoV-2 vaccination with both frequency and severity appearing greater than that of the reported results from the vaccine clinical trials. Several of the endorsed AEs such as fever, fatigue and arthralgias can also be commonly seen in rheumatologic diseases, mimicking flares. While SARS-CoV-2 immunization is crucial in patients with autoimmune diseases, this study demonstrates the importance of understanding the AEs experienced by this patient population to better inform patients of possible expected side effects of SARS-CoV-2 vaccination and further management in the future.

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POS1256 SINGLE DOSE TOCILIZUMAB PHARMACOKINETICS IN GLUCOCORTICOID PRE-TREATED COVID-19 PATIENTS DURING CYTOKINE STORM SYNDROME HYPERINFLAMMATORY EPISODE: LESS IS MORE

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Background: The cytokine storm syndrome (CSS) associated with COVID-19 pneumonia occurs in up to 20% of the admitted patients causing high morbidity and mortality [1]. In the COVID High-intensity Immunosuppression in Cytokine storm syndrome (CHIC) study [1] we reported that CSS patients, who despite high-dose methylprednisolone (MP) treatment still showed severe respiratory deterioration, received subsequent single dose tocilizumab (TCZ) treatment. Our clinical experience with TCZ, every 4 weeks in RA, where a pre-dose serum concentration of > 1 µg/ml is sufficient to block all interleukin (IL)-6 receptors and thereby induce and maintain clinical remission, prompted further investigation of TCZ pharmacokinetics in patients with COVID-19 CSS [1,2].
Objectives: In this pharmacokinetic study we investigated the clinical-pharmacokinetic rationale for a single TCZ dose in a subset of COVID19 induced CSS patients.
Methods: Patients with COVID-19-associated CSS, defined as rapid respiratory deterioration plus at least two biomarker elevations (C-reactive protein (CRP) >100 mg/L; ferritin >900 µg/L; D-dimers >1500 µg/L), received per protocol high-dose intravenous MP for 5 consecutive days. If the respiratory condition had not improved sufficiently, TCZ (8 mg/kg, max. 800 mg) single infusion was added on or after day 2[1]. TCZ serum samples were drawn at TCZ day 1, 3 and 10 to assess TCZ serum concentrations with a validated ELISA-method. A nonlinear-mixed effects model was developed based on all concentration time data to characterise TCZ pharmacokinetics (NONMEM). Subsequently individual pharmacokinetic parameters (AUC0-inf, Cmax, time above 1 µg/ml) were estimated and TCZ concentration-time observations were plotted against the individual predicted concentrations to visualize the complete TCZ concentration-time curve.
Results: In total, 34 patients with COVID19 induced CSS still showing clinical deterioration upon MP treatment received TCZ per protocol [mean (SD) age: 62 (12) years, 22% female, baseline mean (SD) bodyweight: 87 (17) kg, CRP: 108 (833) mmol/L, ferritin: 1653 (911) µg/L, D-dimers 4462 (7272) µg/L]. TCZ clearance was described by a homogeneous population-kinetics model yielding 87 serum samples. TCZ serum concentrations followed a biphasic course [Distribution volume 5.0 L (3.3-7.3), Area Under the Curve$_{0-\infty}$ 1st dose (682 (397-913) mg/L*days), Cmax 137 mg/L (88 – 199), half-life (linear) 3.5 days (2.3-4.1)]. In all patients, TCZ serum concentrations remained above the theoretical maximum IL-6 receptor occupancy concentration of 1 µg/ml for at least 12 days, depicted in Figure 1.

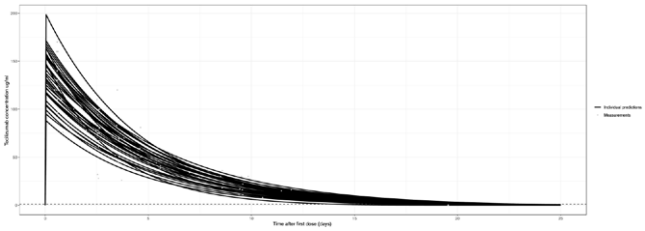

Figure 1. Predicted concentration-time profiles after single dose tocilizumab in 34 methylprednisolone pretreated patients with COVID-19 induced cytokine storm syndrome. Dashed line: maximum IL-6 receptor occupancy concentration 1 µg/ml

Conclusion: Based on our study results on the pharmacokinetics of TCZ in patients with severe COVID-19 induced CSS we conclude that the clearance of TCZ is faster compared to RA-patients at steady state. However, our observations indicate that a single dose of tocilizumab in CSS-patients is enough to cover IL-6 mediated hyperinflammation. Restricting TCZ to a single dosage can prevent overtreatment, drug shortage and saves costs, while still maintaining efficacy, as most patients will have overcome their hyperinflammatory period of the CSS after 10-14 days.
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POS1257 **HYPOGAMMAGLOBULINEMIA IS A SIGNIFICANT RISK FACTOR FOR MORTALITY IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS AND COVID-19**

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Background: The negative impact of COVID-19 in patients with ANCA associated vasculitis (AAV) and patients on rituximab (RTX) treatment have been reported (1). Risk factors for severe course of COVID-19 and increased mortality in these patients are unclear.
Objectives: To evaluate the course of COVID-19 in our AAV cohort and identifying risk factors for mortality.
Methods: Patients with AAV who were classified according to CHCC and whose scheduled last visit were after December 2019 were screened and evaluated for COVID-19 either by phone call or in the clinic. Records of patients with a history of hospital admission due to COVID-19 were evaluated. Cumulative clinical findings and treatment history were noted. Hypogammaglobulinemia (hIgG) was defined as IgG level below 700 mg/dl. All inpatients with a diagnosis of COVID-19 were screened for hIgG and IVIG was administered if necessary.
Results: Eighty-nine patients (47.2% female, mean age 56 + 12.5 (28-81)) were included into the study. The diagnosis was GPA in 56 (62.9%) and MPA in 33 (37.1%) patients. Mean follow up time was 91 + 53.4 (26-272) months. Anti-PR3 and anti-MPO were positive in 46 (51.7%) and 32 (35.9%) patients, respectively. Lower respiratory tract (LRT) involvement was present in 72 (80.9%) and 10 patients had a history of diffuse alveolar haemorrhage (DAH). Sixty-one patients (68.2%) had a history of rapidly progressive glomerulonephritis (RPGN) and 21 (23.6%) had peripheral nervous system (PNS) involvement.
Fifteen (16.9%) patients had COVID-19; 14 of them were PCR positive, one patient had symptoms and thorax CT findings compatible with COVID-19. Pulmonary infiltrates were observed in 13 patients (86.7%); 9 (60%) had severe pneumonia. Twelve patients (85.7%) were hospitalized, 6 patients (42.9%) needed ICU admission and 5 patients (35.7%) died. Tocilizumab and anakinra for hyperinflammation during COVID-19 were used in 1 (6.7%) and 4 (26.7%) patients, respectively.
Four out of five deceased patients (3 on RTX treatment, 1 with renal transplant) were in remission at the time of COVID-19. COVID-19 was detected in a patient with disease flare and DAH, during treatment with high dose steroids and plasmapheresis. hIgG was detected in all deceased patients from COVID-19 during hospital admission (mean IgG: 495±113.2 mg/dL).

Table 1. Comparison of risk factors for CI and mortality in patients with AAV

	COVID-19 (n=15)	Non-infected (n=74)	p	OR	Death (n=5)	Survive (n=10)	p2	OR2
Age	53.4±11.9	56.6±12.6	NS		51.2±12.6	54.6±12.1	NS	
Sex (female)	6	35	NS		4	2	0.036	14 (0.9-207)
LRT Involvement	14	58	NS		5	9	NS	
DAH	4	6	0.038	4.1 (1-16.9)	1	3	NS	
RPGN	15	46	0.004	8.5 (1-68.4)	5	7	NS	
PNS involvement	3	18	NS		3	0	0.005	9 (1.4 - 57)
RTX treatment	10	33	NS		3	7	NS	
hIgG in outpatient visits	6	7	0.02	6.3 (1.8-23.3)	4	2	0.02	16 (1.5-234)
hIgG during hospitalization due to CI	-	-	-	-	5	4	0.025	2.5 (1.2-5.4)
Flares≥1	7	25	NS		4	3	NS	
Chronic Renal Insufficiency	7	22	NS		4	3	NS	