Methods: The patients, fulfilling the International Criteria for Behçet's disease (ICBD), and healthy controls, of a comparable age, were evaluated in the Rheumatology and Urology Clinics. The demographic and clinical data was collected. Disease activity of the patients was assessed using Behçet's Syndrome Activity Score (BSAS). For both groups, the sexual function and the psychological status were evaluated using the International Index of Erectile Functions (IIEF-5) and the Beck Depression Inventory (BDI), respectively. Spearman's rho, Chi-Square and Mann-Whitney U tests were used as appropriated.

Results: The number of BD patients was 26 and that of the controls was 27. The mean age of the patients was 36 ± 7.4 and that of controls was 40.9 ± 5.2 . Though BD patients were younger in age they exhibited significantly lower scores in sexual function, and scored higher in depression as illustrated in **Table 1**.

Abstract THU308 – Table 1. Demographic and clinical data of the participants

	Patients (n=26)	Controls (n=27)	P value
Smoking, n (%)	8 (30.8%)	4 (14.8%)	0.4
Disease duration (years), mean $\pm$ SD	4.2 $\pm$ 1.9	NA	NA
Erectile dysfunction (IIEF-5 score), median (Interquartile range)	15 (9-20)	20 (20-25)	<0.001*
Depression score (Beck questionnaire), median (Interquartile range)	13 (9-18)	9 (7-14)	0.039*

There were no associations between the disease duration, smoking status or different clinical phenotypes and the sexual or psychological functions. However, there was an inverse relationship between BSAS and the sexual function ($\rho = -0.443$, $p = 0.024$). The duration of corticosteroids intake was negatively correlating with the sexual function ($\rho = -0.604$, $p = .001$) as well. The depression scores correlated significantly with the presence of inflammatory back pain ($\rho = .413$, $p = .036$).

There was no association between the severity of sexual dysfunction and that of depression. The patients showed different degrees of depression, and there was a tendency towards increased rates of erectile dysfunction in all groups as shown in **Table 2**.

Abstract THU308 – Table 2. Correlation of IIEF-5 and BDI

Sexual function (IIEF-5 score)	Beck Depression Inventory (BDI)			Total	P value
	Minimal (n=14)	Mild (n=7)	Moderate (n=5)		
No ED or Mild ED ≥ 17 , n (%)	4 (28.6%)	3 (42.9%)	2 (40%)	9	0.78
ED ≤ 16 , n (%)	10 (71.4%)	4 (57.1%)	3 (60%)	17	

ED; erectile dysfunction.

Conclusion: BD has a negative impact on men's psychological state and sexual function. Severe disease states, evident in the long duration of corticosteroids use and the high activity scores, are linked to sexual dysfunction.

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THU0309

NONLINEAR PHARMACOKINETICS OF RITUXIMAB IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS

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Background: Rituximab (RTX) was approved in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV).

Objectives: To describe the pharmacokinetics of rituximab in AAV patients and to explore its sources of variability

Methods: Rituximab pharmacokinetics was described in 92 AAV patients from the RAVE trial (rituximab for ANCA-associated vasculitis) using a population modeling approach. A semi-mechanistic model including a latent target antigen turnover allowed the estimation of specific target-mediated elimination of rituximab in addition to its non-specific elimination. Sex, body surface area (BSA), BVAS/WG score, and status newly diagnosed on pharmacokinetic parameters were investigated as covariates.

Results: A two compartments model including target mediated elimination best described rituximab pharmacokinetics. The mean (interindividual standard deviation) estimated central volume of distribution was 3.06 L (2.61%), systemic clearance was 0.135 L days⁻¹ (6.43%), and target-mediated elimination rate constant was 19.13×10^{-6} nmol⁻¹ days⁻¹ (fixed to 0). The initial activity of the disease was higher in male than in female ($p = 4.09 \times 10^{-14}$), and in patients newly diagnosed at inclusion ($p = 7.91 \times 10^{-5}$). Moreover, systemic clearance was slightly lower in granulomatosis with polyangiitis group than in other AAV groups ($p = 3.6 \times 10^{-3}$). Neither BVAS/WG score nor BSA were significant covariates in a multivariate analysis.

Conclusion: We report a nonlinear target-mediated elimination of rituximab in AAV patients. Granulomatosis with polyangiitis patients have a lower global clearance of rituximab than other AAV groups. Our study not support the utility of BSA based individualized dosing protocols, as previously reported (1).

REFERENCE:

- [1] Cornec D, *et al.* Pharmacokinetics of rituximab and clinical outcomes in patients with anti-neutrophil cytoplasmic antibody associated vasculitis. *Rheumatology*. 2018;57:639-50.

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THU0310

OPTIMAL INITIAL DOSE OF GLUCOCORTICOID FOR ELDERLY-ONSET ANCA ASSOCIATED VASCULITIS: SAFTY OUTCOME ANALYSIS OF TWO NATIONWIDE, PROSPECTIVE, INCEPTION COHORT STUDIES

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Background: Glucocorticoid (GC) is still the mainstay of treatment for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) while GC use, disease severity, and older age are risk factors for accrual of damage and infection in AAV^{1,2}.

Objectives: To explore optimal initial dose of GC for patients with elderly-onset AAV based on safety outcome analysis using data from two nationwide prospective inception cohort studies (RemIT-JAV and RemIT-JAV-RPGN).

Methods: RemIT-JAV and RemIT-JAV-RPGN enrolled consecutive patients with newly diagnosed AAV fulfilling the criteria for primary systemic vasculitis as proposed by the European Medicines Agency algorithm and requiring immunosuppressive treatment. From the cohort studies, elderly-onset (≥ 65 years) patients with microscopic polyangiitis and granulomatosis with polyangiitis, classified as generalized or severe disease type according to the European Vasculitis Study Group-defined disease severity, were enrolled in this analysis. The primary outcome measures were Vasculitis Damage Index (VDI) at 24th month and serious infections during 2 years after starting treatment for AAV. The patients were divided into three groups based on initial dose of GC: high-dose (HD) group, prednisolone (PSL) ≥ 0.8 mg/kg/day; medium-dose group (MD), $0.6 \leq$ PSL < 0.8 mg/kg/day; low-dose (LD) group, PSL < 0.6 mg/kg/day. The VDI were classified into treatment-related VDI¹⁾ and disease-related VDI

(excluding treatment-related VDI from total VDI). We evaluated associations between initial GC dose and the primary outcomes.

Results: Of 477 patients registered in the original cohort studies, 161 patients were enrolled in the present study. Mean age ($\pm$ SD) were 74 ($\pm$ 5) in HD group, 74 ($\pm$ 5) in MD group, and 78 ($\pm$ 6) years in LD group, respectively. There was no significant difference in sex, disease severity, type of ANCA, C-reactive protein levels at baseline, Birmingham Vasculitis Activity Score at baseline, remission rates, and relapse rates. HD group exhibited significantly lower creatinine levels at baseline than MD and LD groups (216 ± 207 in HD, 339 ± 263 in MD, 331 ± 301 μ mol/L in LD, respectively; $p = 0.0012$). Proportion of concomitant cyclophosphamide use during 90 days after starting treatment for AAV decreased (58% in HD, 36% in MD, and 15% in LD, respectively; $p < 0.0001$) while disease activity-related VDI at 24th month increased (2.09 ± 1.39 in HD, 2.54 ± 1.16 in MD, and 2.83 ± 1.60 in LD, respectively; $p = 0.018$) as the initial GC dose went down. HD group developed serious infections more frequently than MD and LD groups (25/65 [38%] in HD, 10/50 [20%] in MD, 9/46 [20%], respectively; $p = 0.033$).

Conclusion: Based on safety outcome analysis, $0.6 \leq \text{PSL} < 0.8$ mg/kg/day might be optimal initial dose of GC for treatment of elderly-onset patients with AAV.

REFERENCES:

- [1] Robson J, et al. *Rheumatology* (Oxford). 2015 Mar;54(3):471-81.
- [2] Watanabe-Imai K, et al. *Mod Rheumatol*. 2017 Jul;27(4):646-651.

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THU0311

PERSISTENT LOW-GRADE VASCULAR INFLAMMATION IN LARGE VESSEL VASCULITIS: A LONGITUDINAL STUDY USING FULLY INTEGRATED 18F-FDG PET/MR

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Background: Persistent low-grade vascular inflammation in large vessel vasculitis (LVV) treated patients could represent the expression of persistent subclinical disease activity or post-inflammatory vascular remodelling. Whether these findings have any impact on future vascular outcomes is still an unmet need¹.

Objectives: To evaluate the frequency and evolution of the low-grade vascular inflammation using a fully integrated 18F-FDG PET/MR in a longitudinally followed cohort of LVV patients.

Methods: All consecutive patients with LVV who underwent at least 2 PET/MR scans (median time 9[6] months) between January 2015 and January 2019 were included. For each scan vessel's metabolic activity was assessed using the Meller's grading and the standard uptake value². Low-grade inflammation was defined as Meller 1 and 2 (inferior or equal to liver), as previously reported. Demographic and clinical data, as well as disease remission or flares, were recorded and compared to vascular metabolic activity.

Results: In total, 107 PET scans were performed (from min. 2 scans to max. 5 scans per patient), mainly during follow-up (78.8%) in 33 LVV patients (72.7% GCA, 27.3% TAK), predominantly female (84.8%), with a regular BMI ($24.1[5.3]$) and with a long-standing disease ($30[29]$ months). At PET examination, low-grade metabolic activity was reported in 60% of the cases (86.4% GCA and 13.6% TAK), while complete remission in 15% and highly pathological in 25%. Comparing patients with low-grade vascular inflammation to those with complete remission (Meller 0), they resulted significantly older ($64[12]$ vs $57[33]$ years, $p=0.005$), with a lower disease duration ($26.5[21.4]$ vs $52.5[34.8]$ months, $p=0.001$) and with higher daily prednisone dosage, but without significance ($5[7.5]$ vs $2.5[8.75]$, $p=0.096$). No significant differences were noted in acute phase reactants and type of treatment. Moreover, when compared to those with high metabolic activity (Meller 3), patients with low-grade inflammation resulted significantly older ($64[12]$ vs $62[25]$ years, $p=0.025$), with a lower disease duration ($26.5[21.4]$ vs $33[46]$ months, $p=0.041$), lower CRP level, but without significance ($3.05[5.92]$ vs $10.35[13.75]$, $p=0.069$). Clinical remission, before PET examination, was registered in 55.6% of patients with Meller 3 activity, significantly lower compared to those with Meller 1 +2 (87.5%, $p=0.002$). Steroids and immunosuppressants tapering rate did not differ between patients with low-grade metabolic activity and those without activity.

Among all patients with low-grade vascular inflammation, 60% underwent to steroids or immunosuppressants tapering. At the subsequent PET examination, a persistence/worsening of metabolic activity was found in 88.9% of them. Change or increase of the treatment regimen led to an improvement (complete remission) in 58.9% of the cases. Low-grade metabolic activity was associated with a significant increased risk of worsening/flare at the subsequent PET examination (RR $5.29[1.87-16.11]$, $p=0.002$).

Conclusion: Low-grade vascular inflammation at PET examination is a common feature in LVV treated patients, especially GCA. It is significantly associated with an older age, lower disease duration and clinical remission. However, steroids or immunosuppressants tapering in these patients is associated with an increased risk of worsening/flare. Further research is urgently needed to address this issue.

REFERENCES:

- [1] DeJaco C, et al. *Ann Rheum Dis* 2018.
- [2] Meller J, et al. *Eur. J. Nucl. Med. Mol. Imaging*, 2003.

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THU0312

ADVENTITIAL FIBROBLAST, AN IMPORTANT PLAYER IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a systemic vasculitis affecting large vessels. The diagnosis is based on the temporal artery biopsy (TAB) which shows a segmental and focal arterial infiltration composed of CD4 T cells and macrophages. It is accompanied by a destruction of the internal elastic layer of the media and a hyperplasia of the intima by proliferation of myofibroblasts (Weyand). The origin of these myofibroblasts is controversial (Ly). Evidences suggest the activation of adventitial fibroblasts into myofibroblasts and their migration into the intima (Stenmark).

Objectives: The objective of this study was to determine whether adventitial fibroblasts migrate to the intima and thereby contribute to intimal hyperplasia during CGA.

Methods: Arterial sections from TAB of patients with GCA (n=24) and control subjects (n=24) were analyzed. Immunohistochemical analysis was