(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.

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Disclosure of Interests: Keiji Ohashi: None declared, KENEI SADA Speakers bureau: Ken-Ei Sada received speaker honoraria from Chugai, Yosuke ASANO: None declared, Keigo Hayashi: None declared, Sumie Hiramatsu Asano: None declared, Yuriko Yamamura: None declared, Michiko Morishita: None declared, Haruki Watanabe: None declared, Mariko Narazaki: None declared, Yoshinori Matsumoto: None declared, Tomoko Kawabata: None declared, Jun Wada Grant/research support from: Jun Wada received grant support from Astellas, Bayer, Chugai, Daiichi Sankyo, Kissei, Kyowa Hakko Kirin, MSD, Otsuka, Teijin, Torii, Pfizer, Takeda, and Taisho Toyama., Speakers bureau: Jun Wada received speaker honoraria from Astellas, Boehringer Ingelheim, Novartis, and Tanabe Mitsubishi., masayoshi harigai Grant/research support from: Tokyo Women's Medical University (TWMU) has received unrestricted research grants for

Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases from Ayumi Pharmaceutical Co. Ltd., Bristol Meyers Squib, Chugai Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp., and with which TWMU paid the salary of MH. MH has also received research grants from AbbVie Japan GK, Eisai Co. Ltd., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd., Hirofumi Makino Consultant for: Hirofumi Makino is a consultant for AbbVie, Boehringer-Ingelheim and Teijin Pharma., Speakers bureau: Hirofumi Makino receives speaker honoraria from Boehringer-Ingelheim (less than \$10,000 each).

DOI: 10.1136/annrheumdis-2019-eular.3420

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.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.7151

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

performed using antibodies directed against fibroblasts (CD90, vimentin), myofibroblasts (alpha smooth muscle actin {ASMA}) and vascular smooth muscle cells (desmin). Staining of prolyl-4-hydroxylase (P4H) and myosin were also performed. Stainings were quantified using the ODPviewer® software (Kamax Innovative System, France) by two double-blind observers. Moreover, co-expression of CD90 with different stainings (ASMA, myosin and P4H) was also performed. Cells in culture were identified by immunocytochemistry using anti-CD90 and markers of activity such as myosin and P4H. Functional assays were performed using culture cells obtained from GCA patients' BATs (n=4) and controls (n=4). The BATs were dissected to separate the adventitia from the other two layers. Each dissected fragment was seeded separately. The proliferation was studied using a bromodeoxyuridine incorporation test under different conditions: DMEM, fetal calf serum (FCS), PDGF and supernatants of cells in culture. The study of migration was performed using a scratch test under the same conditions.

Results: CD90 was significantly higher in GCA than controls in adventitia and intima. Vimentin and ASMA were significantly higher in the 3 tunics of patients with GCA. Expression of desmin was only present in the media for both groups with no significant difference. P4H was present in adventice significant differences between both groups. The adventitial and intimal CD90+ cells co-expressed P4H, ASMA and myosin more importantly during GCA. Cultured cells from BATs' adventices expressed CD90 and did not express desmin. These cells had a greater myosin staining during GCA and had an increased proliferation ability during GCA in the presence of FCS, PDGF and fibroblast supernatants of control or GCA patients. The migration rates of these cells were also significantly increased during GCA in the presence of FCS or PDGF.

Conclusion: Vascular remodeling during GCA would start in the adventitial layer with a key role of fibroblasts. Adventitial fibroblasts could be activated into myofibroblasts and acquire proliferative and migratory abilities. They would participate in the intimal hyperplasia, responsible for ischemic complications. Their inhibition could be a therapeutic way to limit these complications. The activating signal of adventitial fibroblasts into myofibroblasts is not yet known during GCA and requires further studies.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6138

THU0313 COMPARATIVE STUDY OF CLINICAL, ANALYTICAL AND VASCULAR 18F-FDG UPTAKE EVOLUTION IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH METHOTREXATE VS TOCILIZUMAB

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Background: Glucocorticoids remain to be the cornerstone therapy in giant cell arteritis (GCA). However, relapses are common when the prednisone dose is tapered. Thus, additional therapies are required in relapsing GCA. The most widely used conventional immunosuppressive drug is methotrexate (MTX) which efficacy is modest. Consequently, in some cases biological therapy is needed. Among them, the most frequently used is the recombinant humanized anti-IL6 receptor antibody tocilizumab (TCZ).¹

Objectives: To compare clinical evolution, normalization of acute phase reactants and normalization of vascular ¹⁸F-FDG uptake assessed by PET/CT in patients with GCA treated with MTX vs TCZ.

Methods: Comparative multicentric study of 23 patients with GCA treated with MTX vs 36 patients with GCA treated with TCZ who had a baseline and follow-up PET/CT scan. We assessed clinical improvement (no improvement/partial/complete), normalization of acute phase reactants (CRP ≤ 0.5mg/dL and/or ESR ≤ 20 mm/1st hour) and reduction of ¹⁸F-FDG uptake in PET/CT (no reduction/partial/complete normalization). Images were evaluated qualitatively by experienced nuclear medicine physicians. Prednisone tapering was also assessed. Statistical analysis was performed with SPSS. Student's t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher's exact test for categorical variables as appropriate.

Results: We included 23 patients with GCA treated with MTX (20 women/3 men); mean age 65.6 ± 7.9 years; and 36 patients treated with TCZ (27 women/9 men); mean age 67.5 ± 8.3 years. Clinical, analytical and vascular ¹⁸F-FDG uptake evolution is shown in the TABLE. After one year of treatment, the percentage of patients who experienced complete clinical improvement was higher in those who received TCZ (88.9% vs 44.4%; p=0.003). Normalization of acute phase reactants was also more frequent in patients who received TCZ (92.6% vs 47.6%; p=0.001). In regard with reduction of vascular ¹⁸F-FDG uptake, complete normalization was only achieved in 25% of patients who received TCZ and 14.3% of those who received MTX.

Conclusion: Patients with GCA who received TCZ experienced a more rapid and effective clinical and analytical improvement than patients who received MTX. Besides, prednisone tapering was quicker in patients with TCZ. However, no significant differences were found in complete normalization of ¹⁸F-FDG vascular uptake between both treatments.

Abstract THU0313 –Table 1.

TABLE

	MTX (n=23)	TCZ (n=36)	P
Age, mean ± DS	65.6 ± 7.9	67.5 ± 8.3	0.39
Sex (woman), n (%)	20 (87.0)	27 (77.1)	0.50
Complete clinical improvement, n/N (%)			
- 6 months	9/23 (39.1)	28/35 (80.0)	0.002
- 12 months	8/18 (44.4)	24/27 (88.9)	0.003
- 18 months	7/11 (63.6)	21/22 (95.4)	0.03
- 24 months	7/9 (77.8)	17/18 (94.4)	0.25
Normalization of ESR and/or CRP, n/N (%)			
- 6 months	6/23 (26.1)	30/35 (85.7)	< 0.01
- 12 months	10/21 (47.6)	25/27 (92.6)	< 0.01
- 18 months	10/11 (90.9)	23/23 (100.0)	0.32
- 24 months	9/9 (100.0)	19/19 (100.0)	0.99
Normalization of ¹⁸F-FDG PET/CT, n/N (%)			
- 6 months	0/11 (0.0)	0/8 (0.0)	0.99
- 12 months	0/14 (0.0)	3/13 (23.0)	0.10
- 18 months	0/5 (0.0)	3/11 (27.3)	0.51
- 24 months	1/7 (14.3)	1/4 (25.0)	0.99
Dose of Prednisone (mg/day), median [IQR]			
- 6 months	7.5 [5.0-15.0]	5.0 [0.3-5.0]	< 0.01
- 12 months	5.0 [5.0-10.0]	0.0 [0.0-5.0]	< 0.01
- 18 months	5.0 [3.0-6.0]	0.0 [0.0-3.3]	0.03
- 24 months	2.5 [0.0-3.0]	0.0 [0.0-0.0]	0.07

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Disclosure of Interests: D. Prieto-Peña: None declared, Monica Calderón-Goercke: None declared, Javier Loricera: None declared, J. Narváez Consultant for: Bristol-Myers Squibb, Elena Aurrecochea: None declared, Ignacio Villa-Blanco: None declared, Santos Castañeda Consultant for: Amgen, BMS, Lilly, MSD, Roche, Sanofi, UCB, Catalina Gomez-Arango: None declared, ANTONIO MERA VARELA: None declared, Eva Perez-Pampín: None declared, Vicente Aldasoro: None declared, Noelia Alvarez-Rivas: None declared, Nagore Fernández-Llanio: None declared, María Álvarez del Buero: None declared, Luisa Marena Rojas: None declared, Francisca Sivera: None declared, Eva Galindez: None declared, Roser Solans-Laqué: None declared, Susana Romero-Yuste: None declared, Isabel Martínez-Rodríguez: None declared, Jose Ignacio Banzo: None declared, Miguel A González-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD,