kidney cancer (HR 1.60 [95%CI 1.15-2.23]), sarcoma (HR 2.14 [95%CI 1.41-3.24]), acute-leukemia (HR 1.81 [95%CI 1.06-3.07]), chronic-leukemia (HR 1.82 [95%CI 1.19-2.77]), Hodgkin's lymphoma (HR 2.42 [95%CI 1.12-5.20]), non-Hodgkin's lymphoma (HR 1.66 [95%CI 1.21-2.29]) and multiple myeloma (HR 2.40 [95%CI 1.63-3.53]) (Table 1). The time (mean [months] $\pm$ SD) to the diagnosis of any malignancy was significantly shorter in GCA patients (48.6 ± 41.3) compared to controls (58.1 ± 43.6 ; $p < 0.001$).

Figure 1. Kaplan-Meier cancer-free survival curve

Conclusion: GCA patients are at increased risk for sarcoma, kidney cancer, hematological malignancies and overall malignancies compared to age-and-sex matched controls from the general population.

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OP0144

EFFECT OF TOCILIZUMAB ON VASCULAR INFLAMMATION BY ¹⁸F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY: A PROSPECTIVE, LONGITUDINAL STUDY

K. A. Quinn^{1,2}, H. Dashora¹, M. Ahlman¹, P. Grayson¹. ¹National Institutes of Health, Bethesda, United States of America; ²MedStar Georgetown University Hospital, Washington, DC, United States of America

Background: Two randomized controlled trials have demonstrated clinical efficacy of tocilizumab for the treatment of giant cell arteritis (GCA)(1, 2). In these trials, clinical and laboratory measures were used to define the outcome measures. The direct effect of tocilizumab on vascular inflammation remains poorly characterized.

Objectives: To prospectively evaluate vascular inflammation as measured by ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography (PET) in a longitudinal cohort of patients with GCA treated with tocilizumab over a several year follow-up period.

Methods: Patients with GCA were recruited into a prospective, observational cohort. All patients fulfilled modified 1990 American College of Rheumatology (ACR) Classification Criteria for GCA. All patients underwent FDG-PET computed tomography (CT) prior to initiation of tocilizumab. A single reader reviewed all PET scans, blinded to clinical data. Qualitative assessment of FDG uptake relative to liver uptake by visual assessment (scale 0-3) was assessed in 9 arterial territories. A summary score, PET Vascular Activity Score (PETVAS), was calculated (scale 0-27).

Patients underwent imaging at 6-12 month intervals per a standardized imaging protocol. In a subset of patients in whom tocilizumab was discontinued due to established remission, a repeat FDG-PET scan was obtained within 6 months of drug discontinuation.

Change in PET activity over time was measured by linear regression. PET activity during established remission was compared to PET activity after discontinuation of tocilizumab. For some patients, tocilizumab was added to the existing treatment regimen without a substantive change in concomitant glucocorticoid dose. In a secondary analysis, patients were stratified by prednisone dosing (high dose prednisone >10mg/day prednisone, low dose prednisone $\leq$ 10mg/day prednisone during the imaging interval) to determine if tocilizumab had an effect on vascular inflammation independent of glucocorticoids.

Results: 22 patients were included in the study. All patients had clinically active disease at baseline with median baseline PETVAS 24.5 (23-27). There was a significant reduction in PETVAS over 2 years follow up ($p < 0.01$ for linear trend) (Figure). Of note, there was continued progressive improvement in PETVAS in both year 1 and year 2 of treatment. Eight patients received concomitant high dose glucocorticoids and 14 patients remained on low dose glucocorticoids with the addition of tocilizumab. In patients who only received low dose prednisone, significant reduction in PETVAS was still observed with addition of tocilizumab (PETVAS 25.5 to 19.5, $p = 0.04$). In a subset of 5 patients who discontinued tocilizumab due to established remission [median PETVAS 19 (17.5-22) at time of remission], a repeat FDG-PET scan within 6 months after treatment discontinuation showed worsening PET activity in 4 out of 5 patients [median PETVAS 23 (20-23)]. Two of these patients subsequently experienced a clinical disease relapse.

Conclusion: Tocilizumab was associated with improved vascular inflammation as assessed by FDG-PET. There was continued improvement of vascular inflammation at both year 1 and year 2 of treatment, and early evidence suggests a rebound of vascular inflammation when tocilizumab was discontinued. These data provide rationale for long-term tocilizumab therapy in patients with GCA and for consideration of FDG-PET as an outcome measure in future clinical trials.

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PET Activity vs. Elapsed Time on Tocilizumab

Figure. XXX

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OP0145

MALIGNANCY IN ANCA-ASSOCIATED VASCULITIS AND POLYARTERITIS NODOSA: AN AUSTRALIAN POPULATION-BASED STUDY

J. Tieu^{1,2,3,4}, S. Lester^{1,2}, W. Raymond⁵, H. Keen^{5,6}, C. Hill^{1,2,4}, J. Nossent^{5,7}. ¹Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, Australia; ²Basil Hetzel Institute, Adelaide, Australia; ³Lyell McEwin Hospital, Adelaide, Australia; ⁴The Queen Elizabeth Hospital, Adelaide, Australia; ⁵University of Western Australia, Rheumatology, Perth, Australia; ⁶Fiona Stanley Hospital, Rheumatology Dept, Perth, Australia; ⁷Sir Charles Gairdner Hospital, Rheumatology Dept, Perth, Australia

Background: The increased risk of malignancy in patients with ANCA-associated vasculitis (AAV) and polyarteritis nodosa (PAN) has been attributed to late

treatment related effects, with non-melanoma skin and genitourinary cancers most frequently reported in European studies^{1,2,3}. Malignancy has not been examined in patients with AAV/PAN in Australia, where environmental factors may influence risk.

Objectives: To determine the risk and timing of incident cancer in Western Australian (WA) AAV/PAN patients compared to controls.

Methods: Patients and controls were ascertained through the WA Hospital Morbidity Data collection System (HMDS). Administrative hospitalisation data were linked with the WA cancer and death registries. Data was available between 1980-2015. Patients were classified into two sub-groups using International Classification of Disease (ICD) -9 and/or -10 codes: (1) GPA/MPA- granulomatosis with polyangiitis (GPA)/microscopic polyangiitis (MPA), and (2) other-AAV/PAN-eosinophilic granulomatosis with polyangiitis (EGPA), PAN, and other patients with any AAV or PAN where more specific ICD-10 coding was not available. Controls were age, sex and temporally matched (at patient diagnosis date) and had no rheumatological diagnosis. Patients and controls with prior cancer were excluded from the analysis.

Spline-based estimation of time-varying hazard ratios (HR) for incident cancer in patients vs controls was performed using the Stata library *stpm2*⁴. Results for cause-specific models, which treated deaths in patients without cancer as censored, were confirmed using models treating death as a competing risk. The risk of specific cancers was analysed by Cox regression.

Results: The analysis included 391 patients (165 GPA/MPA, 217 other-AAV/PAN) and 4913 controls, with 86 incident cancers (over 3556.7 person-years) observed in patients and 1119 (over 64997.0 person-years) in controls. Patients and controls were well matched for age (mean $\pm$ standard deviation GPA/MPA: 55 $\pm$ 18 years, other AAV/PAN: 59 $\pm$ 17 years, controls 57 $\pm$ 16 years), and sex (female: GPA/MPA 48%, other AAV/PAN 46%, controls 46%).

Incident cancer risk and timing differed between the two patient subgroups (Figure 1). The risk of incident cancer in GPA/MPA patients, compared to controls, increased with disease duration, whilst other-AAV/PAN patients had a greater risk within the first two years of diagnosis, but a similar risk to controls in the longer term.

By specific cancers, GPA/MPA patients had an increased risk of skin cancers (excluding squamous and basal cell carcinomas): hazard ratio (HR) 2.71 95% confidence interval (CI) 1.55 – 4.74, and genitourinary cancers: HR 3.64, 95% CI 1.58, 8.39, which was not observed in other-AAV/PAN patients. While there was trend for an overall increase in haematological cancers, this was inconclusive.

Conclusion: Incident cancer risk, driven by skin and genitourinary cancers, increased with disease duration in GPA/MPA patients, consistent with previous studies, suggestive of a treatment related effect. In contrast, cancer was more frequently observed early after diagnosis in other-AAV/PAN patients. Our findings suggest that vigilance for incident cancers is required for all patients with AAV and PAN after diagnosis and in long term management, considering distinct periods of greater risk by disease subgroup.

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Figure 1: Incident Cancer Risk

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OP0146

LONG TERM OUTCOME AND PROGNOSIS FACTORS OF ISOLATED AORTITIS

Y. Ferfar¹, S. Morinet², O. Espitia³, C. Agard³, M. Vautier¹, C. Comarmond¹, A. C. Desbois¹, F. Domont¹, M. Resche-Rigon², P. Cacoub¹, L. Biard², D. Saadoun¹. ¹University Hospitals Pitié Salpêtrière - Charles Foix, Paris, France; ²Hospital Saint-Louis Ap-Hp, Paris, France; ³Chu Nantes, Nantes, France

Background: Aortitis is a group of disorders characterized by the inflammation of the aorta. The most common causes of aortitis are the large-vessel vasculitis i.e. giant cell arteritis (GCA) and Takayasu arteritis (TA). However, aortitis may be isolated. Because of the wide variation in the course of aortitis, predicting outcome is challenging. The optimal management strategy of isolated aortitis (IA) is still unclear as IA is poorly defined, with data consisting of small retrospective and case control studies.

Objectives: To assess the long-term outcome and prognosis factors for vascular complications in patients with isolated aortitis.

Methods: Retrospective multicenter study of 353 patients with non-infectious aortitis including 136 giant cell arteritis (GCA), 96 Takayasu arteritis (TA) and 73 isolated aortitis (IA). Factors associated with event-free survival, vascular event-free survival and revascularization-free survival were assessed. Risk factors for vascular complications were identified in multivariate analysis.

Results: After a median follow up of 52 months, vascular complications were observed in 32.3 %, revascularization in 30 % and death in 7.6%. The 5-year cumulative incidence of vascular complications was 58% (41; 71), 20% (13; 29), and 19 % (11; 28) in IA, GCA and TA, respectively. In multivariate analysis, IA [HR, 1.85 (1.19 to 2.88), $p=0.017$] and male gender [1.77 (1.26 to 2.49), $p<0.0001$] were independently associated with vascular events. The 5-year surgery-free survival was 45% (31; 65), 71% (62; 81) and 76% (68; 86) in IA, TA and GCA, respectively.

Conclusion: IA has a worse vascular prognosis than GCA and TA. Sixty percent of IA patients will experience a vascular complication within 5 years from diagnosis.

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OP0147

MEASUREMENT OF FLOW VELOCITIES OF THE CENTRAL RETINAL ARTERY IN PATIENTS WITH GIANT CELL ARTERITIS WITH VISUAL SYMPTOMS AND CONTROLS

L.C. Burg¹, P. Brossart², K. I. Reinking³, R. P. Finger³, C. Behning⁴, V. S. Schäfer¹. ¹Clinic for Internal Medicine III, University Hospital Bonn, Rheumatology, Bonn, Germany; ²Clinic for Internal Medicine III, University Hospital Bonn, Oncology, Haematology and Rheumatology, Bonn, Germany; ³Clinic for Ophthalmology, University Hospital Bonn, Ophthalmology, Bonn, Germany; ⁴University Hospital Bonn, Institute for Medical Biometry, Informatics and Epidemiology, Bonn, Germany

Background: Giant cell arteritis (GCA) is the most common form of systemic vasculitis in patients aged 50 years and older.¹ Visual symptoms such as amaurosis, diplopia, temporary or permanent visual field loss secondary to optic nerve ischemia are common manifestations.² The value of vascular ultrasound of extra-ocular vessels in diagnosing GCA is well established.³ However, the role of transocular ultrasound of the central retinal artery in GCA patients has not yet been established.

Objectives: To identify changes in flow velocities of the central retinal artery in GCA patients with visual symptoms and controls with transocular high resolution ultrasound.

Methods: Prospective analysis of GCA patients with visual symptoms and controls. Ultrasound of the central retinal artery was performed in 18 newly diagnosed consecutive GCA patients with visual symptoms (GCA-group) and 25 controls without ocular pathology. Visual symptoms included amaurosis, diplopia and temporary or permanent visual field loss. For each eye, peak systolic values (PS) and end diastolic values (ED) were recorded. Furthermore, the resistance index of each central retinal artery was measured.

Results: Twenty-one of 36 eyes of 18 GCA patients were affected. Therefore 21 central retinal were measured. The control group consisted of 50 central retinal arteries of 25 eye-healthy individuals. The mean age and gender distribution of the GCA-group were 75.6 years (SD $\pm$ 8.1) with eight females (44 %) and 67 years (SD $\pm$ 8.9) with twelve females (48%) in the control group. The mean flow velocity of the central retinal artery was PS 12.2 cm/s (SD $\pm$ 3.5) and ED 3.7 cm/s (SD $\pm$ 1.2) in the GCA group and PS 14.4 cm/s (SD $\pm$ 3.2) and ED 5.1 cm/s (SD $\pm$ 1.6) in the control group. The mean RI was 0.9 (SD $\pm$ 0.3) in the GCA group and 0.8 (SD $\pm$ 0.3) in the control group. Mean reduction