OP0235

INTERFERON-FREE ANTIVIRALS FOR HEPATITIS C VIRUS-ASSOCIATED CRYOGLOBULINEMIA VASCULITIS: A LONG-TERM FOLLOW-UP STUDY

P. Cacoub¹, S.N. Si Ahmed², Y. ferfar¹, S. Pol³, D. Thabut¹, C. Hezode⁴, L. Alric⁵, C. Comarmond¹, G. Ragab⁶, L. Quattuocci⁷, M. Hegazy⁶, T. Poinard¹, M. Resche Rigon⁸, D. Saadoun¹. ¹Hôpital Pitié Salpêtrière, Paris; ²CH Orleans, Orleans; ³Hôpital Cochin, PARIS; ⁴Hôpital H Mondor, Creteil; ⁵CH Purpan, Toulouse, France; ⁶Cairo university, Cairo, Egypt; ⁷University Hospital Udine, Udine, Italy; ⁸Hôpital Saint Louis, Paris, France

Background: In small-size and short term studies of hepatitis C virus (HCV)-cryoglobulinemia vasculitis (CryoVas), direct antiviral agents (DAAs) showed a better response rate and tolerance than interferon containing regimens.

Objectives: To evaluate the effectiveness and tolerance of all oral interferon-free DAA in a large CryoVas cohort with long-term follow-up.

Methods: This prospective international multicenter cohort study included 148 symptomatic HCV-CryoVas patients (53.7% with cirrhosis and 49.3% antiviral-naïve). They all received DAA, i.e. sofosbuvir (SOF) plus daclatasvir (n=53), SOF plus ribavirin (n=51), SOF plus ledipasvir (n=23), or SOF plus simeprevir (n=18), for 12 or 24 weeks. The primary endpoint was the clinical response of CryoVas symptoms at week 12 after stopping DAAs.

Results: 106 (72.6%) patients showed a complete response, 33 (22.6%) a partial response and 7 (4.8%) no response of CryoVas symptoms. Cryoglobulinemia was no longer found in 53.1%. A sustained virological response was obtained in 97.2%. Premature DAA withdrawal was noted in 4.1%. Two factors were associated with a poor response: a severe form of CryoVas [OR 0.33, 95% CI: 0.12 to 0.91; p=0.03] and peripheral neuropathy [OR 0.31, 95% CI: 0.11 to 0.84; p=0.02]. After a median follow-up of 15.3 months, 4 (2.8%) patients died. The final clearance rates of CryoVas manifestations were as follows: purpura (97.2%), renal involvement (91.5%), arthralgia (85.7%), neuropathy (77.1%) and cryoglobulinemia (53.8%). Only SOF plus ledipasvir regimen showed significant superiority [OR 4.09, 95% CI: 1.19 to 19.00; p=0.04].

Conclusions: The different DAA combinations showed high response rates of HCV-CryoVas symptoms. The tolerance was good, and the mortality rate was very low. We identified prognosis factors of response to DAA.

Disclosure of Interest: P. Cacoub Consultant for: Janssen, BMS, Abbvie, GSK, Astra zeneka, Gilead, Merck, Roche, Servier, Vifor, S. N. Si Ahmed Consultant for: BMS, Abbvie, Gilead, Roche, Janssen, Y. ferfar: None declared, S. Pol Consultant for: Sanofi, Novartis, Vertex, Boehringer, Janssen, BMS, Abbvie, GSK, Astra zeneka, Gilead, Merck, Roche, Servier, Vifor, D. Thabut: None declared, C. Hezode Consultant for: BMS, Merck, Abbvie, Gilead, Roche, Janssen, L. Alric Consultant for: BMS, Abbvie, Gilead, Janssen, Merck, C. Comarmond: None declared, G. Ragab: None declared, L. Quattuocci: None declared, M. Hegazy: None declared, T. Poinard: None declared, M. Resche Rigon: None declared, D. Saadoun Consultant for: medimmune, BMS, Abbvie, GSK, Astra zeneka, Gilead, Merck, Roche, Servier,

DOI: 10.1136/annrheumdis-2018-eular.2324

OP0236

RISK OF CARDIOVASCULAR DISEASE AND VENOUS THROMBOEMBOLISM AMONG PATIENTS WITH INCIDENT ANCA-ASSOCIATED VASCULITIS: A 20 YEAR POPULATION-BASED COHORT STUDY

A. Berti^{1,2}, E. Matteson³, C.S. Crowson³, U. Specks⁴, D. Cornes⁵. ¹Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Scientific Institute, Milan; ²Rheumatology Clinic, Santa Chiara Hospital, Trento, Italy; ³Division of Rheumatology; ⁴Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, USA; ⁵Lymphocytes B et Autoimmunité, Université de Bretagne Occidentale, Brest, France

Background: Although modern treatments have greatly improved survival in ANCA-associated vasculitis (AAV), many patients suffer cardiovascular and thrombotic complications during long-term follow up.

Objectives: We aimed to assess the cardiovascular disease (CVD) and venous thromboembolism (VTE) risks among patients with newly diagnosed AAV.

Methods: A population-based incident AAV cohort of 58 patients diagnosed between 1996 and 2015 in Olmsted County (Minnesota, USA) was identified by medical record review. For each patient, 3 age- and sex-matched non-AAV comparators were randomly selected from the same population and assigned an index date corresponding to the AAV incidence date. Medical records of cases and comparators were reviewed for CVD events, which included cardiac events (coronary artery disease, heart failure and atrial fibrillation), cerebrovascular accidents (CVA), peripheral vascular disease (PVD) and VTE, which included deep vein thrombosis (DVT) and pulmonary embolism (PE).

Results: Baseline total cholesterol, high-density lipoprotein and current smoking rate were lower in AAV than comparators (p=0.03, p=0.01 and p=0.04, respectively), while other CVD risk factors and Framingham risk score were not significantly different between the 2 groups. CVD events developed in 13 patients and

17 comparators, corresponding to a >3 fold increased risk (hazard ratio [HR] 3.15; 95% confidence interval [CI]: 1.51–6.57) (figure 1). By subtypes, risks were increased for cardiac events (HR 2.96, 95% CI: 1.42 to 6.15) and CVA (HR 8.16, 95% CI: 2.45 to 27.15), but not for PVD. The HR for VTE was 3.26 (95% CI: 0.84 to 12.60), significantly increased for DVT (HR 6.25, 95% CI: 1.16 to 33.60), but not for PE (HR 1.33, 95% CI: 0.23 to 7.54).

Conclusions: Despite a similar prevalence of CVD risk factors at baseline, the risk of CVD is >3 fold higher and for CVA 8-fold higher in patients with incident AAV than matched comparator subjects.

REFERENCES:

- [1] Avina-Zubieta JA, Mai A, et al. Risk of myocardial infarction and stroke in patients with granulomatosis with polyangiitis (Wegener's): A population-based study. *Arthritis Rheumatol* 2016;68(11):2752–9.
- [2] Morgan MD, et al. Increased incidence of cardiovascular events in patients with antineutrophil cytoplasmic antibody-associated vasculitides: A matched-pair cohort study. *Arthritis Rheum* 2009;60(11):3493–500.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7206

OP0237

A COMPARISON OF PK AND PD OUTCOMES OF TOCILIZUMAB IN GIANT CELL ARTERITIS AFTER SC AND IV DOSING

N.L. Mallatieu¹, J.H. Stone², P. Villiger³, M. Kleiman⁴, L. Brockwell⁵, S. Dimonaco⁵, J.E. Charion⁵. ¹Roche Innovation Ctr, New York; ²Massachusetts Gen Hosp Rheumatol Unit, Harvard Med School, Boston, USA; ³Dept Rheumatology, Immunology and Allergy, U Bern, Bern, Switzerland; ⁴Genentech, South San Francisco, USA; ⁵Roche Products Ltd, Welwyn Garden City, UK; ⁶Roche Innovation Ctr, Basel, Switzerland

Background: Tocilizumab (TCZ), a humanised anti-interleukin-6 (IL-6) receptor monoclonal antibody, was recently approved for the treatment of patients with giant cell arteritis (GCA). Evidence was based on results of a double-blind randomised controlled trial (RCT) in GCA patients given 162 mg TCZ either weekly (QW) or every other week (Q2W) via subcutaneous (SC) route (GiACTA trial¹). A second RCT conducted using 8 mg/kg TCZ given intravenously (IV) every 4 weeks (Q4W) also showed positive outcomes in GCA patients.² The double-blind dosing portion of each study lasted approximately 1 year. All three regimens (SC 162 mg QW, SC 162 mg Q2W, IV 8 mg/kg Q4W) resulted in positive outcomes for sustained remission of GCA. However, a higher benefit was noted in some key secondary efficacy outcomes with the QW vs the Q2W SC regimen.¹

Objectives: To characterise the pharmacokinetics (PK) of TCZ in the GCA population and to assess the impact of the exposure differential from the three regimens on pharmacodynamic (PD) markers.

Methods: TCZ levels and PD biomarkers (soluble IL-6 receptor [sIL-6R], IL-6, erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP]) were measured using validated assays at regular intervals throughout the dosing period from all patients in each trial. A comparison of PK and PD outcomes was conducted to understand the dose exposure–response relationships.

Results: At week 52, mean trough steady state exposure (C_{trough}), a primary PK driver of TCZ efficacy, was highest from SC 162 mg QW, followed by IV 8 mg/kg Q4W, and finally SC Q2W (figure 1). Of the PD end points, at week 52, sIL-6R levels were similar for the SC QW and IV regimens but lower for the SC Q2W regimen

(figure 1), possibly demonstrating a higher level of target engagement from the SC QW and IV regimens compared with the Q2W regimen. IL-6 levels increased vs baseline after TCZ administration for all three regimens, reflecting displacement of bound, endogenous IL-6 from its receptor, consistent with the mechanism of action of TCZ. ESR levels decreased to a similar extent in response to TCZ administration with all three regimens. Change from baseline in CRP was comparable between the two SC regimens (~79%–93% reduction from baseline from the QW and Q2W regimens, respectively). Quantitative changes in CRP values are not available for the IV study.

Abstract OP0237 – Figure 1 Mean (SD) baseline and week 52 PK/PD markers after chronic dosing with TCZ after IV and SC regimens in GCA patients.

Conclusions: Comparison of C_{trough} after 52 weeks of dosing with TCZ from the 8 mg/kg IV regimen with that obtained from two SC regimens showed that exposures from the IV regimen were within the range of exposures of the QW and Q2W regimens. Comparison of PD outcomes showed that all three regimens had comparable results, with the possible exception of lower levels of sIL-6R (a mechanistic marker reflecting serum concentration and target engagement) from the SC Q2W regimen. Comparability of PD results is consistent with the similar efficacy outcomes seen in the SC and IV trials.

REFERENCES:

- [1] Stone JH, et al. *N Engl J Med* 2017;377:317–328.
- [2] Villiger PM, et al. *Lancet* 2016;387:1921–1927.

Acknowledgements: This study was sponsored by F. Hoffmann-La Roche Ltd.
Disclosure of Interest: N. L. Mallalieu Shareholder of: Roche, Employee of: Roche, J. H. Stone Grant/research support from: Roche, Genentech, Xencor, Consultant for: Roche, Genentech, Xencor, P. Villiger: None declared, M. Klearman Employee of: Genentech, L. Brockwell Employee of: Roche, S. Dimonaco Employee of: Roche, J. E. Charon Employee of: Roche
DOI: 10.1136/annrheumdis-2018-eular.2633

OP0238

ASSOCIATION BETWEEN AGE AT DIAGNOSIS AND CLINICAL PRESENTATION AND OUTCOMES OF ANCA-ASSOCIATED VASCULITIS. ANALYSIS FROM THE DCVAS STUDY

S.Monti^{1,2}, A. Craven³, C. Klersy⁴, C. Montecucco², R. Caporali², R. Watts⁵, P. A. Merkel⁶, R. Luqmani³. ¹University of Pavia, PhD in Experimental Medicine; ²Rheumatology, IRCCS Policlinico S. Matteo Foundation, Pavia, Italy; ³Rheumatology, NDORMS, University of Oxford, Oxford, UK; ⁴Biometry and Clinical Epidemiology, IRCCS Policlinico S. Matteo Foundation, Pavia, Italy; ⁵Norwich Medical School, University of East Anglia, Norwich, UK; ⁶Rheumatology and Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania, Philadelphia, PA, USA

Background: ANCA-associated vasculitis (AAV) can affect all age groups. Nevertheless, the differences in disease presentation and outcome between younger and elderly-onset patients are still incompletely understood.²

Objectives: To identify distinguishing characteristics of clinical presentations, short-term outcomes and accumulated damage for AAV, based on age of disease onset.

Methods: We included patients with a final diagnosis of AAV: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) enrolled in The Diagnostic and Classification Criteria for Primary Systemic Vasculitis (DCVAS) study through May 2017. We divided the population according to age at diagnosis: <65 years old (group A) or ≥65 (group B).

Results: We included 1338 patients. 66% had a disease onset <65 years of age (male:50%; mean age 48.4±12.6 years); 34% had an elderly-onset (male: 46%; mean age 73.6±6). The diagnoses of GPA and EGPA were more frequent in group A (73% and 74% of patients, respectively) compared to MPA (56%), $p<0.001$ for comparisons within each diagnostic group. P-ANCA/anti-MPO positivity was more frequent in group B (48% vs 27%, $p=0.001$); c-ANCA/PR3

predominated in group A (48% vs 35%; $p<0.001$). The clinical presentation at onset significantly differed between the two groups. Patients from group A had higher rates of ocular, cutaneous, and musculoskeletal involvement compared to patients in group B who experienced more systemic, renal, cardiovascular, and neurological manifestations (figure 1). Pulmonary and gastrointestinal manifestations were equally distributed between the two age groups. Vasculitis Damage Index (VDI) was significantly higher in patients from group B, with 12% of patients with a 6 months VDI score ≥5, compared to 7% in group A; $p=0.01$. There were 13 (1.5%) deaths amongst patients belonging to group A compared to 22 (4.8%) in group B, HR 3.44 (1.65–7.18); $p=0.001$.

Abstract OP0238 – Table 1. Clinical characteristics and outcome according to age groups

	Group A (<65 years) n=878	Group B (≥65 years) n=460	p
Mean Age	48.4±12.6	73.6±6	<0.001
Diagnostic delay	14.6±34.4	11.8±32.2	0.036
Symptoms duration	19.9±35.1	18.1±33.1	0.145
Type of AAV:			
GPA	536 (61%)	199 (43%)	<0.001
EGPA	148 (17%)	186 (40%)	<0.001
MPA	189 (22%)	66 (14%)	0.004
p-ANCA/anti-MPO	240 (27%)	222 (48%)	0.001
c-ANCA/anti-PR3	421 (48%)	161 (35%)	<0.001
VDI at 6 months follow-up			
=0	236 (28%)	90 (22%)	base
=1/2	378 (44%)	184 (41%)	0.186
=3/4	187 (22%)	116 (26%)	0.010
≥5	57 (7%)	55 (12%)	0.001

Conclusions: Patients with AAV with elderly-onset disease display a different pattern of organ-involvement and an increased risk of significant damage and mortality compared to younger patients. A better understanding of the influence of age of onset on the clinical course of AAV could improve diagnostic and classification criteria and has implications on their pattern of presentation and subsequent clinical course.

REFERENCES:

- [1] Watts RA, et al. Epidemiology of systemic vasculitis. *Arthritis Rheum* 2000;43:414–19.
- [2] Chen M, et al. Antineutrophil cytoplasmic autoantibody-associated vasculitis in older patients. *Medicine* 2008;87:203–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4797

OP0239

PREGNANCY OUTCOMES IN PATIENTS WITH IGA VASCULITIS

J.Nossent^{1,2}, W. Raymond², H. Keen^{2,3}, C. Inderjeeth^{1,2}, D. Preen⁴.

¹Rheumatology, Sir Charles Gairdner Hospital, Nedlands; ²Rheumatology, School of Medicine, University of Western Australia, Crawley; ³Rheumatology, Fiona Stanley Hospital, Murdoch; ⁴School of Population and Global Health, University of Western Australia, Crawley, Australia

Background: IgA vasculitis (IgAV) is usually a self-limiting condition, but women with a history of IgAV are reported to have an increased risk of complications during pregnancy. There is however little international data regarding obstetric outcomes and risk factors for IgAV patients.¹

Objectives: To compare pregnancy outcomes between matched controls and patients hospitalised for IgA vasculitis in Western Australia (WA), where birth centres attached to public hospitals are the principal source for delivery of free midwifery-led care.