REFERENCES:
[1] Diaz-Perez JL, De Lagran ZM, Diaz-Ramon JL, Winkelmann RK. Cutaneous polyarteritis nodosa. Semin Cutan Med Surg. 2007 Jun;26:77–86.
[2] Morgan AJ, Schwartz RA. Cutaneous polyarteritis nodosa: a comprehensive review. Int J Dermatol. 2010 Jul;49:750–6.
[3] Daoud MS, Hutton KP, Gibson LE. Cutaneous periarteritis nodosa: a clinicopathological study of 79 cases. Br J Dermatol. 1997 May;136:706–13.
[4] Nakamura T, Kanazawa N, Ikeda T, Yamamoto Y, Nakabayashi K, Ozaki S, et al. Cutaneous polyarteritis nodosa: revisiting its definition and diagnostic criteria. Arch Dermatol Res. 2009 Jan;301:117–21.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.1037

FRI0287 EFFICACY OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS TREATMENTS ACCORDING TO THE TYPE OF MANIFESTATIONS BASED ON ANALYSIS OF 636 PATIENTS

Matthias Papo[1], Renato A. Sinico[2], Vítor Teixeira[3], Maria-Letizia Urban[4], Juliane Mahrhold[5], Sara Monti[6], Giulia Cassone[7], Franco Schiavon[8], Benjamin Seeliger[9], Thomas Neumann[10], Claus Kroegel[11], Matthieu Groh[12], Chiara Marvisi[13], Maxime Samson[14], Thomas Barba[15], David Jayne[3], Bernhard Hellmich[5], Carlomaurizio Montecucco[6], Carlo Salvarani[7], Jean-Emmanuel Kahn[12], Bernard Bonnotte[14], Cécile-Audrey Durel[15], Xavier Puéchal[1], Luc Mouthon[1], Loïc Guillevin[1], Giacomo Emmi[1,4], Augusto Vaglio[13], Benjamin Terrier[1], French Vasculitis Study Group EGPA European Collaborative Initiative. *[1]Internal Medicine, Paris, France*; *[2]Medicine and Surgery, Milan, Italy*; *[3]Medicine, Cambridge, Italy*; *[4]Experimental and Clinical Medicine, Florence, Italy*; *[5]Internal Medicine, Kirchheim, Germany*; *[6]Rheumatology, Pavia, Italy*; *[7]Rheumatology, Reggio Emilia and Modena, Italy*; *[8]Rheumatology, Padova, Italy*; *[9]Respiratory Medicine, Hannover, Italy*; *[10]Rheumatology, St. Gallen, Switzerland*; *[11]Pneumology, Jena, Germany*; *[12]Internal Medicine, Suresnes, France*; *[13]Nephrology, Parma, Italy*; *[14]Internal Medicine, Dijon, France*; *[15]Internal Medicine, Lyon, France*

Background: Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Glucocorticoids (GCs) represent the treatment cornerstone. So far, EGPA management has been based on conventional immunosuppressants, but GC-dependence remains frequent. Recently, therapies targeting B cells and interleukin-5 have been prescribed, but data on large cohorts are lacking.
Objectives: This study aimed to describe therapeutic management and efficacy of treatments in EGPA patients.
Methods: We set up a multicenter European cohort that included 636 EGPA patients. Treatments used, complete remission rates and vasculitis relapse-free survival were recorded. Complete remission was defined as absence of vasculitis relapse and prednisone dose <5 mg/d at last follow-up. Efficacy to treat GC-dependent asthma/ENT signs was defined as the absence of asthma/ENT symptoms and prednisone dose ≤7.5mg/d within the 6 months after initiation.
Results: For induction, cyclophosphamide (CYC) was the most frequently prescribed immunosuppressant (36.2%), more often in patients with FFS ≥1 (P<0.0001). GCs alone were used in 37.3%, azathioprine (AZA) in 14.4% and methotrexate (MTX) in 6.2%. No difference was found in the 10-years overall survival between patients with FFS=0, FFS=1 and FFS≥2.
Complete remission rates were similar between conventional immunosuppressants (CYC, AZA or MTX) and GCs alone. Vasculitis relapse-free survival was also similar between CYC, AZA or MTX and GCs alone. Similar results were observed for first vasculitis relapse treatments.
During follow-up, GC-dependent asthma and/or ENT manifestations were treated with AZA (40%), MTX (25%), mycophenolate mofetil (16%), rituximab (RTX) (21%), CYC (19%), cyclosporine (6%), omalizumab (5.9%) and mepolizumab (5.5%), allowing GC-tapering ≤7.5mg/in 23%, 31%, 17%, 43%, 5%, 71%, 25% and 50%, respectively. Conventional immunosuppressants were mostly used in first and second line, while eosinophil-targeted biotherapies were used in 4th or 5th lines.
Conclusion: In EGPA patients, the response to conventional immunosuppressants, in addition to GCs, is often disappointing compared to GCs alone, without clear benefit on complete remission rates and relapse-free survival. In contrast, notwithstanding a small number of treated patients, eosinophil-targeted therapies seemed promising to treat asthma and/or ENT manifestations.
Disclosure of Interests: Matthias Papo: None declared, Renato A. Sinico: None declared, Vítor Teixeira: None declared, Maria-Letizia Urban: None declared, Juliane Mahrhold: None declared, Sara Monti: None declared, Giulia Cassone: None declared, Franco Schiavon: None declared, Benjamin Seeliger: None declared, Thomas Neumann: None declared, Claus Kroegel: None declared, Matthieu Groh: None declared, Chiara Marvisi: None declared, Maxime Samson: None declared, Thomas Barba: None declared, David Jayne Grant/research support from: David Jayne has received research grants from Chemocentryx, GSK, Roche/Genentech and Sanofi-Genzyme. He has received consultancy fees from Astra-Zeneca, Boehringer-Ingelheim, Chemocentryx, Chugai, GSK, Infla-RX, Insmed and Takeda, Bernhard Hellmich Consultant for: Roche, Speakers bureau: Abbvie, MSD, Roche, Novartis, Pfizer, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Carlo Salvarani Grant/research support from: Roche, Consultant for: Eli Lilly and Company, Roche, Abbvie, Jean-Emmanuel Kahn: None declared, Bernard Bonnotte: None declared, Cécile-Audrey Durel: None declared, Xavier Puéchal: None declared, Luc Mouthon: None declared, Loïc Guillevin: None declared, Giacomo Emmi: None declared, Augusto Vaglio: None declared, Benjamin Terrier: None declared
DOI: 10.1136/annrheumdis-2019-eular.4156

FRI0288 OPHTHALMOLOGICAL MANIFESTATIONS AND ENDOTHELIN-1 PLASMA LEVELS IN PATIENTS WITH SYSTEMIC NECROTIZING VASCULITIS (SNV)

Liubov Petelytska[1], Oleg Iaremenko[1], Kateryna Iaremenko[2]. *[1]Bogomolets National Medical University, The Department of Internal Medicine#3, Kyiv, Ukraine*; *[2]Oleksandrivska City Clinical Hospital, The Laboratory Department, Kyiv, Ukraine*

Background: Inflammatory eye disease is described in 50% to 60% of patients with ANCA-positive vasculitis and in 10–20% of patients with polyarteritis nodosa, and for 8% to 16% of patients it is an initial manifestation [1,2]. Endothelin-1 (ET-1) as a potential participant in the local regulation of intraocular pressure, ocular blood vessel tone, and iris smooth muscle tone, suggesting that it may be an important mediator in the development of ocular pathologic conditions [3]. The lower ET-1 plasma levels were found in the optic neuropathy [4].
Objectives: to provide a more complete description of the ocular disease in patients with systemic necrotizing vasculitis (SNV), to evaluate the serum level of ET-1 in patients with SNV with and without eye involvement.
Methods: The study included 36 patients with SNV (polyarthritis nodosa - 8, ANCA - associated vasculitis - 28) and healthy controls (n=26). The 17 patients with SNV had ophthalmological manifestations. Clinical activities of patients were calculated according to the Birmingham Vasculitis Activity Score (BVAS). The serum levels of ET-1 (pmol/L) were determined by immunoassay analysis using the kits of Biomedica. The outcomes of this study were the differences in marker levels between SNV patients with and without eye involvement and healthy controls estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves (AUC).
Results: The ocular manifestation of patient with SNV included episcleritis (n=10), anterior uveitis (n=3), ischaemic optic neuritis (n=3) and occlusive retinal vasculitis (n=1). All patients had active disease (BVAS>11). There were no significant differences of BVAS, ESR and CRP between SNV patients with and without eye involvement. In 14% patients with SNV eye involvement was an initial manifestation. The level of ET-1 (M ± σ) in group of SNV patients with eye involvement (n=17) was 0.28 ± 0.13 and did not differ significantly from the control group (0.27 ± 0.10, p> 0.05). At the same time, in patients without eye involvement (n=19), it was significantly elevated (0.36 ± 0.34) compared with control group and with group of SNV patients with eye involvement (p < 0,001). ROC analysis showed that the AUC for ET-1 is 0.5±0.10 (p=0.98), which indicates not acceptable capacity for ET-1 differentiate groups of patients with ocular involvement and patients without ocular involvement (sensitivity - 59%, specificity - 57%).

Conclusion: The most common ocular manifestation in patients with SNV was episcleritis, which occurred in almost one third of patients. The serum levels of ET-1 were decreased in patients with SNV with eye involvement compared with patients without eye involvement, but this cannot be used for diagnostic purposes.

REFERENCES:

[1] Pakrou N, Selva D, Leibovitch I. Wegener's granulomatosis: ophthalmic manifestations and management. Semin Arthritis Rheum. 2006;35(5):284–92.

[2] Pagnoux, C., Seror, R., Henegar, C., Mahr, A., Cohen, P., Le Guern, V., Bienvenu, B., Mouthon, L., and Guillevin, L. (2010). Clinical features and outcomes in 348 patients with polyarteritis nodosa: a systematic retrospective study of patients diagnosed between 1963 and 2005 and entered into the French Vasculitis Study Group Database. Arthritis and Rheumatism, 62, 616–26

[3] Sugiyama T. Involvement of Endothelin-1 in the Pathophysiology of Normal-Tension Glaucoma. International Journal of Ophthalmic Research 2015; 1(2): 36-40 Available from: URL: http://www.ghrnet.org/index.php/ijor/article/view/1221.

[4] Ohguro I, Ohguro H, Ohkuro K, Nakazawa M: Study of contribution of low levels of plasma endothelin-1 concentrations to pathogenesis of glaucomatous optic neuropathy. Hirosaki Med J, 2006; 57: 59–64

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3944

FRI0289 THE CYCLOPHOSPHAMIDE-SPARING ROLE OF AN INTENSIFIED B-CELLS DEPLETION PROTOCOL IN ANCA-ASSOCIATED VASCULITIS

Dario Roccatello[1,2], Savino Sciascia[2], Roberta Fenoglio[1], Daniela Rossi[2]. [1]*San Giovanni Bosco Hospital, Tuirn, Italy*; [2]*University of Turin, Turin, Italy*

Background: ANCA-associated vasculitis (AAV) are systemic diseases with relapsing chronic course. The management of AAV requires the use of immunosuppressive drugs whose use is associated with potential toxicity.
Objectives: This case-control study aims to evaluate the immunosuppressive-sparing effect of rituximab (RTX) used with cyclophosphamide (CYC), compared to a traditional regimen based on high-dose CYC.
Methods: 26 patients (pts) with AAV with a necrotising extracapillary glomerulonephritis were prospectively enrolled. 13 pts received the intensified protocol of B-lymphocyte depletion therapy (IBCDT) "4+2" with RTX and CYC (4 weekly infusions of RTX followed by 2 monthly followed by prednisone tapered to 5 mg/day in 3 months). 13 pts treated with the high-dose CYC treatment protocol followed by azathioprine as maintenance therapy were enrolled as controls.
Results: In the 13 cases treated with the IBCDT we observed a significant reduction in mean values of parameter of disease activity. After administration of RTX, a significant reduction of the mean s-creatinine values and BVAS was observed. All pts had full B-cell depletion on peripheral blood after the first IBCDT protocol after 1 year. No further maintenance therapy was given. In the cases, a response was observed in 8/13 cases. 4 pts did not respond and a death was observed for cardiovascular causes. No significant difference was observed in terms of response to therapy between the two groups. The IBCDT allows a significant reduction in the cumulative dose of CYC to which each patient was exposed during follow-up, reaching statistical significance levels ($p < 0.001$). Calculated on a monthly basis, the "4+2" protocol allowed an average reduction in the CYC cumulative dose equivalent to 827 mg/month.
Conclusion: In a selected sample of patients with AAV with renal involvement, the IBCT regimen appeared to be non inferior in terms of the efficacy when compared to CYC-based standard regimens. Moreover, the IBCDT regimen allowed a net reduction in the cumulative average dose of CYC to which pts are exposed, quantifiable in approximately 1g/month.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.4820

FRI0290 EFFICACY AND SAFETY OF TOCILIZUMAB IN PATIENTS WITH GIANT CELL ARTERITIS AND VISUAL DISTURBANCES

Andrea Rubbert-Roth[1], Scott Tschuppert[2], Thomas Neumann[1], Ulf Benecke[3], Ian Pirker[1], Johannes von Kempis[1]. [1]*Rheumatology Clinic, Kantonspital St Gallen, St Gallen, Switzerland*; [2]*Opthalmology Clinic, Kantonspital St Gallen, St Gallen, Switzerland*; [3]*Angiology Clinic, Kantonspital St Gallen, St Gallen, Switzerland*

Background: Giant cell arteritis (GCA) affects cranial arteries and, as a complication, may lead to visual disturbances and ultimately blindness. Tocilizumab (TCZ) has recently been approved for treatment of GCA. Data on its efficacy and safety in patients who present with visual affection are limited.
Objectives: To study the outcome of patients with GCA and visual affection treated with TCZ.
Methods: We performed this retrospective single center study of all patients with GCA and visual disturbances consecutively seen in our clinic between April 2013 and January 2019 who underwent treatment with tocilizumab in addition to glucocorticosteroids (GC).
Results: 16 GCA patients (13 women, 3 male) with a mean age of 76.3 ± 9.7 yrs at GCA diagnosis and 25 affected eyes were treated with tocilizumab in addition to GC.
2/16 patients presented with visual disturbances under treatment with under prednisone, and 1/16 patient under leflunomide for polymyalgia. 2 patients experienced unilateral blindness while receiving iv pulse GC. AAION was diagnosed in 20/25 eyes, PION in 1/25 eyes and occlusion of the central retinal artery in 4/25 eyes. Loss of vision below 10% occurred in 12/25 eyes. None of the patients had bilateral blindness at baseline. 5/25 eyes were affected by hemi- or sectorial anopsia, blurred vision was reported in 8/25 eyes. 14 patients were treated with TCZ iv 8mg/kg every 4 weeks, 2 patients received sc TCZ at 162mg every 2 weeks.
All patients with visual symptoms received intravenous GC boluses, followed by prednisone 1mg/kg/day with subsequent stepwise reduction. Concomitant treatment consisted of low dose ASS in 11/16 and anticoagulants/NOAKs in 5/16 patients. Statins were used in 9/16 patients. Mean disease duration before initiation of tocilizumab was 3.8 ± 5.7 months. 13/16 patients started with TCZ within 2 months after diagnosis of GCA, in 3 patients TCZ was started because of refractory and/or relapsed disease.
Mean duration of TCZ therapy was 14.8 ± 9.4 months. 9/16 patients were able to stop GC after a mean duration of 14.8 ± 9.5 months and have been steroid-free for an average time of 14.7 ± 10 months (as of January 2019). 4/7 patients with a disease duration of less than 6 months are still on a GC taper at present. In addition to cessation of GC, 4 patients have discontinued TCZ and are drug-free at present for 4, 9, 31 and 35 months, respectively. In 2 additional patients, TCZ dose was decreased and/or the dosing interval extended. None of the 12 eyes with vision < 10% have recovered, but no new vision disturbances occurred during TCZ or after cessation of either TCZ/or GC.
Overall, TCZ was well tolerated with no major side effects. 22 patients experienced vascular complications (stroke, development of an aortic aneurysm) during treatment with TCZ.
Conclusion: Although TCZ was unable to reverse unilateral blindness, no new visual symptoms occurred during or after TCZ treatment and the majority of patients were able to stop or reduce GC.
Disclosure of Interests: Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Scott Tschuppert: None declared, Thomas Neumann: None declared, Ulf Benecke: None declared, Ian Pirker: None declared, Johannes von Kempis Consultant for: Pfizer, UCB, Lilly, Sanofi.
DOI: 10.1136/annrheumdis-2019-eular.1748