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

Matthias Papo1, Renato A. Sinico2, Vitor Teixeira2, Maria-Letizia Urban8, Juliane Mahfood3, Sara Moret4, Olija Cassone4, Franco Schiavon4, Benjamin Seelig5, Thomas Neumann5, Claus Kroegel5, Mathieu Gho5, Chiara Marvisi6, Maxine Samson6, Thomas Barba7, David Jayne3, Jean-Emmanuel Kahn1, bernard Bonnotte1, Cécile-Audrey Durel1, Xavier Puéchal1, Luc Mouthon1, Loïc Guillevin1, Giacomo Emmi1, Augusto Vaglio1, Benjamin Terrier1, French Vasculitis Study Group EGPA European Collaborative Initiative, 1Internal Medicine, Paris, France, 2Medicine and Surgery, Milan, Italy, 3Medicine, Cambridge, Italy, 4Experimental and Clinical Medicine, Florence, Italy, 5Internal Medicine, Kirchheim, Germany, 6Rheumatology, Pavia, Italy, 7Rheumatology, Reggio Emilia and Modena, Italy, 8Rheumatology, Padova, Italy, 9Respiratory Medicine, Hannover, Italy, 10Rheumatology, St. Gallen, Switzerland, 11Rheumatology, Jena, Germany, 12Internal Medicine, Suresnes, France, 13Nephrology, Parma, Italy, 14Internal Medicine, Dijon, France, 15Internal 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 <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 <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 <5 mg/d at last follow-up.

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/d 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.

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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:

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

Dario Roccato1,2, Savino Sciascia3, Roberta Feroglio4, Daniela Rossi2. 1San Giovanni Bosco Hospital, Turin, Italy; 2University 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 toxicities.

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 IBCDT 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.

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

Andrea Rubbert-Roth1, Scott Tschuppert2, Thomas Neumann1, Ulf Benecke3, Ian Pirker4, Johannes von Kemps5, 6Rheumatology Clinic, Kantonspral St Gallen, St Gallen, Switzerland; 6Angiology Clinic, Kantonspral 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 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 occulsion 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 treatment 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.

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