Table 1. ANCA in EGPA cohort (n = 73). BPI = bactericidal permeability-increasing protein.

IFT / ELISA	No. of patients (%)
P-ANCA	11 (15.1)
C-ANCA	5 (6.8)
MPO-ANCA	8 (10.9)
PR3-ANCA	2 (2.7)
BPI-ANCA	1 (1.4)
PTX3-ANCA	5 (6.8)
OLM4-ANCA	2 (2.7)

Conclusion: We report on the detection of PTX3-, BPI- and OLM4-ANCA in addition to MPO- and PR3-ANCA in EGPA. OLM4-ANCA has been reported in 2 patients with non-vasculitic inflammatory symptoms previously [5]. Herein, detection of OLM4-ANCA in EGPA is reported for the first time. Our study shows that the presence of ANCA with various specificities other than MPO and PR3 contribute to a higher prevalence of ANCA in EGPA. Moreover, clinical manifestations differ between ANCA-negative EGPA and ANCA-positive EGPA, and between patients with different ANCA-specificities.

REFERENCES:
[1] Schönermarck U, et al. Prevalence and spectrum of rheumatic diseases associated with proteinase 3-antineutrophil cytoplasmic antibodies (ANCA) and myeloperoxidase-ANCA. Rheumatology 2001;40:178-84.
[2] Bremer P, et al. Getting rid of MPO-ANCA: a matter of disease subtype. Rheumatology 2013:752-4.
[3] Comarmond C, et al. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss): clinical characteristics and long-term followup of the 383 patients enrolled in the French Vasculitis Study Group cohort. Arthritis Rheum 2013;65:270-81.
[4] Padoan R, et al. IgG anti-Pentraxin 3 antibodies are a novel biomarker of ANCA-associated vasculitis and better identify patients with eosinophilic granulomatosis with polyangiitis. J Autoimmun 2021;124:102725.
[5] Amirbeagi F, et al. Olfactomedin-4 autoantibodies give unusual c-ANCA staining patterns with reactivity to a subpopulation of neutrophils. J Leukoc Biol 2015;97:181-9.

POS0830

SYSTEMATIC LITERATURE REVIEW INFORMING THE 2022 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF ANCA-ASSOCIATED VASCULITIS: FOCUS ON TREATMENT STRATEGIES

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Background: The 2008 and 2016 European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of ANCA-associated vasculitis (AAV)[1,2] have supported clinicians with comprehensive recommendations for the treatment of patients with AAV in daily practice. During the past 5 years, the publication of several high-impact randomized-controlled studies have further improved the standard of care of AAV.
Objectives: The aim of this systematic review was to collect evidence supporting the 2022 update the AAV management recommendations.
Methods: The recommendations were developed based on an evidence-based approach as outlined in the 2014 EULAR standardized operating procedures (SOP)[3]. Areas of interest were adopted from the 2016 recommendations and updated by identifying additional topics through a Delphi process. Key questions were framed in the PICO (Population, Intervention, Comparator, Outcome) format and a search strategy consisting of keywords identifying treatment-related topics of interest was created based on the PICO questions. Aspects of drug treatment and other therapeutic interventions in AAV were included in the search, with a focus on remission induction, maintenance treatment and steroid sparing protocols. Outcomes such as survival, remission/relapses, infectious complications and malignancies were also covered. PubMed (Medline), Embase and the Cochrane Library databases were searched for articles providing data on the search questions. Abstracts of the annual meetings of EULAR, ACR, ERA-EDTA, ASN and the Vasculitis and ANCA Workshops were also screened, but restricted to randomized controlled clinical trials (RCTs). After deduplication publications were sorted by title and abstract first. There was full text review for articles eligible after title/abstract screening. The data were extracted from included articles and grouped according to the PICO questions. Data extraction results were collected in evidence tables.

The Cochrane revised tool for assessing risk of bias for RCTs (RoB2), ROBINS-1 for observational studies and AMSTAR II for meta-analyses were used for bias assessment. Evidence was categorized based on the GRADE system as per EULAR SOP[3].
Results: Based on the results of the Delphi, 11 topics related to therapeutic interventions were identified that were transformed into PICO questions (Table 1). Other items that received lower scores were added in the format of subquestions. Based on these research questions, search strings for the SLR were created.

Table 1. Key topics of interest for treatment strategies identified in the Delphi exercise grouped according to the PICO format

Patients	Intervention & Comparators	Outcome
Diagnosis	Cyclophosphamide	Disease-related outcomes
Granulomatosis with Polyangiitis	Rituximab	Treatment-related adverse events
Microscopic Polyangiitis	Mycophenolate	
Eosinophilic Granulomatosis with Polyangiitis	Methotrexate	
Disease severity	Azathioprine	
New-onset disease	Glucocorticoids	
Relapsing disease	Avacopan	
Organ- or life-threatening disease	Mepolizumab	
Not organ- or life-threatening disease	Plasma exchange	

The SLR was still ongoing at the time this abstract has been written and results of the SLR will be presented at the meeting.
Conclusion: This SLR identified recent developments affecting key areas of AAV treatment, that provide systematic evidence to inform the 2022 update of the EULAR recommendations for the management of AAV, which will also be presented at this meeting.

REFERENCES:
[1] Mukhtyar C, et al. EULAR Recommendations for the management of primary small and medium vessel vasculitis. Ann Rheum Dis. 2008;68:310-317.
[2] Yates M et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis. 2016 Sep;75(9):1583-94
[3] van der Heijde D et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. Ann Rheum Dis. 2015 Jan;74(1):8-13.

POS0831

IGA VASCULITIS IN ADULTS, PEDIATRICS AND NON-VASCULITIC IGA NEPHROPATHY

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Background: IgA vasculitis (IgAV) has been extensively studied in children, while its natural history remains poorly studied in adults. Sparse data comparing childhood and adult-onset disease has shown significant differences in their clinical presentation, especially in the severity of renal involvement, which accounts for the major long-term morbidity. IgAV shares similar renal histologic features with IgA nephropathy (IgAN), while clinically IgAN is a chronic kidney disease which may lead to end stage renal disease and dialysis. The extent of kidney injury among adults with IgAV is still a matter of uncertainty.
Objectives: We aimed to evaluate clinical manifestations, laboratory data, treatment patterns and long-term outcomes of pediatric and adult-onset IgAV in comparison to IgAN.
Methods: This retrospective collaborative study examined medical records of adults and children with IgAV and IgAN adult patients admitted to rheumatology clinic and in hospital pediatric departments in a 13-year period (2007-2019). Diagnosis of adults with IgAV relied on the Ankara criteria and was confirmed by a consistent skin biopsy with positive IgA staining by immunofluorescence. Children with IgAV were included in our study on a clinical basis. All IgAN patients had a kidney biopsy proven disease. We analyzed and compared frequencies of clinical manifestations, laboratory findings, treatment regimens and long-term outcomes at one year follow-up. Finally, we assessed long term outcomes, such as time to dialysis and all-cause mortality, till the end of the follow-up time.

Results: A total of 60 adult IgAV, 60 pediatric IgAV and 45 IgAN patients were included in our study. There were significantly more males in the IgAN group compared to the adult and pediatric IgAV groups (77.8%, 41.7% and 55% respectively, p=0.01). Adult IgAV patients were significantly older than IgAN patients (53.1±17.4 years vs. 45.1±15.7 years, p=0.02) and had significantly higher rates of diabetes (43.3% vs. 24.4%, p=0.05) and ischemic heart disease (18.3% vs. 4.4%, p=0.03). The pediatric IgAV group had a statistically higher rate of previous infection compared to the adult IgAV group (44.8% vs. 20%, p=0.02). At one year follow-up, IgAN patients had higher levels of serum creatinine compared to the adult IgAV group (2.002 vs. 1.100, p<0.01). Data observed until the end of the follow-up time showed no difference in time to dialysis (IgAV adults: 9.8-12.4 years, IgAN: 5.0-6.6 years, p>.41). Nevertheless, IgAV adult patients had significantly shorter survival time (5.5 years, 95% CI: 4.8-6.2 years) than IgAN patients (7.0 years, 95% CI: 6.6-7.5 years, p<.01).

Conclusion: This retrospective study demonstrates that IgAV in adults presents substantial clinical manifestations, including high risk of progression to persistent renal impairment and possesses higher mortality rate in comparison with pediatric-onset disease and IgAN.

REFERENCES:

[1] Blanco R, Martínez-Taboada VM, Rodríguez-Valverde V, García-Fuentes M, González-Gay MA. Henoch-Schönlein purpura in adulthood and childhood: two different expressions of the same syndrome. Arthritis Rheum. 1997 May;40(5):859-64. doi: 10.1002/art.1780400513. PMID: 9153547.

[2] Nossent J, Raymond W, Isobel Keen H, Preen D, Inderjeeth C. Morbidity and mortality in adult-onset IgA vasculitis: a long-term population-based cohort study. Rheumatology (Oxford). 2021 Dec 24;61(1):291-298. doi: 10.1093/rheumatology/keab312. PMID: 33779729.
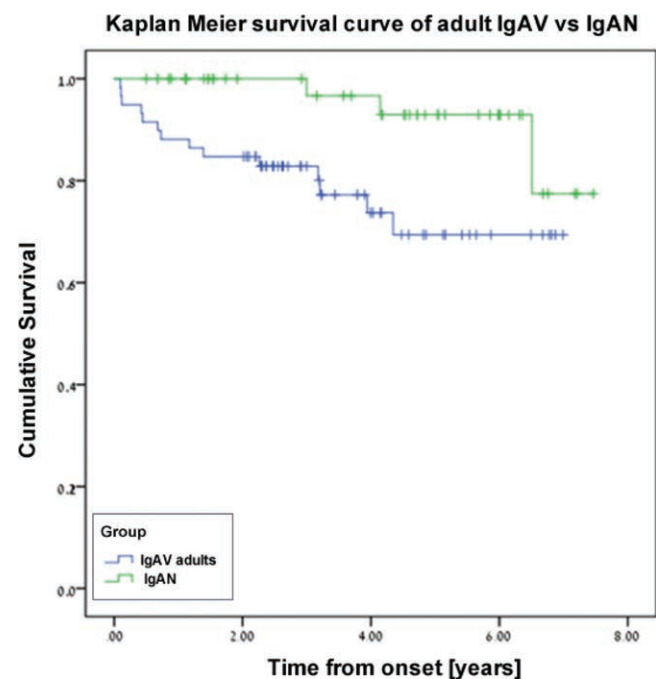

Figure 1.

POS0832 | **MORTALITY TRENDS IN ANCA-ASSOCIATED VASCULITIDES (AAVS): DATA FROM A CONTEMPORARY, MULTICENTER ANCA REGISTRY**

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Background: AAVs are a group of rheumatic diseases with excess morbidity and mortality (~3-fold higher compared to the general population). Long-term studies looking at mortality trends in contemporary patient cohorts are limited.

Objectives: To investigate the overall long-term survival and all-cause mortality in a contemporary AAV patient cohort.

Methods: Multicenter cohort study of patients registered and prospectively followed in the Greek ANCA Registry.

Results: Data for 165 patients (989.38 patient-years of follow up) with a diagnosis of AAV (GPA n=95, 58%, MPA n=54, 33%, EGPA n=16, 9%) were analyzed (January 1, 1998 - January 10, 2022). 53% of patients were female, with a mean age of 65 (±16.4) years; the majority (97%) had generalized disease and were ANCA positive (76%). The mean follow-up since diagnosis was 5.9 (±5.1) years. At the end of follow-up, the overall mortality rate was 20% (33/165), whereas the cumulative mortality rates at 5 and 10 years were 24% and 26% respectively. Overall cumulative survival at 5 years was worse in patients with MPA (57%) compared to GPA (81%) and EGPA (92%), (p<0.001). There was no difference in long-term survival among those treated with different induction regimens including cyclophosphamide (CYC, n of deaths=24/83, 28.9%), rituximab (RTX, n=4/40, 10%) or the CYC+RTX combination (n=3/16, 18.7%). Furthermore, there was no difference in survival between relapsing (≥1 relapses) and non-relapsing (n=76) patients (Figure 1). Cumulative survival was worse in patients who initially presented with lung (66% *vs.* 90% at 5 years, p=0.007), kidney (56% *vs.* 96% at 5 years, p<0.001) and simultaneous lung and kidney (39% *vs.* 93% at 5 years, p<0.001) involvement. Among the 33 registered deaths, the most frequent causes were infections (52%), followed by cardiovascular events (24%), disease flares (14%) and malignancies (10%).
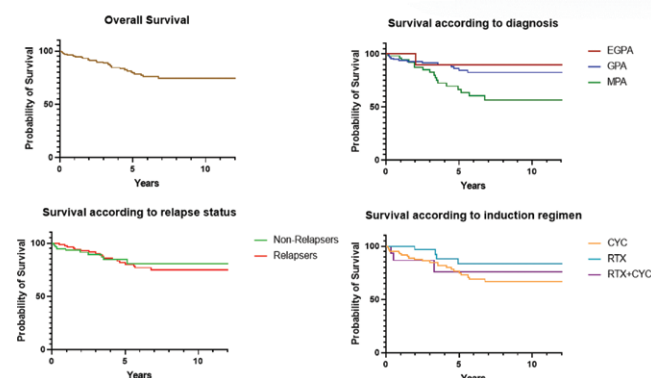

Figure 1.

Conclusion: In a contemporary multi-center AAV cohort, the cumulative mortality rates at 5 and 10 years were 24% and 26% respectively. Overall survival was worse in patients with MPA as well as those with combined lung and kidney involvement at baseline while there were no survival differences according to the initial induction regimen. Infection was the most common cause of death. These findings emphasize the unmet needs for better, less toxic therapies.

POS0833 | **DIFFERENCES BETWEEN AVACOPAN AND PREDNISONE FOR THE TREATMENT OF ANCA-ASSOCIATED VASCULITIS AT DIFFERENT THRESHOLDS OF GLUCOCORTICOID TOXICITY**

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Background: Treatment with glucocorticoids (GCs) for ANCA-associated vasculitis (AAV) is associated with substantial toxicity. The Glucocorticoid Toxicity Index (GTI) was developed to measure change in GC toxicity over time.[1] Data from the composite GTI domains provide both an Aggregate Improvement Score (AIS) and a Cumulative Worsening Score (CWS) of GC toxicity, permitting the