numbers of extrarenal manifestations, remission-inducing immunosuppressants and median follow-ups (three years) between groups, relapse rates were similar: 9.1% of DPP and 10% of AAVP. Please, see the table 1 for more detailed data.

Conclusion: Although DPP have features of both kinds of eponymous vasculitis, the anti-GBM component is the dominant phenotype, with more severe renal presentation and prognosis compared to AAVP with severe renal failure. Simultaneous testing of both antibodies and a systematically performed renal biopsy should be recommended in all rapidly progressive glomerulonephritis patients to recognize this difficult-to-treat, rare disease.

Table 1. Comparison of clinical characteristics and outcomes between the cohorts of DPP and AAVP

	DPP n = 33	AAVP n = 45	p
Age (year)	71,5 [14 - 89]	63 [45 - 93]	0.14
Male	16 (48)	19 (42)	0.65
Birmingham Vasculitis Activity Score	18,1 ± 4,8	20,4 ± 5,4	0.07
Organ involvement (except kidney)	1,7 ± 0,8	1,9 ± 1,1	0.31
Serum creatinine (μmol/L)	719 [238 - 2412]	501 [310 - 1683]	0.006
ANCA (MPO/PR3)	22/11	34/11	0.45
Berden classification	n = 31	n = 44	0.003
s (sclerotic) / c (crescentic)	6 (19) / 22 (71)	12 (27) / 16 (37)	
f (focal) / m (mixed)	0 / 3 (10)	11 (25) / 5 (11)	
Brix renal risk score	n = 27	n = 44	0.000014
Low / Medium / High	0 (0) / 4 (15) / 23 (85)	1 (2) / 29 (66) / 14 (32)	
Initial immunosuppressive therapy			
IV Cyclophosphamide	25 (76)	40 (82)	0.14
Rituximab	1 (3)	3 (7)	0.64
Plasma exchanges	25 (76)	19 (42)	0.005
Maintenance treatment	17 (48)	40 (89)	0.046
Initial RRT requirement	27 (82)	16 (36)	0.00007
Renal recovery (% initial RRT requirement)	4 (12)	6 (38)	0.9
1 year renal survival	9 (27)	29 (64)	0.0002

Values are displayed as absolute number (%) or as median [range]. DPP: double positive patients; AAVP: ANCA associated vasculitis patients; MPO: myeloperoxidase; PR3: proteinase 3; RRT: renal replacement therapy; IV: intravenous.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3089

POS0118

A WORLDWIDE PHARMACOEPIDEMOLOGICAL UPDATE OF DRUG-ASSOCIATED ANCA-ASSOCIATED VASCULITIS AT THE TIME OF TARGETED THERAPIES

S. Deshayes¹, C. Dolladille², A. Dumont¹, N. M. Silva¹, B. Chretien², H. De Boysson¹, J. Alexandre², A. Aouba¹. ¹CHU de Caen Normandie, Internal Medicine, Caen, France; ²CHU de Caen Normandie, Pharmacology, Caen, France

Background: Several pharmacological classes are involved in drug-associated anti-neutrophil cytoplasmic antibody-associated vasculitis (DA-AAV). However, the literature data supporting the role a drug in the onset of DA-AAVs mainly rely on case reports or short series and implicate old treatments. Moreover, the advent of new treatments, including targeted therapies, may have modified the epidemiology of these adverse drug reactions (ADRs).

Objectives: To update this list by using a pharmacovigilance-based data mining approach.

Methods: We collected data on ADRs reported with the MedDRA preferred term "Anti-neutrophil cytoplasmic antibody positive vasculitis" up to November 2020, from the World Health Organization pharmacovigilance database. For each retrieved drug, a case/noncase analysis was performed, and disproportionate reporting was calculated by using the information component (IC). A positive IC025 value, which is the lower end of the 95% credibility interval, was considered significant.

Results: A total of 483 deduplicated individual case safety reports of DA-AAV involving 15 drugs with an IC025>0 were retrieved. DA-AAV occurred in 264 (71.2%, n=371) women, the median age at onset was 62 years [45-72], and the median time to onset between the introduction of the suspected drug and DA-AAV was 9 months [1-36]. DA-AAV occurrence was considered serious in 472 (97.7%, n=481) cases and fatal in 43 (8.9%) cases. The drugs associated with the highest disproportionate reporting were hydralazine, propylthiouracil, thiazole, sofosbuvir, minocycline, carbimazole, mirabegron, and nintedanib (Table 1).

Table 1. List of the 15 drugs associated with ANCA-associated vasculitis in the World Health Organization pharmacovigilance database with significant disproportional reporting, sorted by decreasing IC₀₂₅

Drug	N _{observed}	N _{fatal} (%)	IC ₀₂₅ / IC ₉₅	ROR [95%CI]	Delay (in days) between the introduction of the drug and AAV, median [Q1-Q3] (n available)
Hydralazine	208	19 (9%)	8.2 / 8.4	2683.5 [2269.3-3173.3]	1277 (n=1)
Propylthiouracil	108	4 (4%)	7.2 / 7.5	1201.5 [974.8-1480.9]	1003 [425-1959] (n=19)
Thiamazole	40	5 (13%)	5.2 / 5.6	138.7 [100.7-191.1]	411 [58-966] (n=6)
Sofosbuvir	46	0	4.9 / 5.3	74.6 [55.3-100.8]	(n=0)
Minocycline	17	0	3.8 / 4.6	72.4 [44.7-117.3]	(n=0)
Carbimazole	6	0	2.0 / 3.4	44.9 [20.1-100.4]	92 (n=1)
Mirabegron	7	2 (29%)	1.5 / 2.7	11.1 [5.3-23.3]	291 [289-415] (n=3)
Nintedanib	6	2 (33%)	1.4 / 2.8	14.2 [6.3-31.7]	56 [36-132] (n=4)
Penicillamine	4	1 (25%)	1.4 / 3.1	170.3 [63.5-456.3]	(n=0)
Influenza vaccine	29	2 (7%)	1.3 / 1.9	4.1 [2.8-6.0]	24 [20-26] (n=7)
Allopurinol	7	2 (29%)	1.2 / 2.4	8.0 [3.8-16.8]	(n=0)
Rifampicin	7	2 (29%)	0.6 / 1.9	4.7 [2.2-9.8]	(n=0)
Peginterferon alfa-2b	4	0	0.3 / 2.1	7.0 [2.6-18.6]	98 (n=1)
Montelukast	4	4 (100%)	0.2 / 1.9	5.8 [2.2-15.5]	(n=0)
Rosuvastatin	6	0	0.1 / 1.5	3.4 [1.5-7.5]	(n=0)

IC: information component; ROR: reporting odds ratio; CI: confidence interval; AAV: ANCA-associated vasculitis

Conclusion: This study strengthens the previously suspected association but also identifies 3 new drugs that may cause DA-AAV. Particular attention should be given to these drugs by prescribers and in experimental studies.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1465

POS0119

RENAL INVOLVEMENT AND NEED OF RENAL REPLACEMENT THERAPY IN ANCA ASSOCIATED VASCULITIS IN A SPANISH SINGLE-CENTER STUDY

J. Álvarez Troncoso¹, J. C. Santacruz Mancheno², A. Díez Vidal¹, S. Afonso Ramos³, A. Noblejas Mozo¹, T. Olea Tejero³, J. J. Ríos¹, B. Rivas³, Á. Robles Marhuenda¹, M. C. Vega Cabrera³, E. Martínez Robles¹, C. Soto Abánades¹, F. Arnalich Fernández¹. ¹Hospital Universitario La Paz, Internal Medicine, Madrid, Spain; ²Clínica de los Riñones Menydia, Nephrology, Quito, Ecuador; ³Hospital Universitario La Paz, Nephrology, Madrid, Spain

Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EPGA). Renal involvement is frequent in AAV and is an important factor for morbidity and mortality.

Objectives: The main objective of this study was to analyze the demographic, clinical, histological and therapeutic characteristics of renal involvement in patients with AAV and the risk of renal replacement therapy (RRT) or death.

Methods: Retrospective observational study of 56 patients with AAV fulfilling classificatory criteria and renal involvement diagnosed between 1995 and 2020 from a Spanish tertiary centre. We studied the histological involvement (according to the 2010 classification in focal, crescentic, mixed or sclerotic), immunofluorescence (IF) and the treatment received with the risk of RRT or death.

Results: We included 56 patients diagnosed with AAV and renal involvement. The mean age was 61.08±4.05 years; 58.9% were women. The mean follow-up

time of these patients was 16.14 ± 8.80 years. Only 57.1% of patients presented systemic involvement. Most frequent non-renal AAV manifestations were lung involvement (39.3%), central nervous system (30.4%), otorhinolaryngology (ORL) (14.3%), skin (8.9%) and cardiac involvement (8.9%). Main immunological findings were ANCA-MPO+ (69.6%), ANCA-PR3+ (23.2%), ANCA-negative (5.4%). Low C3 was found in 19.6% patients. Histologic classification (HC) and need of RRT is described in table 1. Main HC in renal AAV was crescentic, mixed, focal and sclerotic respectively. Eight patients had not biopsy performed. IF was positive for C3 deposits in 20 patients (35.7%). Half of the patients presented <50% normal glomeruli.

The treatment of renal involvement in AAV in our cohort was as follows: 83.9% (47) corticosteroids (CS) and cyclophosphamide (of which 40 received intravenous and 7 oral cyclophosphamide; and 12 patients associated plasma exchange (PE) with this treatment), 5.36% CS alone, 2 patients received CS and mycophenolate; 1 CS and rituximab, 1 CS and PE, and 2 patients received no treatment. A total of 13 patients received PE and 18 RRT. The mean time to RRT was 65.44 ± 32.72 months. Relapses were not uncommon, 33.93% of the patients presented ≥ 1 relapse and 10.71% presented ≥ 2 . Infections were very frequent since they were present in 91.07% of the patients. Other frequent non-immunological complications observed in the follow-up of these patients were thrombosis in 31.14%, cardiovascular events in 28.57% and cancer in 19.64%. Patients with ANCA-PR3+ were younger at diagnosis ($p < 0.001$), were more likely to present cardiac ($p = 0.045$) and ORL involvement ($p < 0.001$). However, neither ANCA-PR3+ nor ANCA-MPO+ were specifically associated with the need of RRT or higher risk of death in our cohort. Use of CS alone for the treatment of renal AAV was associated with higher mortality ($p = 0.006$) but CS and cyclophosphamide with lower mortality ($p = 0.044$). ANCA-negative patients were more likely to receive no treatment. Having <50% normal glomeruli and C3 deposits on IF were associated with an increased need for RRT. Presenting focal disease on HC was protective for the need of RRT. Older age at diagnosis, systemic involvement of AAV and need of RRT was associated with higher mortality.

Conclusion: AAVs are complex vasculitides with frequent renal involvement. Increased C3 deposition, non-focal histological forms, and <50% normal glo-

		OR	IC (95%)	p
RRT	Number of glomeruli <50% normal	9.66	2.56-36.39	$p < 0.001$
	IF: C3 deposits	6	1.69-21.26	$p = 0.009$
Death	Age >70	6.53	1.84-23.15	$p < 0.001$
	Systemic disease	1.89	0.95-3.73	$p = 0.029$
	RRT	5.54	1.60-19.13	$p = 0.005$

meruli were related to the need for RRT. In turn, the need for RRT, a later age at diagnosis, and systemic involvement were associated with higher mortality. Holistic and multidisciplinary early management of AAVs in experience centers can help improve renal prognosis and decrease mortality.

REFERENCES:

- [1] Binda et al. ANCA-associated vasculitis with renal involvement. *J Nephrol.* 2018 Apr;31(2):197-208.
- [2] Kronbichler et al. Clinical associations of renal involvement in ANCA-associated vasculitis. *Autoimmun Rev.* 2020 Apr;19(4):102495.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.345

POS0120 INCIDENCE OF MALIGNANCIES IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS DIAGNOSED BETWEEN 1988 AND 2020

A. Masiak¹, M. Ziętkiewicz¹, A. Dębska-Ślizień², Z. Zdrojewski¹. ¹Medical University of Gdańsk, Department of Internal Medicine, Connective Tissue

Diseases and Geriatrics, Gdańsk, Poland; ²Medical University of Gdańsk, Department of Nephrology, Transplantology and Internal Diseases, Gdańsk, Poland

Background: Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) is a group of systemic necrotizing small vessel vasculitides. Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) are two most common types of AAV affecting mainly middle-aged and elderly people. Previous data indicated an increased occurrence of cancer in AAV patients [1], which has been mainly attributed to exposure to cyclophosphamide [2].

Objectives: The purpose of this paper was to analyze cancer incidence in unselected patients with GPA and MPA treated in one academic center since 1988 with follow-up until 2020.

Methods: With case record review, the baseline characteristics, outcomes and malignancy development in a cohort of 251 patients were assessed. Patients were followed up from time of diagnosis to their death or most recent hospital or outpatient's assessment.

Results: Twenty-eight of 251 patients with AAV (65% cANCA, 26% pANCA, 9.0% ANCA-negative) developed a total of 32 malignancies during a mean follow-up of 8.6 years. Patients characteristic is presented in table 1. Mean time since AAV onset to cancer diagnosis was 5.86 ± 6.78 years. Of these malignancies, 2 melanoma, 6 were non-melanoma skin cancers, 4 gastrointestinal tract cancer (2 colon, 1 stomach, 1 liver), 3 bladder cancer, 2 breast cancer, 2 uterine cancer, 1 ovarian cancer, 2 prostate cancer, 1 testis cancer, 2 lung cancer, 6 haematological malignancies (1 lymphoma, 1 chronic myeloid leukemia, 4 monoclonal gammopathy of unknown significance), additionally 1 benign salivary gland tumor was found. Four of the 16 patients with renal transplants developed a total of 6 malignancies. There were no differences in the incidence of cancer by gender, age, severity and activity of the disease, ANCA status, smoking status, number of relapses and treatment. There was no association between cancer and cumulative dose of cyclophosphamide.

Conclusion: In the AAV group, 11% of patients developed different type of cancer. The most common was non-melanoma skin cancer. The risk of developing malignancy increased with follow-up time. We found no association of tumor development and cumulative cyclophosphamide dose.

REFERENCES:

- [1] Rahmattulla et al. Incidence of malignancies in patients with antineutrophil cytoplasmic antibody-associated vasculitis diagnosed between 1991 and 2013. *Arthritis Rheum.* 2015;67(12):3270-3278.
- [2] Faurschou M et al. Prolonged risk of specific malignancies following cyclophosphamide therapy among patients with granulomatosis with polyangiitis. *Rheumatology (Oxford)* 2015; 54:1345-1350.

Table 1. Characteristics of the AAV patients included in the study.

	Total sample (n=251)	No malignancy occurrence (n=223)	Malignancy occurrence (n=28)	P value
Age at diagnosis, mean $\pm$ SD years	53.0 $\pm$ 15.9	52.4 $\pm$ 16.4	57.9 $\pm$ 9.45	NS
Female, n (%)	115 (45.8%)	106 (47.5%)	9 (32.1%)	NS
Mean observation time (years)	5.72 $\pm$ 5.17	5.35 $\pm$ 4.93	8.61 $\pm$ 6.17	0.002
BVASv3	18.9 $\pm$ 8.49	18.9 $\pm$ 8.46	18.6 $\pm$ 8.90	NS
DEI	7.03 $\pm$ 2.86	7.04 $\pm$ 2.90	6.96 $\pm$ 2.62	NS
Organ involvement, n (%)				
Upper respiratory tract	170 (67.7%)	151 (67.7%)	19 (67.9%)	NS
Lungs	163 (64.9%)	142 (63.7%)	21 (75.0%)	NS
Kidney	171 (68.1%)	151 (67.7%)	20 (71.4%)	NS
Skin	62 (24.7%)54 (21.5%)	55 (24.7%)49 (22.0%)	7 (25.0%)	NS
Eyes	11 (4.4%)	11 (4.9%)	5 (17.9%)	NS
Heart	30 (12.0%)	24 (10.8%)	0 (0.0%)	NS
Gastrointestinal tract	34 (13.5%)	32 (14.3%)	6 (21.4%)	NS
Follow-up				
0-5 years	145 (57.8%)	136 (61.0%)	9 (32.1%)	0.004
> 5-10 years	62 (24.7%)	52 (23.3%)	10 (35.7%)	NS
> 10 years	44 (17.5%)	35 (15.7%)	9 (32.1%)	0.031
Deaths, n(%)	56 (23.0%)	45 (20.8%)	11 (39.3%)	0.029
Renal transplantation, n(%)	16 (6.4%)	12 (5.4%)	4 (14.3%)	NS
Cumulative Cyclophosphamide dose (g)	14.7 $\pm$ 30.0	14.5 $\pm$ 30.8	16.6 $\pm$ 23.6	NS

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3840