Supplementary material

Methods

Patients

Patients with newly diagnosed or relapsing GPA/MPA/EGPA as classified by the Chapel Hill Consensus Conference (CHCC) classification[11] during the COVID-19 pandemic period of January-July 2020 were included in the study. Patients were enrolled from 12 different centers from the US, UK, and Europe (Johns Hopkins (n=15), University of North Carolina (n=12), Washington University, St. Louis (n=7) Northwell Health (n=7), Ohio State University, Wexner Medical Center (n=3), Tallaght hospital and Beaumont hospital, Ireland (n=12), Imperial College, London (n=21), Lancashire Teaching hospitals (n=36), Manchester University Foundation trust (n=26), LMU university, Munich (n=14), Medical University Innsbruck, Austria (n=10) and Charles University, Prague (n=28). The study was approved by the institutional review board at each center.

Data collection

Data regarding demographics, disease type, ANCA type, organ involvement by AAV, new or relapsing disease, co-morbidities, e-GFR at presentation, dialysis requirement at entry, remission at 6 months and at last follow up were collected. Details of induction therapy including the type and dose of immunosuppressive medications, use of plasma exchange and use of PJP prophylaxis were collected. We collected data on bone marrow suppression, infections requiring hospitalization, COVID-19 infection, ESKD and death at last follow up. Complete remission was defined as a Birmingham Vasculitis Activity Score (version 3) [12] of zero with patients either off prednisone or with prednisone doses less than 10 mg daily. ESKD was defined as need for renal replacement therapy. Bone marrow suppression was defined by the presence of leukopenia and thrombocytopenia.

Outcomes and Follow-Up

Our primary outcome was achievement of complete remission at 6 months. Secondary outcomes included eGFR at 6 months, change in eGFR over 6 months, death, bone marrow suppression, steroid dosing at 16 weeks and 6 months, infection requiring hospitalization, and ESRD. eGFR was calculated using the CKD-EPI creatinine equation.[13] Renal recovery is defined as becoming dialysis independent after presenting in ESKD during relapse or diagnosis. All patients were followed until death or date of last follow up.

Statistical analyses

Comparisons of categorical variables were performed using a chi-squared test. Comparisons of continuous variables were performed using Kruskal Wallis and ANOVA test. All statistical tests used a P value of 0.05 to determine statistical significance. Stata version 16.1 was used for all statistical analyses.

Table 3. Different clinical outcomes by different treatment regimens.

		Rituximab alone	Cyclophosphamide alone	Rituximab + Cyclophosphamide	p-value
	Number of subjects	n=84	n=49	n=49	
Age at diagnosis	Median (IQR) years	66 (58-72.5); n=84	71 (62-77); n=49	62 (53-69); n=49	0.007
Sex, n (%)	Female	40 (48); n=84	27 (55); n=49	26 (53); n=49	0.671
ANCA type, n (%)	GPA	46 (55); n=84	20 (42); n=48	19 (39); n=49	0.324
	MPA	36 (43); n=84	25 (52); n=48	28 (57); n=49	
	EGPA	2 (2); n=84	3 (6); n=48	2 (4); n=49	
Kidney involvement during relapse or diagnosis, n (%)		67 (80); n=84	43 (88); n=49	40 (82); n=49	0.498
GFR (ml/min/1.73 m2)	Mean (SD) at start of the study (n=180)	34 (30); n=82	24 (24); n=49	40 (36); n=49	0.0351
	6 months mean (SD); n=154	43 (29); n=67	33 (24); n=44	47 (27); n=43	0.0659
	Δ Over 6 months (median IQR); n=156	+6 (0-15), n=67	+6 (-1.8-16.2); n=45	+6 (-5.5-15.7); n=44	0.68
Remission at 6 months (n=170), n (%)		73 (92); n=79	42 (91); n=46	39 (87); n=45	0.564
Dialysis Independence (n=30), n (%)		6 (60) n=10	8 (62); n=13	5 (71); n=7	0.877
ESKD by end of study n=177, n (%)		8 (10); n=82	7 (14); n=49	2 (4); n=46	0.259
Death (n=182), n (%)		5 (6); n=84	6 (12); n=49	5 (10); n=49	0.43
Bone Marrow suppression (n=182), n (%)		2 (2); n=84	2 (4); n=49	6 (12); n=49	0.048
Infection requiring hospitalization (n=182), n (%)		10 (12); n=84	6 (12); n=49	13 (27); n=49	0.06

Mean (SD) Cumulative steroid dose in mg (n=166)		**2640 (1851); n=79**	**3428 (1567); n=45**	**3154 (2054); n=42**	**0.0585**
Mean (SD) Cumulative Dose of IV pulse methylprednisolone in mg (n=168)		**916 (1145); n=75**	**1047 (805); n=45**	**979 (866); n=48**	**0.7765**
Use of pulse steroids (n=182), n (%)		**42 (50); n=84**	**39 (80); n=49**	**36 (73); n=49**	**<0.001**
Mean (SD) Daily Prednisone dose at 16 weeks		**7.0 (5.5); n=76**	**9.4 (4.3); n=45**	**8.7 (8.0) n=45**	**0.0644**
Mean (SD) Daily Prednisone dose at 6 months		**4.1 (3.6); n=76**	**7.1 (4.8); n=42**	**4.9 (4.3); n=45**	**0.0009**

Table 4. Treatment differences among patients tested positive and negative for COVID-19

Treatment variables		Entire COVID-19 tested cohort	COVID-19 (-)	COVID-19 (+)	P-value
	Number of subjects	n=115	n=99	n=16	
Use of pulse steroids, n (%)		82 (71)	70 (71)	12 (75)	0.725
Cumulative Dose of IV pulse methylprednisolone in mg	Mean (SD)	1144 (1021); n=107	1172 (1039); n=91	984 (924); n=16	0.7275
	Median (IQR)	1000 (250-1500); n=107	1000 (250-1500); n=91	750 (375-1250); n=16	0.7258
Cumulative steroid dose (mg)	Mean (SD)	3111 (1857); n=103	3124 (1829); n=92	2999 (2175); n=11	0.8341
	Median (IQR)	2830 (1680-4230); n=103	2951 (1691-4127); n=92	1952 (1500-4888); n=11	0.7977
Rituximab use only, n (%)		43 (37); n=115	40 (40); n=99	3 (19); n=16	0.097
Cyclophosphamide use only, n (%)		26 (23); n=115	22 (22); n=99	4 (25); n=16	0.805
Rituximab and Cyclophosphamide, n (%)		42 (37); n=115	34 (34); n=99	8 (50); n=16	0.228
Cyclophosphamide cumulative dose	Mean (SD)	3.4 (2.5); n=56	3.4 (2.5); n=56	3.1 (1.9); n=12	0.7095
	Median (IQR)	3 (1.6-4.5); n=56	3 (1.6-4.5); n=56	2.5 (1.7-4.8); n=12	0.8716
PLEX, n (%)		20 (17); n=115	18 (18); n=99	2 (13); n=16	0.578

Table 5. Outcomes of patients diagnosed with COVID-19

Outcomes		Death	Hospitalized for infectious cause	Median (IQR) interval from AAV to COVID-19 in days	ESKD at end of study, n (%)	Kidney recovery, n (%)	Δ Over 6 months (median IQR)
	Total COVID patients n=16	4 (25); n=16	7 (44); n=15	33 (4-168); n=15	0; n=15	1 (100); n=1*	5.0 (-1.9-15.5); n=12

* One other patient had a dialysis dependent AKI on entry, but they died before renal recovery data was observed.

Table 6. Patient outcomes of the US, UK, & European cohorts

Treatment variables		Entire cohort	United States	United Kingdom	Europe	P-value
	Number of subjects	n=191	n=44	n=83	n=64	
Median (IQR) Δ eGFR Over 6 months		6 (-2-15.4); n=162	12.5 (4.5-19.5); n=36	1.5 (-6-8) n=70	7 (0.20-16.9) n=56	0.0005
Remission at 6 months, n (%)		160 (90); n=178	37 (90); n=41	64 (85); n=75	59 (95); n=62	0.164
Infection requiring hospitalization, n (%)		29 (15); n=191	9 (20); n=44	8 (10); n=83	13 (20); n=64	0.13
Kidney Recovery, n (%)		19 (61); n=31	6 (60); n=10	4 (36); n=11	9 (90); n=10	0.042
ESKD by end of study, n (%)		19 (10); n=186	7 (17); n=41	10 (12); n=83	2 (3); n=62	0.058
Bone Marrow suppression, n (%)		10 (5); n=190	1 (2); n=43	7 (8); n=83	2 (3); n=64	0.233
Death, n (%)		16 (8); n=191	3 (7); n=44	8 (10); n=83	5 (8); n=64	0.845

Table 7. Outcomes of patients with new and relapsing AAV

Outcome variables	New Disease	Relapsing Disease	P-value
Number of patients	n=132	n=59	
Median (IQR) Δ eGFR Over 6 months	7 (0-16.9); n=108	0.59 (-6-9); n=54	0.0042
Remission at 6 months, n (%)	108 (89); n=122	52 (93); n=56	0.373
Kidner Recovery, n (%)	19 (68); n=28	0; n=3	0.022
ESRD by end of study, n (%)	14 (11); n=128	5 (9); n=58	0.629
Death, n (%)	12 (9); n=132	4 (7); n=59	0.594
Bone Marrow suppression, n (%)	6 (5); n=131	4 (7); n=59	0.53
Infection requiring hospitalization, n (%)	21 (16); n=132	4 (7); n=59	0.909

Table 8. Treatment variables of patients with new and relapsing AAV

Treatment variables	New disease	Relapse	P-value
	n=132	n=59	
Use of pulse steroids, n (%)	95 (72); n=132	22 (37); n=59	<0.001
Mean (SD) cumulative dose of IV pulse Solumedrol in mg	1106 (1015); n=124	502 (744); n=51	0.0002
Mean (SD) cumulative steroid dose for remission induction in mg	3221 (1827); n=116	2414 (1762); n=55	0.007
Mean (SD) steroid dose at 16 weeks in mg	7.8 (5.8); n=118	9.2 (7.8); n=56	0.1902
Mean (SD) steroid dose at 6 months in mg	4.8 (4.3); n=116	5.8 (4.7); n=55	0.1733
Proportion off steroids at 6 months, n (%)	34 (28); n=122	12 (21); n=56	0.362
Rituximab use only, n (%)	49 (37); n=13	35 (59); n=59	0.004
Cyclophosphamide use only, n (%)	44 (33); n=132	5 (8); n=59	<0.001
Rituximab and cyclophosphamide , n (%)	34 (26); n=132	15 (25); n=59	0.961
Mean (SD) cyclophosphamide cumulative dose in grams	3.6 (2.4); n=75	2.9 (3.3); n=20	0.2978
PLEX, n (%)	21 (16); n=132	5 (8); n=59	0.166
Use of hydroxychloroquine	1 (1); n=130	0; n=58	0.503
Use of PJP prophylaxis	119 (90); n=132	43 (73); n=59	0.002
IVIG	21 (16); n=132	5 (8); n=59	0.166