

SUPPLEMENTARY MATERIAL

Supplementary Table S1: Clinical features of the study cohort in subgroups by Berden histopathological class and according by induction treatment.....	2
Supplementary Table S2: eGFR at baseline, 6 and 12 months and changes in eGFR from baseline at 6 and 12 months in the overall cohort and in groups stratified by Berden histological classes.....	6
Supplementary Table S3: eGFR at baseline, 6 and 12 months and changes in eGFR from baseline at 6 and 12 months, according to induction treatment and after stratification by Berden histological classes.....	7
Supplementary Table S4: Multivariable logistic regression model predicting eGFR recovery 6 months after induction therapy	8
Supplementary Table S5: Multivariable Firth's penalized logistic regression models to predict eGFR recovery in patient subgroups by Berden class.....	9
Supplementary Table S6: Multivariable Cox regression model with Firth's penalized partial likelihood predicting the kidney failure outcome.....	11
Supplementary Table S7: Multivariable Cox regression models with Firth's penalized partial likelihood to predict kidney failure in patient subgroups by Berden class	12
Supplementary Figure S1: Proportions of kidney remission rates at 6 months according to induction immunosuppression in subgroups stratified by Berden histopathological classes	13
Supplementary Figure S2: eGFR at baseline, 6 and 12 months after induction in the cohort stratified by Berden histopathological classes	14
Supplementary Figure S3: Kaplan Meier curves showing time to the kidney failure outcome in the cohort stratified by Berden histopathological classes.....	15

Supplementary Table S1: Clinical features of the study cohort in subgroups by Berden histopathological class and according by induction treatment

Values are reported as mean \pm standard deviation, median [interquartile range] or count (percentage). P values refer to ANOVA, Kruskal-Wallis Rank Sum Test or Fisher's exact tests, as appropriate, to compare the 3 groups. When these tests reached statistical significance ($p < 0.05$), post-hoc pairwise comparisons were performed. The superscript symbols indicate post-hoc pairwise comparisons with $p < 0.05$ (with Hommel correction for multiple testing). Absolute numbers (percentages) of missing data are reported in the "missing" column.

A. Focal class

	Overall	CYC	RTX	RTX-CYC	P-value	Missing
n	71	39	14	18		
Age at baseline (years)	62.2 \pm 12.7	63.8 \pm 10.5	63.6 \pm 15.8	57.7 \pm 14.2	0.221	-
Male sex	45 (63.4%)	26 (66.7%)	11 (78.6%)	8 (44.4%)	0.127	-
ANCA specificity						-
PR3	37 (52.1%)	19 (48.7%)	6 (42.9%)	12 (66.7%)	0.331	
MPO	34 (47.9%)	20 (51.3%)	8 (57.1%)	6 (33.3%)	0.331	
PR3 and MPO	1 (1.4%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1	
Negative	1 (1.5%)	1 (2.7%)	0 (0.0%)	0 (0.0%)	1	
Clinical diagnosis						-
GPA	30 (42.3%)	15 (38.5%)	3 (21.4%) [°]	12 (66.7%) [°]	0.033	
MPA	41 (57.7%)	24 (61.5%)	11 (78.6%) [°]	6 (33.3%) [°]	0.033	
eGFR (ml/min per 1,73m ²)	41.0 [19.5, 77.0]	34.0 [15.0, 79.0]	29.0 [15.8, 61.0]	53.5 [37.5, 77.5]	0.061	-
Dialysis dependence	5 (7.0%)	4 (10.3%)	1 (7.1%)	0 (0.0%)	0.387	-
Proteinuria (mg/day)	1430.0 \pm 1412.1	1315.5 \pm 1558.3	1728.4 \pm 1341.5	1456.8 \pm 1147.1	0.687	8 (11.3%)
Hypertension	19 (31.1%)	14 (35.9%)	2 (14.3%)	3 (37.5%)	0.302	10 (14.1%)
BVAS v3	18.2 \pm 5.6	18.0 \pm 6.3	15.5 \pm 2.7	20.1 \pm 5.1	0.106	9 (12.7%)
Extrarenal involvement						
Lung	39 (54.9%)	26 (66.7%) [*]	3 (21.4%) [*]	10 (55.6%)	0.014	-
Peripheral nervous system	7 (9.9%)	2 (5.1%)	1 (7.1%)	4 (22.2%)	0.131	-
Central nervous system	3 (4.2%)	1 (2.6%)	0 (0.0%)	2 (11.1%)	0.253	-
Ocular	7 (9.9%)	4 (10.3%)	0 (0.0%)	3 (16.7%)	0.417	-
Musculoskeletal	13 (18.3%)	9 (23.1%)	2 (14.3%)	2 (11.1%)	0.648	-
Gastrointestinal	4 (5.6%)	3 (7.7%)	0 (0.0%)	1 (5.6%)	0.808	-
Cardiovascular	1 (1.4%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1	-
ENT	23 (32.4%)	15 (38.5%)	3 (21.4%)	5 (27.8%)	0.517	-
Skin	15 (21.1%)	8 (20.5%)	3 (21.4%)	4 (22.2%)	1	-
RTX cumulative dose (g) ^a	2.0 [2.0, 2.0]	-	2.0 [1.9, 2.9]	2.0 [2.0, 2.0]	0.326	-
CYC cum dose (g) ^b	4.0 [2.2, 6.0]	6.0 [3.3, 7.1]	-	2.2 [2.2- 2.2]	<0.001	6 (10.5%)
PLEX	12 (28.6%)	9 (40.9%)	2 (40.0%)	1 (6.7%)	0.055	29 (40.8%)
IV glucocorticoids	43 (61.4%)	23 (60.5%)	13 (92.9%) [°]	7 (38.9%) [°]	0.005	1 (1.4%)
IV glucocorticoid dose (g) ^c	1.5 [1.5, 2.0]	1.5 [0.5, 2.0]	1.5 [1.5, 3.0]	1.5 [1.0, 1.6]	0.594	2 (4.6%)
Oral glucocorticoids	70 (98.6%)	39 (100.0%)	14 (100.0%)	17 (94.4%)	0.451	-
Starting dose (mg/day) ^d	60.0 [40.0, 60.0]	60.0 [40.0, 60.0]	55.0 [37.5, 60.0]	60.0 [60.0, 60.0]	0.414	4 (5.7%)
Maintenance therapy at 6 months						11 (18.3%)
Azathioprine	26 (43.3%)	16 (48.5%)	1 (11.1%)	9 (50.0%)	0.106	
RTX	8 (13.3%)	4 (12.1%)	3 (33.3%)	1 (5.6%)	0.129	
CYC	2 (3.3%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	0.429	
MMF	3 (5.0%)	1 (3.0%)	0 (0.0%)	2 (11.1%)	0.340	
Glucocorticoids only	17 (28.3%)	8 (24.2%)	5 (55.6%)	4 (22.2%)	0.143	
Combination/other	4 (6.7%)	2 (6.1%)	0 (0.0%)	2 (11.1%)	0.540	

B. Mixed class

	Overall	CYC	RTX	RTX-CYC	P-value	Missing
n	101	56	14	31		
Age at baseline (years)	63.2±12.3	62.3±12.1	68.9±11.8	62.3±12.5	0.172	-
Male sex	60 (59.4%)	34 (60.7%)	5 (35.7%)	21 (67.7%)	0.133	-
ANCA specificity						-
PR3	35 (34.7%)	18 (32.1%)	3 (21.4%)	14 (45.2%)	0.274	
MPO	67 (66.3%)	39 (69.6%)	12 (85.7%)	16 (51.6%)	0.069	
PR3 and MPO	4 (4.0%)	3 (5.4%)	1 (7.1%)	0 (0.0%)	0.45	
negative	3 (3.3%)	2 (4.1%)	0 (0.0%)	1 (3.3%)	1	3 (3.0%)
Clinical diagnosis						
GPA	32 (32.7%)	14 (25.9%)	4 (28.6%)	14 (46.7%)	0.158	
MPA	66 (67.3%)	40 (74.1%)	10 (71.4%)	16 (53.3%)	0.158	
eGFR (ml/min per 1,73m ²)	19.0 [12.0, 28.0]	18.0 [10.2, 27.0]	18.5 [14.8, 30.2]	23.0 [14.5, 33.5]	0.149	-
Dialysis dependence	14 (13.9%)	9 (16.1%)	2 (14.3%)	3 (9.7%)	0.72	-
Proteinuria (mg/day)	2439.8±1923.6	2264.1±2074.8	2347.8±1479.3	2844.5±1800.6	0.478	16 (15.8%)
Hypertension	45 (54.2%)	32 (57.1%)	8 (57.1%)	5 (38.5%)	0.509	18 (17.8%)
BVAS v3	18.0±5.4	18.6±6.0	14.5±4.5	18.3±4.2	0.060	5 (4.9%)
Extrarenal involvement						-
Lung	47 (46.5%)	32 (57.1%) [^]	6 (42.9%)	9 (29.0%) [^]	0.04	
Peripheral nervous system	8 (7.9%)	6 (10.7%)	0 (0.0%)	2 (6.5%)	0.601	
Central nervous system	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	
Ocular	4 (4.0%)	2 (3.6%)	0 (0.0%)	2 (6.5%)	0.79	
Musculoskeletal	17 (16.8%)	11 (19.6%)	0 (0.0%)	6 (19.4%)	0.215	
Gastrointestinal	4 (4.0%)	2 (3.6%)	1 (7.1%)	1 (3.2%)	0.614	
Cardiovascular	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	
ENT	22 (21.8%)	14 (25.0%)	3 (21.4%)	5 (16.1%)	0.625	
Skin	12 (11.9%)	7 (12.5%)	1 (7.1%)	4 (12.9%)	1	
RTX cumulative dose (g) ^a	2.0 [2.0, 2.0]	-	2.0 [1.6, 2.0]	2.0 [2.0, 2.0]	0.12	2 (4.4%)
CYC cum dose (g) ^b	3.0 [2.2, 6.0]	3.6 [3.0, 6.0]	-	2.2 [2.2, 2.2]	<0.001	5 (5.7%)
PLEX	11 (15.7%)	10 (27.8%)	0 (0.0%)	1 (3.6%)	0.018	31 (30.7%)
IV glucocorticoids	59 (60.2%)	45 (80.4%) [^]	8 (66.7%) ^o	6 (20.0%) ^{^o}	<0.001	3 (3.0%)
IV glucocorticoid dose (g) ^c	1.5 [1.0, 2.2]	1.5 [0.7, 2.1]	1.5 [1.5, 2.4]	1.0 [0.7, 1.5]	0.247	2 (3.4%)
Oral glucocorticoids	99 (98.0%)	55 (98.2%)	13 (92.9%)	31 (100.0%)	0.351	-
Starting dose (mg/day) ^d	60.0 [32.0, 60.0]	60.0 [32.0, 60.0]	60.0 [25.0, 60.0]	60.0 [60.0, 60.0]	0.789	10 (10.1%)
Maintenance therapy at 6 months						10 (9.9%)
Azathioprine	50 (54.9%)	28 (54.9%) [*]	1 (9.1%) ^{*o}	21 (72.4%) ^o	0.002	
RTX	3 (3.3%)	1 (2.0%)	2 (18.2%)	0 (0.0%)	0.012	
CYC	4 (4.4%)	4 (7.8%)	0 (0.0%)	0 (0.0%)	0.194	
MMF	5 (5.5%)	1 (2.0%)	0 (0.0%)	4 (13.8%)	0.057	
Glucocorticoids only	23 (25.3%)	14 (27.5%)	6 (54.5%) ^o	3 (10.3%) ^o	0.014	
Combination/other	6 (6.6%)	3 (5.9%)	2 (18.2%)	1 (3.4%)	0.234	

C. Crescentic class

	Overall	CYC	RTX	RTX-CYC	P-value	Missing
n	96	61	12	23		
Age at baseline (years)	58.4±13.7	60.0±11.1	59.5±16.0	53.7±17.7	0.158	-
Male sex	56 (58.3%)	38 (62.3%)*	2 (16.7%)**	16 (69.6%)*	0.007	-
ANCA specificity						-
PR3	50 (52.1%)	30 (49.2%)	7 (58.3%)	13 (56.5%)	0.791	
MPO	40 (41.7%)	24 (39.3%)	6 (50.0%)	10 (43.5%)	0.753	
PR3 and MPO	1 (1.0%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	0.125	
Negative	7 (7.6%)	7 (12.3%)	0 (0.0%)	0 (0.0%)	0.159	
Clinical diagnosis						1 (1%)
GPA	46 (48.4%)	29 (47.5%)	4 (36.4%)	13 (56.5%)	0.563	
MPA	49 (51.6%)	32 (52.5%)	7 (63.6%)	10 (43.5%)	0.563	
eGFR (ml/min per 1,73m ²)	14.0 [5.0, 28.5]	11.0 [5.0, 22.0] ^	14.5 [6.5, 32.5]	23.0 [14.5-40.5] ^	0.005	-
Dialysis dependence	28 (29.2%)	24 (39.3%) ^	3 (25.0%)	1 (4.3%) ^	0.003	-
Proteinuria (mg/day)	2349.8±2425.3	2743.8±2885.8	2044.6±1646.3	1546.8±785.2	0.156	18 (18.7%)
Hypertension	44 (51.2%)	31 (51.7%)	7 (58.3%)	6 (42.9%)	0.756	10 (10.4%)
BVAS v3	18.6±6.8	18.2±6.9	17.7±5.4	20.0±7.1	0.52	2 (2.1%)
Extrarenal involvement						
Lung	48 (50.0%)	33 (54.1%)	8 (66.7%)	7 (30.4%)	0.075	-
Peripheral nervous system	8 (8.3%)	3 (4.9%)	1 (8.3%)	4 (17.4%)	0.164	-
Central nervous system	2 (2.1%)	2 (3.3%)	0 (0.0%)	0 (0.0%)	1	-
Ocular	2 (2.1%)	1 (1.6%)	0 (0.0%)	1 (4.3%)	0.599	-
Musculoskeletal	22 (22.9%)	11 (18.0%)	3 (25.0%)	8 (34.8%)	0.226	-
Gastrointestinal	4 (4.2%)	3 (4.9%)	0 (0.0%)	1 (4.3%)	1	-
Cardiovascular	2 (2.1%)	1 (1.6%)	0 (0.0%)	1 (4.3%)	0.599	-
ENT	29 (30.2%)	12 (19.7%) ^	4 (33.3%)	13 (56.5%) ^	0.005	-
Skin	13 (13.5%)	3 (4.9%)*	5 (41.7%)*	5 (21.7%)	0.001	-
Induction treatment						
RTX cumulative dose (g) ^a	2.0 [2.0, 2.0]	-	2.0 [1.0, 2.1]	2.0 [2.0, 2.0]	0.585	6 (17.1%)
CYC cum dose (g) ^b	3.0 [2.2, 4.9]	3.0 [3.0, 6.0]	-	2.2 [2.2, 2.2]	<0.001	6 (7.1%)
PLEX	31 (44.9%)	25 (59.5%) [^]	4 (44.4%)	2 (11.1%) [^]	0.002	27 (28.1%)
IV glucocorticoids	72 (76.6%)	52 (86.7%) [^]	9 (75.0%)	11 (50.0%) [^]	0.003	2 (2.1%)
IV glucocorticoid dose (g) ^c	1.5 [0.4, 2.1]	1.2 [3.7, 2.2]	1.5 [1.5, 1.5]	1.5 [1.5, 1.9]	0.115	4 (5.5%)
Oral glucocorticoids	92 (98.9%)	59 (98.3%)	12 (100.0%)	21 (100.0%)	1	3 (3.1%)
Starting dose (mg/day) ^d	60.0 [32.0, 60.0]	50.0 [32.0, 60.0]	50.0 [30.0, 60.0]	60.0 [60.0, 60.0]	0.236	12 (13%)
Maintenance therapy at 6 months						15 (15.6%)
Azathioprine	45 (55.6%)	33 (66.0%)*	1 (10.0%)*	11 (52.4%)	0.005	
RTX	9 (11.1%)	0 (0.0%)* [^]	4 (40.0%)*	5 (23.8%) [^]	<0.001	
CYC	6 (7.4%)	6 (12.0%)	0 (0.0%)	0 (0.0%)	0.134	
MMF	6 (7.4%)	3 (6.0%)	0 (0.0%)	3 (14.3%)	0.302	
Glucocorticoids only	11 (13.6%)	4 (8.0%)*	5 (50.0%)* ^o	2 (9.5%) ^o	0.002	
Combination/other	4 (4.9%)	4 (8.0%)	0 (0.0%)	0 (0.0%)	0.271	

D. Sclerotic

	Overall	CYC	RTX	RTX-CYC	P-value	Missing
n	36	22	12	2		
Age at baseline (years)	60.2±16.4	57.1±16.7	65.9±16.3	62.5±3.5	0.351	1 (2.8%)
Male sex	20 (55.6%)	9 (40.9%)*	10 (83.3%)*	1 (50.0%)	0.037	-
ANCA specificity						-
PR3	10 (27.8%)	4 (18.2%)	5 (41.7%)	1 (50.0%)	0.222	
MPO	24 (66.7%)	16 (72.7%)	7 (58.3%)	1 (50.0%)	0.518	
PR3 and MPO	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	
Negative	2 (5.6%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0.581	
Clinical diagnosis						2 (5.6%)
GPA	8 (23.5%)	4 (20.0%)	3 (25.0%)	1 (50.0%)	0.539	
MPA	26 (76.5%)	16 (80.0%)	9 (75.0%)	1 (50.0%)	0.539	
eGFR (ml/min per 1,73m ²)	19.0 [12.8, 24.2]	20.0 [13.8, 27.2]	17.5 [11.0, 24.0]	12.0 [8.5, 15.5]	0.513	-
Dialysis dependence	7 (19.4%)	3 (13.6%)	3 (25.0%)	1 (50.0%)	0.285	-
Proteinuria (mg/day)	1864.4±1605.1	1773.6±1729.2	1642.5±1368.0	3524.0±0.0	0.322	9 (25%)
Hypertension	17 (47.2%)	15 (68.2%)*	2 (16.7%)*	0 (0.0%)	0.005	-
BVAS v3	15.2±4.9	16.3±4.4	12.5±4.9	22.0	NA	4 (11.1%)
Extrarenal involvement						
Lung	9 (25.0%)	5 (22.7%)	2 (16.7%)	2 (100.0%)	0.091	-
Peripheral nervous system	3 (8.3%)	2 (9.1%)	1 (8.3%)	0 (0.0%)	1	-
Central nervous system	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	-
Ocular	1 (2.8%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	0.389	-
Musculoskeletal	7 (19.4%)	3 (13.6%)	3 (25.0%)	1 (50.0%)	0.285	-
Gastrointestinal	2 (5.6%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0.581	-
Cardiovascular	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	-
ENT	3 (8.3%)	1 (4.5%)	1 (8.3%)	1 (50.0%)	0.193	-
Skin	3 (8.3%)	2 (9.1%)	0 (0.0%)	1 (50.0%)	0.119	-
Induction treatment						
RTX cumulative dose (g) ^a	2.0 [1.0, 2.5]	-	1.9 [1.0, 2.7]	2.0 [2.0, 2.0]	0.788	1 (7.1%)
CYC cum dose (g) ^b	3.0 [3.0, 4.5]	3.0 [3.0, 3.7]	-	6.8 [5.5-8.0]	0.063	3 (12.5%)
PLEX	2 (10.5%)	2 (12.5%)	0 (0.0%)	0 (0%)	1	17 (47.2%)
IV glucocorticoids	23 (69.7%)	17 (81.0%)	5 (50.0%)	1 (50.0%)	0.182	3 (8.3%)
IV glucocorticoid dose (g) ^c	1.0 [0.4, 1.5]	0.4 [0.4, 1.5]	3.0 [1.5, 3.0]	2.0 [2.0, 2.0]	0.007	-
Oral glucocorticoids	34 (97.1%)	20 (95.2%)	12 (100.0%)	2 (100.0%)	1	1 (2.8%)
Starting dose (mg/day) ^d	40.0 [32.0, 60.0]	36.0 [32.0, 60.0]	60.0 [40.0, 60.0]	50.0 [45.0, 55.0]	0.769	3 (8.8%)
Maintenance therapy at 6 months						9 (25%)
Azathioprine	13 (48.1%)	11 (68.8%)*	1 (11.1%)*	1 (50.0%)	0.022	
RTX	1 (3.7%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0.354	
CYC	1 (3.7%)	1 (6.2%)	0 (0.0%)	0 (0.0%)	0.700	
MMF	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	
Glucocorticoids only	10 (37.0%)	3 (18.8%)	6 (66.7%)	1 (50.0%)	0.054	
Combination/other	2 (7.4%)	1 (6.2%)	1 (11.1%)	0 (0.0%)	0.831	

Abbreviations: ANCA: antineutrophil cytoplasmic antibody; BVAS v3: Birmingham Vasculitis Activity Score version 3; CYC: cyclophosphamide; eGFR: estimated glomerular filtration rate; ENT: Ear, Nose and Throat; GPA: granulomatosis with polyangiitis; IV: intravenous; MPA: microscopic polyangiitis; MPO: myeloperoxidase; PLEX: Plasma Exchange; PR3: proteinase 3; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide

*P value < 0,05 CYC vs RTX ; ^ P value < 0,05 CYC vs RTX-CYC; ° P value < 0,05 RTX vs RTX-CYC

a. Refers only to patients treated with RTX

b. Refers only to patients treated with CYC

c. Refers only to patients treated with IV glucocorticoids

d. Refers only to patients treated with oral glucocorticoids

Supplementary Table S2: eGFR at baseline, 6 and 12 months and changes in eGFR from baseline at 6 and 12 months in the overall cohort and in groups stratified by Berden histological classes

Data are reported as median (IQR). P values in the last column refer to Kruskal-Wallis rank sum test to compare the groups. When this test reached statistical significance ($p < 0.05$), post-hoc pairwise Wilcoxon tests (with Hommel's correction for multiple testing) were performed. Statistically significant ($p < 0.05$) pairwise comparisons are indicated by superscript symbols.

Paired Wilcoxon test p-values comparing eGFR at 6 or 12 months vs baseline were significant ($p < 0.05$) in all cases, except sclerotic class at 6 months.

Patient cohort	All	n	Focal	n	Mixed	n	Crescentic	n	Sclerotic	n	P-value
Baseline eGFR	20.0 (11.0, 35.2)	304	41.0 (19.5, 77.0) ^{#o•}	71	19.0 (12.0, 28.0) [#]	101	14.0 (5.0, 28.5) ^o	96	19.0 (12.8, 24.2) [*]	36	<0.001
6-month eGFR	39.0 (23.0, 55.0)	261	53.0 (40.2, 82.5) ^{#o•}	60	34.0 (21.0, 48.0) ^{#□}	89	41.5 (23.8, 57.2) ^{o^}	84	18.5 (11.8, 28.0) ^{*^□}	28	<0.001
12-month eGFR	40.0 (24.5, 58.5)	251	57.0 (41.0, 80.0) ^{#o•}	59	35.5 (22.0, 50.0) ^{#□}	90	41.0 (25.0, 58.2) ^{o^}	76	22.5 (17.0, 29.2) ^{*^□}	26	<0.001
Delta eGFR 6 months	12.0 (0.0, 25.0)	261	11.0 (-5.2, 23.0) ^o	60	11.0 (1.0, 21.0) ^{*□}	89	21.0 (7.0, 36.0) ^{**^}	84	0.5 (-1.2, 9.0) ^{^□}	28	<0.001
Delta eGFR 12 months	13.0 (0.5, 28.0)	251	11.0 (-7.0, 27.5) ^o	59	12.5 (1.0, 21.0) ^{*□}	90	22.5 (8.0, 36.5) ^{**^}	76	2.0 (-0.8, 9.2) ^{^□}	26	<0.001

Abbreviations: eGFR-estimated glomerular filtration rate.

*P value < 0.05 crescentic vs mixed ; ^P value < 0.05 crescentic vs sclerotic; °P value < 0.05 crescentic vs focal; # P value < 0.05 focal vs mixed; *P value < 0.05 focal vs sclerotic; □P value < 0.05 mixed vs sclerotic

Supplementary Table S3: eGFR at baseline, 6 and 12 months and changes in eGFR from baseline at 6 and 12 months, according to induction treatment and after stratification by Berden histological classes

eGFR and changes in eGFR from baseline are reported as median (IQR), stratified by Berden class: (A) focal, (B) mixed, (C) crescentic, (D) sclerotic. The “n” columns report sample sizes of the subgroups at the different time points. P-values in the last column refer to Kruskal-Wallis rank sum test to compare the groups. When these tests reached statistical significance ($p < 0.05$), post-hoc pairwise comparisons were performed. Pairwise comparisons with $p < 0.05$ after applying Hommel’s correction for multiple testing are flagged with the superscript symbols. # refers to Wilcoxon signed rank test $p < 0.05$ when performing paired comparisons between eGFR values at 6/12 months and baseline eGFR values

A. Focal class

Patient cohort	Total	n	CYC	n	RTX	n	RTX-CYC	n	P-value
Baseline eGFR	41.0 (19.5, 77.0)	71	34.0 (15.0, 79.0)	39	29.0 (15.8, 61.0)	14	53.5 (37.5, 77.5)	18	0.061
6-months eGFR	53.0 (40.2, 82.5)	60	51.0 (35.0, 78.0) [#]	34	52.0 (41.8, 73.2)	8	75.0 (48.5, 87.8)	18	0.170
12-months eGFR	57.0 (41.0, 80.0)	59	49.0 (36.5, 75.0) [#]	35	67.0 (42.0, 72.0)	11	73.0 (55.0, 88.0)	13	0.187
Delta eGFR 6 months	11 (-5.2, 23.0)	60	10.5 (1.2, 21.0)	34	22.5 (-5.0, 38.8)	8	10.5 (-8.0, 19.2)	18	0.556
Delta eGFR 12 months	11 (-7.0, 27.5)	59	12.0 (-5.5, 26.0)	35	21.0 (-2.0, 37.0)	11	9.0 (-8.0, 19.0)	13	0.621

B. Mixed class

Patient cohort	Total	n	CYC	n	RTX	n	RTX-CYC	n	P-value
Baseline eGFR	19.0 (12.0, 28.0)	101	18.0 (10.2, 27.0)	56	18.5 (14.8, 30.2)	14	23.0 (14.5, 33.5)	31	0.149
6-months eGFR	34.0 (21.0, 48.0)	89	32.0 (21.0, 47.0) [#]	49	42.0 (14.0, 50.5)	11	36.0 (24.0, 51.0) [#]	29	0.586
12-months eGFR	35.5 (22.0, 50.0)	90	32.5 (21.5, 47.2) [#]	48	34.0 (17.5, 50.0)	11	39.0 (24.5, 59.0) [#]	31	0.418
Delta eGFR 6 months	11.0 (1.0, 21.0)	89	13.0 (3.0, 21.0)	49	0.0 (-3.0, 16.0)	11	7.0 (1.0, 19.0)	29	0.098
Delta eGFR 12 months	12.5 (1.0, 21.0)	90	14.0 (2.0, 26.5)	48	3.0 (-0.5, 15.0)	11	9.0 (1.0, 20.5)	31	0.355

C. Crescentic class

Patient cohort	Total	n	CYC	n	RTX	n	RTX-CYC	n	P-value
Baseline eGFR	14.0 (5.0, 28.5)	96	11.0 (5.0, 22.0) [°]	61	14.5 (6.5, 32.5)	12	23.0 (14.5, 40.5) [°]	23	0.005
6-months eGFR	41.5 (23.8, 57.2)	84	40.0 (22.8, 56.2) [#]	52	26.0 (14.5, 52.5)	11	48.0 (33.0, 62.0) [#]	21	0.163
12-months eGFR	41.0 (25.0, 58.2)	76	42.0 (25.0, 58.5) [#]	47	25.0 (16.0, 54.0)	9	49.0 (29.8, 66.2) [#]	20	0.212
Delta eGFR 6 months	21.0 (7.0, 36.0)	84	21.5 (9.0, 36.2)	52	11.0 (-7.5, 28.5)	11	24.0 (7.0, 31.0)	21	0.390
Delta eGFR 12 months	22.5 (8.0, 36.5)	76	23.0 (12.0, 38.0)	47	11.0 (6.0, 25.0)	9	23.0 (7.0, 36.0)	20	0.424

D. Sclerotic class

Patient cohort	Total	n	CYC	n	RTX	n	RTX-CYC	n	P-value
Baseline eGFR	19.0 (12.8, 24.2)	36	20.0 (13.8, 27.2)	22	17.5 (11.0, 24.0)	12	12.0 (8.5, 15.5)	2	0.513
6-months eGFR	18.5 (11.8, 28.0)	28	23.0 (16.8, 27.8)	16	14.0 (5.0, 28.0)	10	10.5 (7.8, 13.2)	2	0.276
12-months eGFR	22.5 (17.0, 29.2)	26	25.0 (17.2, 37.5) [#]	18	17.0 (8.5, 25.0)	7	19.0 (19.0, 19.0)	1	0.407
Delta eGFR 6 months	0.5 (-1.2, 9.0)	28	3.5 (-0.2, 11.0)	16	0.5 (-1.5, 7.8)	10	-1.5 (-2.2, -0.8)	2	0.469
Delta eGFR 12 months	2.0 (-0.8, 9.2)	26	5.5 (0.0, 13.0)	18	0.0 (-4.0, 1.0)	7	0.0 (0.0, 0.0)	1	0.058

Abbreviations: CYC: cyclophosphamide; eGFR: estimated glomerular filtration rate; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide
*P value < 0,05 RTX vs CYC; [#]P value < 0,05 RTX vs RTX-CYC; [°]P value < 0,05 CYC vs RTX-CYC.

Supplementary Table S4: Multivariable logistic regression model predicting eGFR recovery 6 months after induction therapy

Clinically relevant variables with missing data <10% were included as predictors. Missing data were imputed and model estimates were pooled using Rubin's rules, as detailed in the Methods. P values for categorical variables with more than two categories refer to pooled likelihood ratio tests.

Variable	Odds Ratio (95% CI)	p-value
Age at baseline (10 years)	0.48 (0.37-0.64)	< 0.001
Male sex (reference: female)	1.45 (0.77-2.72)	0.248
Baseline eGFR (10 ml/min/1.73m ²)	0.55 (0.45-0.67)	< 0.001
PR3 ANCA-positivity	0.67 (0.26-1.72)	0.399
GPA (reference: MPA)	1.31 (0.49-3.49)	0.588
Berden class		<0.001
Mixed vs focal	0.26 (0.10-0.65)	0.004
Crescentic vs focal	0.69 (0.27-1.76)	0.432
Sclerotic vs focal	0.07 (0.02-0.26)	<0.001
Mixed vs crescentic	0.38 (0.18-0.81)	0.012
Sclerotic vs crescentic	0.10 (0.03-0.33)	<0.001
Mixed vs sclerotic	3.81 (1.20-12.05)	0.023
Induction therapy		0.506
RTX vs CYC	0.59 (0.23-1.48)	0.256
RTX-CYC vs CYC	0.98 (0.43-2.22)	0.964
RTX vs RTX-CYC	0.60 (0.20-1.80)	0.359
IV glucocorticoids	1.68 (0.79 -3.56)	0.174

Abbreviations: CI: confidence interval; CYC: cyclophosphamide; eGFR: estimated glomerular filtration rate; GPA: granulomatosis with polyangiitis; IV: intravenous; MPA: microscopic polyangiitis; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide

Supplementary Table S5: Multivariable Firth's penalized logistic regression models to predict eGFR recovery in patient subgroups by Berden class

Separate models were developed for each subgroup by Berden class, using the same set of predictors. Tables report odds ratios (OR), 95% confidence intervals (CI) and the respective p-values. Missing data were imputed and model estimates were pooled using Rubin's rules, as detailed in the Methods.

A. Focal class

	OR	95% CI	p-value
age (10 years)	0.51	0.27-0.96	0.038
eGFR (10 ml/min)	0.47	0.31-0.71	<0.001
Induction therapy			
RTX vs CYC	2.14	0.28-16.41	0.457
RTX-CYC vs CYC	2.76	0.52-14.64	0.228
RTX vs RTX-CYC	0.78	0.08-7.20	0.820
IV steroids	2.15	0.53-8.74	0.280

B. Mixed class

	OR	95% CI	p-value
age (10 years)	0.57	0.37-0.87	0.009
eGFR (10 ml/min)	0.64	0.44-0.94	0.023
Induction therapy			
RTX vs CYC	0.64	0.15-2.73	0.538
RTX-CYC vs CYC	0.50	0.14-1.81	0.289
RTX vs RTX-CYC	1.27	0.24-6.54	0.775
IV steroids	0.88	0.28-2.82	0.831

C. Crescentic class

	OR	95% CI	p-value
age (10 years)	0.57	0.37-0.88	0.011
eGFR (10 ml/min)	0.59	0.43-0.80	<0.001
Induction therapy			
RTX vs CYC	0.23	0.05-0.98	0.047
RTX-CYC vs CYC	1.16	0.27-4.94	0.84
RTX vs RTX-CYC	0.20	0.03-1.19	0.077
IV steroids	1.90	0.50-7.21	0.340

D. Sclerotic class

	OR	95% CI	p-value
age (10 years)	0.52	0.27-0.99	0.047
eGFR (10 ml/min)	1.21	0.61-2.39	0.574
Induction therapy			
RTX vs CYC	0.30	0.02-4.26	0.355
RTX-CYC vs CYC	0.99	0.03-28.74	0.996
RTX vs RTX-CYC	0.30	0.00-18.00	0.548
IV steroids	2.55	0.14-45.31	0.507

Abbreviations: CI: confidence interval; CYC: cyclophosphamide; eGFR: estimated glomerular filtration rate; IV: intravenous; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide

Supplementary Table S6: Multivariable Cox regression model with Firth's penalized partial likelihood predicting the kidney failure outcome

Missing data were imputed and model estimates were pooled using Rubin's rules, as detailed in the Methods.

Variable	Hazard Ratio (95% CI)	P-value
Age at baseline (10 years)	0.98 (0.79-1.20)	0.827
Male sex (reference: female)	1.06 (0.62-1.79)	0.836
Baseline GFR (10 ml/min/1.73m ²)	0.52 (0.39-0.70)	<0.001
PR3 ANCA-positivity	1.23 (0.56-2.71)	0.605
GPA (reference: MPA)	0.76 (0.31-1.86)	0.549
Berden class		
Mixed vs focal	2.82 (0.88-9.03)	0.081
Crescentic vs focal	2.10 (0.64-6.89)	0.219
Sclerotic vs focal	5.76 (1.70-19.45)	0.005
Mixed vs crescentic	1.34 (0.71-2.53)	0.364
Sclerotic vs crescentic	2.74 (1.29-5.80)	0.009
Mixed vs sclerotic	0.49 (0.23-1.02)	0.056
Therapy		
RTX vs CYC	1.88 (0.93-3.83)	0.080
RTX-CYC vs CYC	0.99 (0.45-2.18)	0.982
RTX vs RTX-CYC	1.90 (0.73-4.93)	0.186
IV glucocorticoids	0.82 (0.43-1.54)	0.530

Abbreviations: CI: confidence interval; CYC: cyclophosphamide; eGFR: estimated glomerular filtration rate; GPA: granulomatosis with polyangiitis; IV: intravenous; MPA: microscopic polyangiitis; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide

Supplementary Table S7: Multivariable Cox regression models with Firth's penalized partial likelihood to predict kidney failure in patient subgroups by Berden class

Separate models were developed for each subgroup by Berden class, using the same set of predictors. Tables report hazard ratios (HR), 95% confidence intervals (CI) and the respective p-values. Missing data were imputed and model estimates were pooled using Rubin's rules, as detailed in the Methods.

Modelling in the focal class was not done due to the low number of events (n=3 events)

Mixed class

	HR	95% CI	p-value
eGFR (10 ml/min)	0.38	0.22-0.67	<0.001
Induction therapy			
RTX vs CYC	2.21	0.69-7.05	0.178
RTX-CYC vs CYC	1.51	0.47-4.86	0.490
RTX vs RTX-CYC	1.47	0.34-6.29	0.601
IV steroids	1.14	0.38-3.45	0.807

Crescentic class

	HR	95% CI	p-value
eGFR (10 ml/min)	0.56	0.34-0.93	0.026
Induction therapy			
RTX vs CYC	3.42	1.03-11.35	0.045
RTX-CYC vs CYC	0.64	0.14-2.99	0.568
RTX vs RTX-CYC	5.33	0.91-31.18	0.063
IV steroids	0.65	0.21-1.94	0.430

Sclerotic class

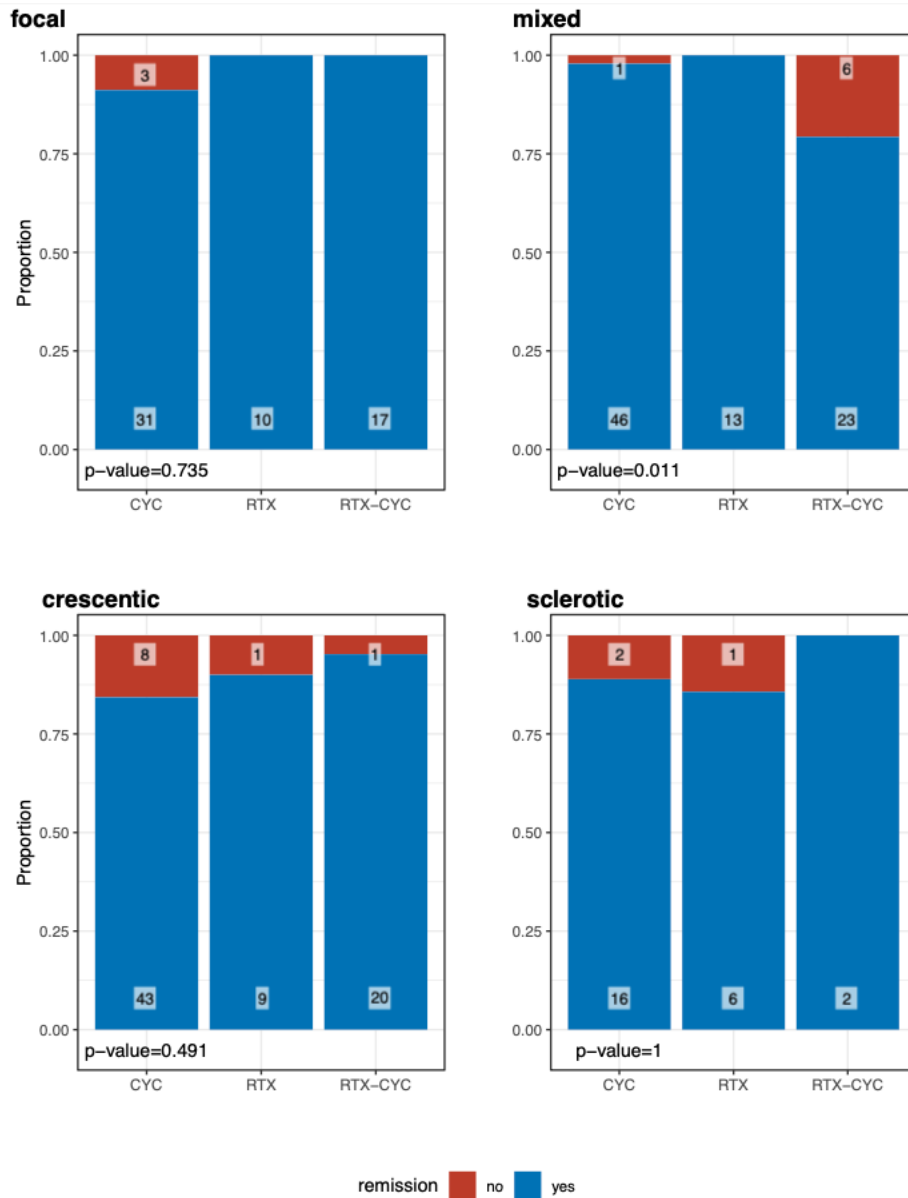
	HR	95% CI	p-value
eGFR (10 ml/min)	0.33	0.14-0.76	0.011
Induction therapy			
RTX vs CYC	0.91	0.17-4.83	0.909
RTX-CYC vs CYC	1.46	0.17-12.38	0.723
RTX vs RTX-CYC	0.62	0.08-4.88	0.644
IV steroids	0.28	0.05-1.53	0.136

Abbreviations: CI: confidence interval; CYC: cyclophosphamide; eGFR: estimated glomerular filtration rate; IV: intravenous; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide

Supplementary Figure S1: Proportions of kidney remission rates at 6 months according to induction immunosuppression in subgroups stratified by Berden histopathological classes

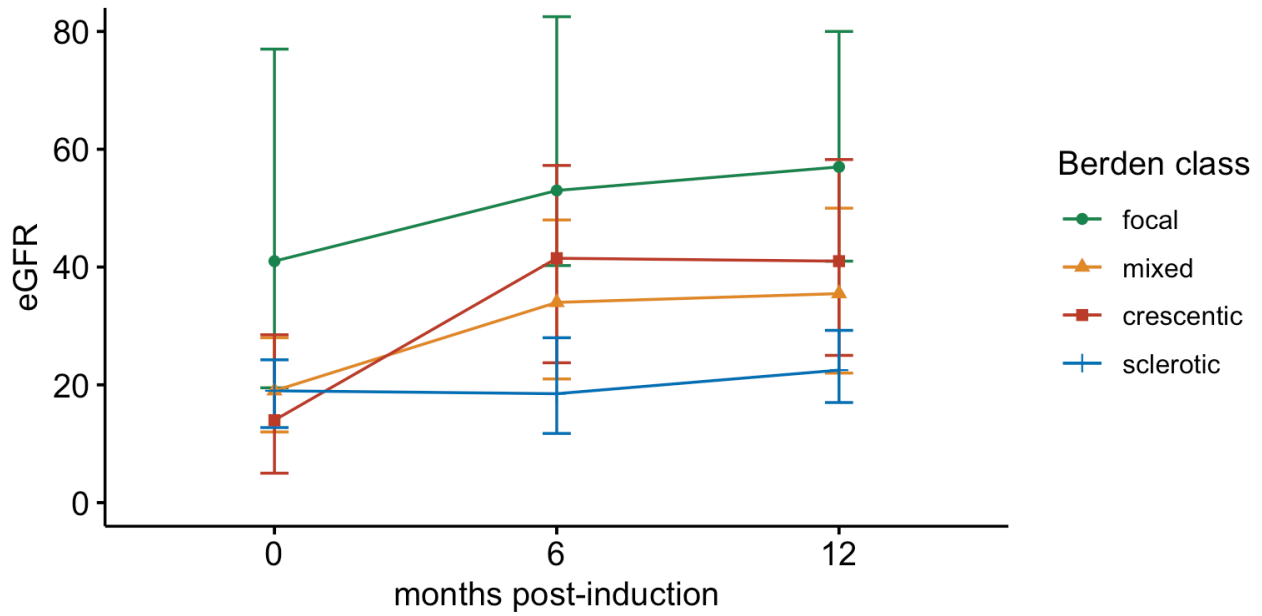
Bars represent proportions, with absolute counts shown as numbers superimposed on each segment. P values refer to Fisher's exact test.

Abbreviations: CYC: cyclophosphamide; RTX: rituximab; RTX-CYC: Rituximab plus Cyclophosphamide

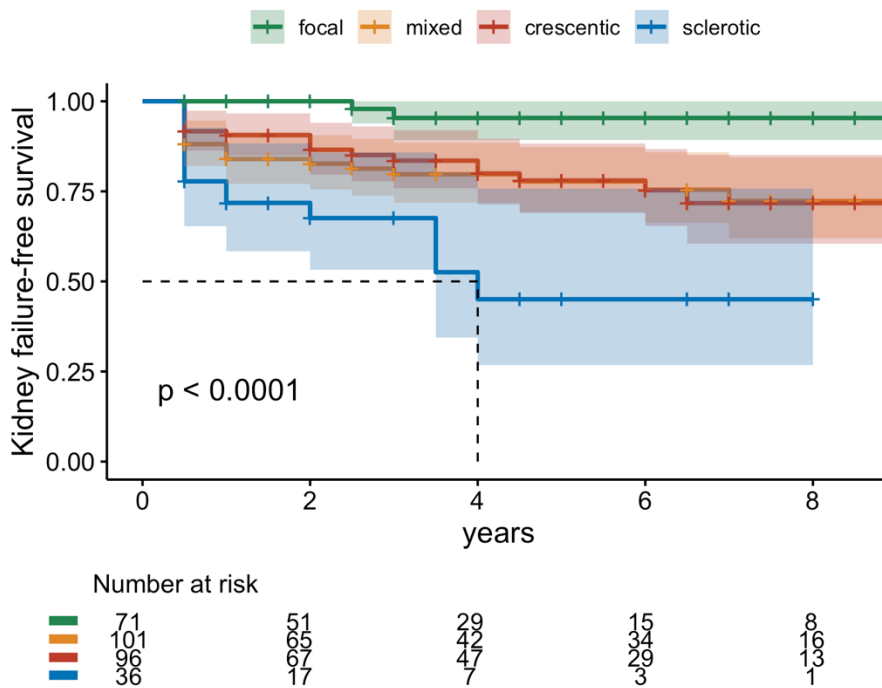


Supplementary Figure S2: eGFR at baseline, 6 and 12 months after induction in the cohort stratified by Berden histopathological classes

Dots indicate medians and lines refer to IQR of eGFR values (ml/min per 1.73 m²).



Supplementary Figure S3: Kaplan Meier curves showing time to the kidney failure outcome in the cohort stratified by Berden histopathological classes



P value refers to overall log-rank test p-value.

Pairwise comparisons using log-rank test:

focal vs. mixed: $p=0.002$

focal vs. crescentic: $p=0.005$

focal vs. sclerotic: $p<0.001$

crescentic vs. mixed: $p=0.846$

crescentic vs. sclerotic: $p=0.003$

sclerotic vs. mixed: $p=0.015$