**Supplemental Material Table of Contents**

**Supplemental Table 1**. Recruiting centers

| City | Hospital Division | No. of patients |
|---|---|---|
| **Italy** | | |
| Brescia | Division of Nephrology, Spedali Civili | 2 |
| Firenze | Division of Nephrology, Meyer Hospital | 9 |
| Firenze | Division of Internal Medicine, Careggi University Hospital | 1 |
| Genova | Division of Nephrology, IRCCS Giannina Gaslini Istitute | 22 |
| Milano | Division of Nephrology, IRCCS Cà Granda Policlinico Hospital | 3 |
| Milano | Division of Paediatric Nephrology, IRCCS Cà Granda Policlinico Hospital | 4 |
| Milano | Immunology Division, Allergy and Rheumatology Unit, San Raffaele Hospital | 1 |
| Milano | Division of Nephrology, San Carlo Borromeo Hospital | 1 |
| Parma | Division of Nephrology, Parma University Hospital | 2 |
| Roma | Rheumatology Unit, Bambino Gesù Children's Hospital | 8 |
| Trieste | Division of Paediatrics, IRCCS Burlo Garofolo Hospital | 1 |
| **Canada** | | |
| Toronto | Division of Nephrology, Hospital for Sick Children | 31* |

*****Of these 31 patients, 7 were new while the remaining 24 were included in a previous study (reference #8). The current study reports an extended follow-up for these 24 cases (median follow-up extension 68 months, range 0-86). For these patients to be included in the present study, we also required additional data as compared with the data reported in the original paper. The new data comprised: Body surface area, PVAS, lung nodules/infiltrates, WBC, proteinuria, haematuria, RPGN, hypertension, ANA, C4, relapse, time to relapse.

**Supplemental Table 2**. Differences in terms of demographics, diagnosis and induction treatment between the Italian and Canadian cohorts.

| | **Italian cohort** | **Canadian cohort** |
|---|---|---|
| No. of patients | 54 | 31 |
| Female gender, n (%) | 34 (62.9) | 21 (67.7) |
| Age at diagnosis, median (range) | 11 (4-18) | 11 (3-17) |
| Diagnosis, n (%) | | |
| MPA | 36 (66.7) | 17 (54.8) |
| GPA | 18 (33.3) | 14 (45.2) |
| | | |
| Induction treatment, n (%) | | |
| GC pulses | 43 (79.6) | 22 (71.0) |
| CYC | 47 (87.0) | 21 (67.7) |
| RTX | 6 (11.1) | 2 (6.5) |
| PEX | 8 (14.8) | 8 (25.8) |
| MMF | 4 (7.4) | 0 (0.0) |

MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; GC: glucocorticoids; CYC: cyclophosphamide; RTX: rituximab; PEX: plasma exchange; MMF: mycophenolate mofetil

**Supplemental Table 3**. Main immunosuppressive therapies used for remission induction and maintenance

| *Induction therapies* | **All (n=85)** | | **GPA (n=32)** | **MPA (n=53)** | | **Focal (n=18)** | **Crescentic (n=43)** | **Mixed (n=11)** | **Sclerotic (n=13)** |
|---|---|---|---|---|---|---|---|---|---|
| **GC alone, n (%)** | 16 (18) | | 3 (9) | 13 (25) | | 10 (55) | 3 (7) | 0 | 3 (24) |
| **GC + CYC, n (%)** | 47 (55) | | 15 (47) | 32 (60) | | 6 (33) | 26 (60) | 9 (82) | 6 (46) |
| **GC + CYC + RTX, n (%)** | 3 (4) | | 1 (3) | 2 (4) | | 0 | 3 (7) | 0 | 0 |
| **GC + CYC + PEX, n (%)** | 11 (13) | | 7 (22) | 4 (7) | | 0 | 7 (16) | 2 (18) | 2 (15) |
| **GC + CYC + RTX + PEX, n (%)** | 5 (6) | | 5 (16) | 0 | | 1 (6) | 2 (5) | 0 | 2 (15) |
| **Other, n (%)** | 3 (4) | | 1 (3) | 2 (4) | | 1 (6) | 2 (5) | 0 | 0 |
| *Drugs used for maintenance* | | | | | | | | | |
| **GC, n (%)** | 77 (91) | | 31 (97) | 46 (87) | | 15 (83) | 40 (93) | 10 (91) | 12 (92) |
| **AZA, n (%)** | 44 (52) | | 19 (59) | 25 (47) | | 8 (44) | 23 (54) | 8 (73) | 5 (39) |
| **MMF, n (%)** | 26 (31) | | 13 (41) | 13 (25) | | 2 (11) | 15 (35) | 3 (27) | 6 (46) |
| **MTX, n (%)** | 9 (11) | | 5 (16) | 4 (8) | | 4 (22) | 4 (9) | 0 (0) | 1 (8) |
| **RTX, n (%)** | 8 (9) | | 5 (16) | 3 (6) | | 1 (6) | 5 (12) | 2 (18) | 0 (0) |
| **Other, n (%)** | 3 (3) | | 0 (0) | 3 (6) | | 1 (6) | 2 (5) | 0 (0) | 0 (0) |

**Abbreviations used in the table**: GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; GC: glucocorticoids; CYC: cyclophosphamide; MMF: mycophenolate moofetil; MTX: methotrexate; RTX: rituximab; PEX: plasma exchange

Focal, crescentic, mixed and sclerotic denote the kidney histopathological classes identified according to Berden AE et al. (reference #20)

**Supplemental Table 4**. Main kidney parameters at different time-points

| | **GPA (n=32)** | **MPA (n=53)** | | **Focal (n=18)** | **Crescentic (n=43)** | **Mixed (n=11)** | **Sclerotic (n=13)** |
|---|---|---|---|---|---|---|---|
| **eGFR at baseline, *mL/min/1.73 m²*** | 40 (15-74) | 34 (16-62) | | 80 (62-105) | 23 (12-58) | 53 (36-68) | 21 (14-29) |
| **eGFR at month 6, *mL/min/1.73 m²*** | 77 (49-100) | 67 (9-108) | | 104 (81-113) | 68 (8-99) | 83 (64-109) | 11 (7-60) |
| **eGFR at last follow-up, *mL/min/1.73 m²*** | 77 (51-101) | 77 (8-112) | | 103 (83-123) | 72 (9-107) | 92 (78-107) | 10 (5-48) |
| | | | | | | | |
| **Patients on RRT at baseline, n (%)** | 2 (6) | 9 (17) | | 0 | 8 (19) | 0 | 3 (23) |
| **Patients on RRT at month 6, n (%)** | 6 (19) | 14 (26) | | 0 | 12 (28) | 1 (9) | 7 (54) |
| **Patients on RRT at last follow-up, n (%)** | 6 (19) | 19 (36) | | 1 (6) | 15 (35) | 1 (9) | 8 (62) |
| | | | | | | | |
| **Proteinuria at baseline, mg/24h** | 1950 (900-3350) | 1660 (1000-3100) | | 1200 (641-2750) | 2800 (1010-3640) | 1400 (440-2070) | 1855 (1226-3175) |
| **Proteinuria at last follow-up, mg/24h** | 265 (203-548) | 171 (100-480) | | 190 (112-380) | 200 (90-480) | 360 (155-435) | 230 (160-595) |

**Abbreviations used in the table**: GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; eGFR: estimated glomerular filtration rate; RRT: renal replacement therapy

Focal. crescentic. mixed and sclerotic denote the kidney histopathological classes identified according to Berden AE et al. (reference #20)

**Supplemental Table 5:** Prognostic indicators of kidney failure and of kidney failure/chronic kidney disease (CKD) stage 3-5 (composite outcome) analyzed using Cox regression models

| | **Risk of kidney failure** | | **Risk of kidney failure or CKD stage 3 to 5** |
|---|---|---|---|
| | *Crude HR (95% CI)* | | *Crude HR (95% CI)* |
| Sex | 1.12 (0.48 – 2.56) | | 1.34 (0.62 – 2.90) |
| Age at diagnosis | 0.98 (0.88- 1.08) | | 0.96 (0.88 – 1.06) |
| Time from symptom onset to diagnosis | 0.93 (0.84 – 1.03) | | 1.00 (0.96- 1.03) |
| Diagnosis | | | |
| GPA | Ref. | | |
| MPA | 2.18 (0.88 – 5.43) | | 1.66 (0.77 – 3.59) |
| Clinical manifestations | | | |
| Constitutional | 1.22 (0.49 – 3.05) | | 1.03 (0.46 – 2.29) |
| Arthralgia | 0.45 (0.17 – 1.20) | | 0.46 (0.19 – 1.11) |
| Weight loss | 1.40 (0.59 – 3.34) | | 1.25 (0.56 – 2.78) |
| Cardiovascular | 1.92 (0.26 – 14.25) | | 1.37 (0.19 – 10.06) |
| Hypertension | 6.15 (2.11 – 17.91) | | 3.13 (1.40 – 7.02) |
| Skin | 0.38 (0.11 – 1.26) | | 0.44 (0.15 – 1.25) |
| Purpura | 0.30 (0.04 – 2.21) | | 0.24 (0.03 – 1.73) |
| CNS | 3.53 (1.56 – 8.00) | | 2.42 (1.11 – 5.27) |
| Eye | 0.54 (0.13 – 2.30) | | 0.66 (0.20 – 2.18) |
| ENT | 1.07 (0.47 – 2.46) | | 0.93 (0.43 – 2.00) |
| Lung | 1.28 (0.59 – 2.77) | | 1.07 (0.54 – 2.15 |
| Alveolar haemorrhage | 1.82 (0.68 – 4.85) | | 1.60 (0.66 – 3.88) |
| Nodules/infiltrates | 2.17 (0.99 – 4.73) | | 1.66 (0.81 – 3.38) |
| Gastrointestinal | 0.69 (0.26-1.83) | | 1.39 (0.66 – 2.95) |
| CRP (mg/dL) | 0.98 (0.88 – 1.09) | | 0.97 (0.88 – 1.08) |
| Serum creatinine (mg/dL) | 1.24 (1.15 – 1.35) | | 1.18 (1.11 – 1.27) |
| eGFR mL/min/1.73 $m^2$ | 0.95 (0.92 – 0.97) | | 0.96 (0.94 – 0.98) |
| Proteinuria (mg/$m^2$/24 h) | 1.00 (0.99 – 1.00) | | 1.00 (0.99 – 1.00) |
| Serum albumin (g/dL) | 0.31 (0.13 – 0.72) | | 0.43 (0.21 – 0.88) |
| ANCA | | | |
| ANCA by IF | | | |
| C-ANCA | Ref. | | |
| P-ANCA | 1.51 (0.59 – 3.90) | | 1.41 (0.62 – 3.21) |
| Negative | 1.60 (0.45 – 5.68) | | 1.08 (0.33 – 3.60) |
| ANCA by ELISA | | | |
| PR3-ANCA | Ref. | | |
| MPO-ANCA | 1.59 (0.57 – 4.46) | | 1.34 (0.55 – 3.26) |
| Negative | 1.75 (0.47 – 6.53) | | 1.15 (0.34 – 3.93) |
| C3 (mg/dL) | 0.99 (0.98 – 1.01) | | 0.99 (0.98 – 1.01) |
| C4 (mg/dL) | 0.97 (0.92 – 1.03) | | 0.98 (0.94 – 1.02) |
| Histological class[§] | | | |
| Focal/mixed | Ref. | | |
| Crescentic | 6.38 (1.46 – 27.80) | | 4.71 (1.39 – 15.93) |
| Sclerotic | 11.80 (2.49 – 55.99) | | 8.88 (2.43 – 32.48) |
| Treatment | | | |
| CYC | 1.08 (0.41 – 2.85) | | 1.13 (0.46 – 2.74) |

§

| | | | |
|---|---|---|---|
| PEX | 2.65 (1.17 – 5.97) | | 2.83 (1.38 – 5.81) |
| RTX | 1.26 (0.38 – 4.21) | | 1.36 (0.48 – 3.88) |

Kidney biopsy class was defined according to Berden AE et al (reference #20)

**Abbreviations used in the table**. CKD: chronic kidney disease; HR: hazard ratio; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; CNS: central nervous system; ENT: ear-nose-throat; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; ANCA: anti-neutrophil cytoplasmic antibodies; IF: immunofluorescence; C-ANCA: cytoplasmic ANCA; P-ANCA: perinuclear ANCA; PR3-ANCA: proteinase 3-ANCA; MPO-ANCA: myeloperoxidase-ANCA; CYC, cyclophosphamide; PEX, plasma exchange; RTX, rituximab

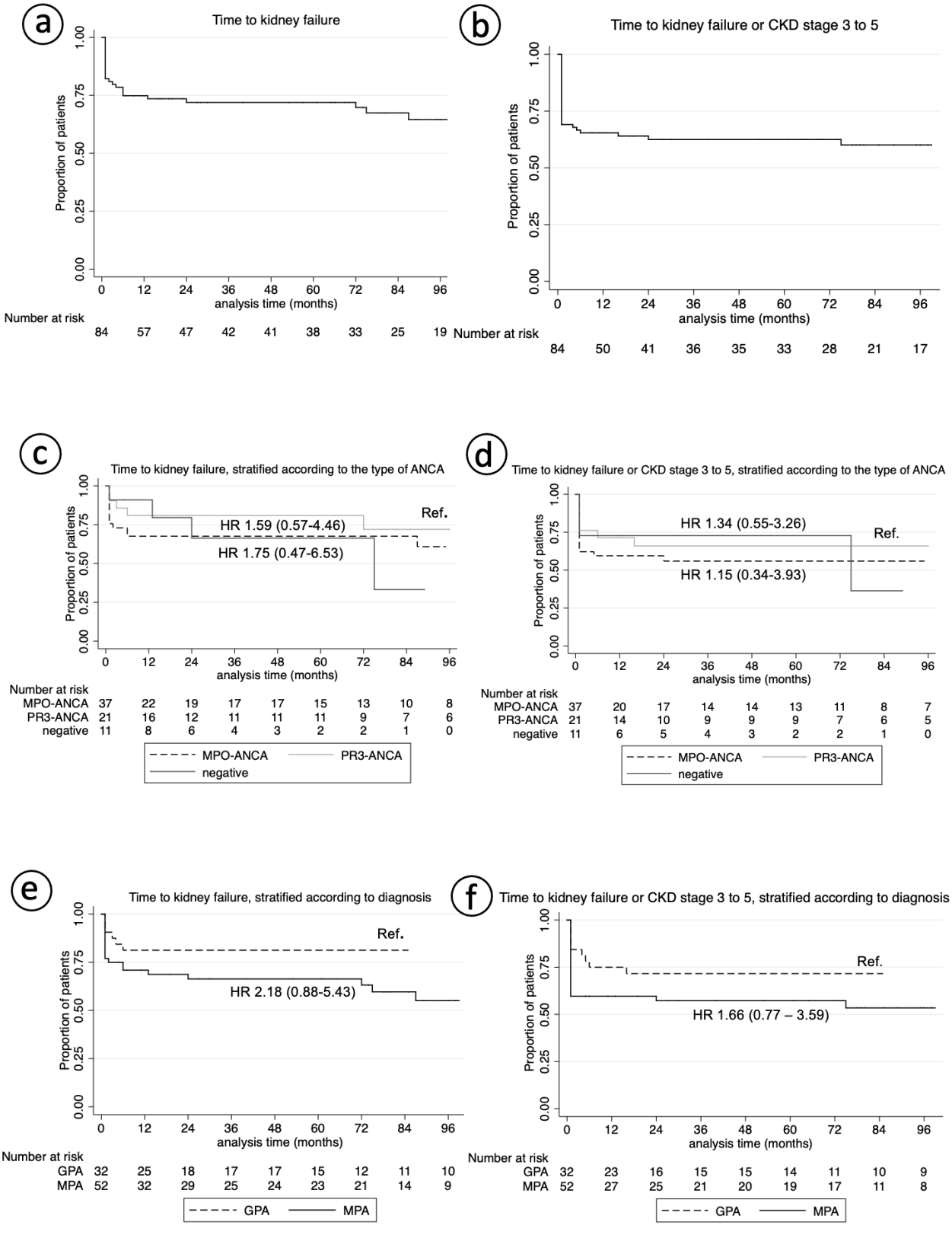
**Supplemental Table 6.** Predictors of kidney failure or kidney failure/chronic kidney disease (CKD) stage 3-5 (composite outcome) analyzed using multivariable Cox regression models

| | **Risk of kidney failure** | | **Risk of kidney failure or CKD stage 3 to 5** | |
|---|---|---|---|---|
| | *Adjusted HR (95% CI)* | *p value* | *Adjusted HR (95% CI)* | *p value* |
| Diagnosis | | | | |
| GPA | Ref. | | | |
| MPA | 2.46 (0.57-10.55) | 0.226 | 1.34 (0.46 – 3.90) | 0.594 |
| Hypertension | 3.14 (0.78-12.67) | 0.109 | 1.48 (0.54 – 4.06) | 0.446 |
| CNS involvement | 1.00 (0.23-4.35) | 1.000 | 0.93 (0.26 – 3.35) | 0.911 |
| Nodules/infiltrates | 2.33 (0.57-9.52) | 0.239 | 1.37 (0.44 – 4.21) | 0.585 |
| eGFR mL/min/1.73 $m^2$ | 0.96 (0.92-0.99) | 0.043 | 0.96 (0.93 – 0.99) | 0.005 |
| Serum albumin (g/dL) | 0.57 (0.19-1.65) | 0.296 | 1.02 (0.42 – 2.47) | 0.962 |
| Histological class[§] | | | | |
| Focal/mixed | Ref. | | | |
| Crescentic | 2.30 (0.26-19.94) | 0.450 | 1.33 (0.26 – 6.69) | 0.731 |
| Sclerotic | 4.33 (0.41-45.88) | 0.223 | 2.46 (0.42 – 14.20) | 0.316 |

HR: hazard ratio; CKD: chronic kidney disease; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; CNS: central nervous system; eGFR: estimated glomerular filtration rate

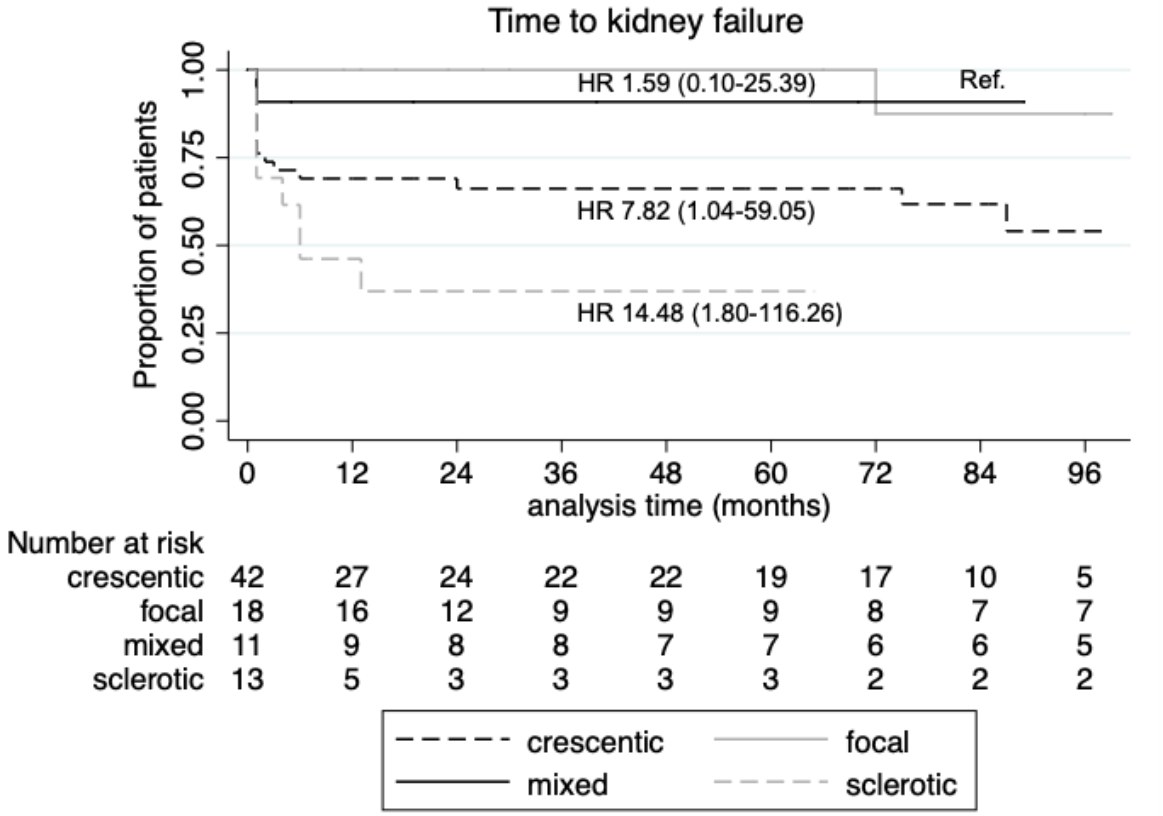
**Supplemental Figure 1. Time to kidney failure or to CKD 3-5/kidney failure, overall and according to diagnosis and ANCA specificity**

(a) Kaplan-Meier curves of the time from diagnosis to kidney failure or last follow-up ("kidney survival") in the whole cohort; (b) Kaplan-Meier curves of the time from diagnosis to chronic kidney disease stage 3-5/kidney failure in the whole cohort; (c) Kaplan-Meier curves of the time to kidney failure in patients with different ANCA specificities (MPO-ANCA, PR3-ANCA- reference category, and negative ANCA); (d) Kaplan-Meier curves of the time from diagnosis to chronic kidney disease stage 3-5/kidney failure in patients with different ANCA specificities (MPO-ANCA, PR3-ANCA- reference category, and negative ANCA); (e) Kaplan-Meier curves of the time to kidney failure in patients with MPA and GPA (reference category);(f) Kaplan-Meier curves of the time from diagnosis to chronic kidney disease stage 3-5/kidney failure in patients with MPA and GPA (reference category). The plots in c, d, e, and f also report Hazard Ratios from unadjusted Cox regression models.


a
Time to kidney failure
Proportion of patients
0.00
0.25
0.50
0.75
1.00
0 12 24 36 48 60 72 84 96
analysis time (months)
Number at risk
84 57 47 42 41 38 33 25 19
b
Time to kidney failure or CKD stage 3 to 5
Proportion of patients
0.00
0.25
0.50
0.75
1.00
0 12 24 36 48 60 72 84 96
analysis time (months)
Number at risk
84 50 41 36 35 33 28 21 17
c
Time to kidney failure, stratified according to the type of ANCA
Proportion of patients
0.00
0.25
0.50
0.75
1.00
Ref.
HR 1.59 (0.57-4.46)
HR 1.75 (0.47-6.53)
0 12 24 36 48 60 72 84 96
analysis time (months)
Number at risk
MPO-ANCA 37 22 19 17 17 15 13 10 8
PR3-ANCA 21 16 12 11 11 11 9 7 6
negative 11 8 6 4 3 2 2 1 0
MPO-ANCA
PR3-ANCA
negative
d
Time to kidney failure or CKD stage 3 to 5, stratified according to the type of ANCA
Proportion of patients
0.00
0.25
0.50
0.75
1.00
HR 1.34 (0.55-3.26)
Ref.
HR 1.15 (0.34-3.93)
0 12 24 36 48 60 72 84 96
analysis time (months)
Number at risk
MPO-ANCA 37 20 17 14 14 13 11 8 7
PR3-ANCA 21 14 10 9 9 9 7 6 5
negative 11 6 5 4 3 2 2 1 0
MPO-ANCA
PR3-ANCA
negative
e
Time to kidney failure, stratified according to diagnosis
Proportion of patients
0.00
0.25
0.50
0.75
1.00
Ref.
HR 2.18 (0.88-5.43)
0 12 24 36 48 60 72 84 96
analysis time (months)
Number at risk
GPA 32 25 18 17 17 15 12 11 10
MPA 52 32 29 25 24 23 21 14 9
GPA
MPA
f
Time to kidney failure or CKD stage 3 to 5, stratified according to diagnosis
Proportion of patients
0.00
0.25
0.50
0.75
1.00
Ref.
HR 1.66 (0.77 – 3.59)
0 12 24 36 48 60 72 84 96
analysis time (months)
Number at risk
GPA 32 23 16 15 15 14 11 10 9
MPA 52 27 25 21 20 19 17 11 8
GPA
MPA

**Supplemental Figure 2. Kidney survival in the different histological classes**

Comparison of kidney survival between patients with the four different kidney histological classes (focal class is the reference category- "Ref"). The plot also reports Hazard Ratios from unadjusted Cox regression models.



**Supplemental Figure 3. Time to relapse in the whole cohort and based on histological class, diagnosis and ANCA specificity**

(a) Kaplan-Meier curves of the time from remission to relapse or last follow-up ("time to relapse") in the whole cohort, (b) in patients with different kidney histological classes (focal/mixed is the reference category), (c) in patients with MPA and GPA (reference category), and (d) in patients with different ANCA specificities (PR3-ANCA, reference category; MPO-ANCA, and negative ANCA). The plots in b-d also report Hazard Ratios from unadjusted Cox regression models.