# Efficacy of Rituximab and Plasma Exchange in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis with Severe Renal Disease

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**Running title**: Treatment in AAV with severe renal impairment

## Supplemental material

## Table of contents

## Supplemental Tables

Supplemental Table 1 – Demographic and clinical characteristics description of patients with Anti-Neutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis (AAV) and non-severe renal disease.

| **Active Non-Severe Renal Disease in AAV (n = 216)** | **eGFR ≥ 30 mL/min/1.73m$^2$** |
|---|---|
| Age at severe renal involvement diagnosis, median (IQR) years | 58 (42-68) |
| Male, n (%) | 130 (60.2) |
| AAV, n (%) | |
| MPA | 88 (40.7) |
| GPA | 128 (59.3) |
| ANCA specificity (ELISA), n (%) | |
| MPO | 95 (44.0) |
| PR3 | 121 (56.0) |
| BVAS/WG at diagnosis, median (IQR) | 8 (7-11) |
| Renal limited disease at diagnosis, n (%) | 26 (12.0) |
| Rapidly progressive glomerulonephritis, n (%) | 47 (21.8) |
| Alveolar hemorrhage BVAS/WG at diagnosis, n (%) | 40 (18.5) |
| Cardiovascular risk factors, n (%) | |
| Arterial hypertension | 125 (57.9) |
| Diabetes mellitus | 21 (9.7) |
| Dyslipidemia | 52 (24.1) |
| BMI > 30 Kg/m$^2$ | 56 (25.9) |

Abbreviations: AAV - antineutrophil cytoplasmic antibody associated vasculitis; ANCA - anti-neutrophil cytoplasmic antibody; BVAS/WG - Birmingham vasculitis activity score for Wegener Granulomatosis; eGFR – estimated glomerular filtration rate; ELISA - enzyme linked immunosorbent assay; ESDR - end-stage renal disease; ESR - erythrocyte sedimentation rate; FU - follow-up; GPA - granulomatosis with polyangiitis; IQR - interquartile range; IV – intravenous; MPA - microscopic polyangiitis; MPO – myeloperoxidase; n- number; PLEX - plasma exchange; PR3 – proteinase 3; RPGN – rapidly progressive glomerulonephritis.

Supplemental Table 2 - Multivariable analysis of predictive factors for severe renal disease in patients with Anti-Neutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis (AAV).

| | Multivariable Logistic Regression | |
|---|---|---|
| | OR (95% CI) | p-value |
| Age >60 years at severe renal involvement diagnosis | 1.738 (1.056 – 2.860) | **0.030** |
| Arterial hypertension | 1.789 (1.075 – 2.980) | **0.025** |
| Diabetes mellitus | 2.459 (1.251 – 4.834) | **0.009** |
| BMI >30 kg/m$^2$ | 2.505 (1.458 – 4.303) | **0.001** |
| Renal limited disease | 4.154 (2.185 – 7.897) | **<0.0001** |
| Hemoglobin (reduction of 0.5 g/dl) | 1.730 (1.499 – 1.996) | **<0.0001** |
| MPO-ANCA | 1.571 (0.958 – 2.574) | **0.073** |

**Abbreviations:** ANCA – anti-neutrophil cytoplasmic antibody; BMI – body mass index; CI – confidence interval; MPO – myeloperoxidase; OR – Odds ratio. *p-value < 0.05 is considered significant (Multivariable Logistic Regression).

Supplemental Table 3 – Analysis of the distribution of the variables included in the propensity score matching analysis in patients with AAV and active severe renal disease treated with cyclophosphamide (CYC) or rituximab (RTX) for remission induction.

| *Variables included in the Propensity-Score Matching Analysis** | *Pre-Matching* | | | *Post-Matching** | | |
|---|---|---|---|---|---|---|
| | CYC n = 161 (64.1%) | RTX n = 64 (25.5%) | ***Std. Diff. (%)* | CYC n = 60(37.3%) | RTX n = 60(93.8%) | ***Std. Diff. (%)* |
| **Alveolar hemorrhage BVAS/WG at diagnosis, n (%)** | 27 (16.8) | 10 (15.6) | **3.3** | 8 (13.3) | 8 (13.3) | **0.0** |
| **eGFR at diagnosis of renal involvement < 15 mL/min/1.73m$^2$, n (%)** | 71 (44.1) | 24 (37.5) | **-13.5** | 22 (36.7) | 22 (36.7) | **0.0** |
| **IV methylprednisolone at induction remission** | 95 (59.0) | 52 (81.3) | **57.0** | 50 (83.3) | 50 (83.3) | **0.0** |
| **Plasma exchange therapy** | 37 (23.0) | 14 (21.9) | **-2.7** | 14 (23.3) | 14 (23.3) | **0.0** |

*** The pairs used for the variables comparison after matching were obtained by analyzing the outcome of Remission at 6 months.** Standardized mean differences.**

**Abbreviations**: AAV - antineutrophil cytoplasmic antibody associated vasculitis; ANCA - anti-neutrophil cytoplasmic antibody; BVAS/WG - Birmingham vasculitis activity score for Wegener Granulomatosis; eGFR – estimated glomerular filtration rate [**GFR is estimated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) method]**; ELISA - enzyme linked immunosorbent assay; ESRD - end-stage renal disease; ESR - erythrocyte sedimentation rate; FU - follow-up; GPA - granulomatosis with polyangiitis; IQR - interquartile range; IV – intravenous; MPA - microscopic polyangiitis; MPO – myeloperoxidase; n- number; PLEX - plasma exchange; PR3 – proteinase 3; RPGN – rapidly progressive glomerulonephritis.

Supplemental Table 4 – Post propensity score matching outcomes comparison of patients with AAV and active severe renal disease treated with cyclophosphamide (CYC) or rituximab (RTX) for remission induction.

| | CYC | RTX | *p-value |
|---|---|---|---|
| **Outcomes** | | | |
| **Vasculitis activity** | | | |
| Remission - 6 months [CYC n = 60/161 (37.3%) vs. RTX n = 60/64 (93.8%)] | 45 (75.0) | 49 (81.7) | 0.375 |
| Complete remission - 6 months [CYC n = 60/161 (37.3%) vs. RTX n = 60/64 (93.8%)] | 12 (25.0) | 18 (31.6) | 0.457 |
| Relapse - 12 months [CYC n = 56/161 (34.8%) vs. RTX n = 56/64 (87.5%)] | 8 (14.3) | 13 (23.2) | 0.226 |
| Death - 24 months [CYC n = 64/161 (39.8%) vs. RTX n = 64/64 (100%)] | 19 (29.7) | 12 (18.8) | 0.149 |
| **Renal** | | | |
| ESRD - 24 months [CYC n = 64/161 (39.8%) vs. RTX n = 64/64 (100%)] | 16 (25.0) | 10 (15.6) | 0.187 |
| **Combined events of ESRD and/or death** | | | |
| 18 months [CYC n = 64/161 (39.8%) vs. RTX n = 64/64 (100%)] | 15 (23.4) | 10 (15.6) | 0.265 |
| 24 months [CYC n = 64/161 (39.8%) vs. RTX n = 64/64 (100%)] | 18 (28.1) | 14 (21.9) | 0.414 |

**Abbreviations**: AAV - antineutrophil cytoplasmic antibody associated vasculitis; ANCA - anti-neutrophil cytoplasmic antibody; BVAS/WG - Birmingham vasculitis activity score for Wegener Granulomatosis; eGFR – estimated glomerular filtration rate; ELISA - enzyme linked immunosorbent assay; ESRD - end-stage renal disease; ESR - erythrocyte sedimentation rate; FU - follow-up; GPA - granulomatosis with polyangiitis; IQR - interquartile range; IV – intravenous; MPA - microscopic polyangiitis; MPO – myeloperoxidase; n- number; PLEX - plasma exchange; PR3 – proteinase 3; RPGN – rapidly progressive glomerulonephritis. * The pairs resultant from the propensity score matching were obtained by the analysis of the outcome of Combined Events of ESRD and/or death at 18 months. ***p*-value < 0.05 is considered significant (Pearson $\chi^2$ test for categorical variables, t-test for continuous variables with normal distribution and Mann-Whitney U test for continuous variables with skewed distribution).

Supplemental Table 5 – Clinical characteristics, and outcomes of patients with AAV and active severe renal disease treated stratified according to eGFR at admission: <15 mL/min/1.73m2 vs. ≥ 15 to 30 mL/min/1.73m$^2$.

| **Active Severe Renal Disease in AAV (n = 251)** | **eGFR ≥ 15 and < 30 mL/min/1.73m$^2$ n = 147 (58.6%)** | **eGFR <15 mL/min/1.73m$^2$ n = 104 (41.4%)** | ***p-value*** |
|---|---|---|---|
| Age at severe renal involvement diagnosis, median (IQR) years | 65 (53-74) | 68 (59-75) | 0.070 |
| Male, n (%) | 72 (49.0) | 56 (53.8) | 0.447 |
| AAV, n (%) | | | 0.798 |
| MPA | 81 (55.1) | 59 (56.7) | |
| GPA | 66 (44.9) | 45 (43.3) | |
| ANCA specificity (ELISA), n (%) | | | 0.374 |
| MPO | 88 (59.9) | 68 (65.4) | |
| PR3 | 59 (40.1) | 36 (34.6) | |
| BVAS/WG at diagnosis, median (IQR) | 8 (7-11) | 7 (7-9) | **0.025** |
| Renal limited disease at diagnosis, n (%) | 38 (25.9) | 46 (44.2) | **0.002** |
| Rapidly progressive glomerulonephritis, n (%) | 52 (35.4) | 45 (43.3) | 0.363 |
| Alveolar hemorrhage BVAS/WG at diagnosis, n (%) | 27 (18.4) | 13 (12.5) | 0.211 |
| Cardiovascular risk factors, n (%) | | | |
| Arterial hypertension | 108 (73.5) | 79 (76.0) | 0.655 |
| Diabetes mellitus | 38 (25.9) | 18 (17.3) | 0.109 |
| Dyslipidemia | 50 (34.0) | 41 (39.4) | 0.380 |
| BMI > 30 Kg/m$^2$ | 94 (63.5) | 41 (51.9) | 0.259 |
| Laboratory findings | | | |
| Hemoglobin, mean (sd) g/dL | 9.9 (8.9 – 11.3) | 9.5 (8.6 – 10.7) | 0.076 |
| ESR > 22 mm/1$^{st}$h, n (%) | 86 (78.2) | 59 (86.8) | 0.152 |
| Remission-induction therapies, n (%) | | | |
| Cyclophosphamide | 90 (61.2) | 71 (68.3) | 0.502 |
| Rituximab | 40 (27.2) | 24 (23.1) | |
| IV methylprednisolone at induction remission | 90 (61.2) | 67 (64.4) | 0.606 |
| Plasma exchange therapy | 22 (15.0) | 29 (27.9) | **0.012** |
| Maintenance treatment, n (%) | | | 0.135 |
| Azathioprine | 49 (33.3) | 30 (29.4) | |
| Mycophenolate mofetil | 78 (53.1) | 65 (63.7) | |
| Rituximab | 20 (13.6) | 7 (6.9) | |
| Other | - | 2 (1.9) | |
| **Outcomes** | | | |
| **Vasculitis, n (%)** | | | |
| Remission | | | |
| At 6 months | 102 (71.8) | 66 (64.7) | 0.236 |
| Total | 124 (91.9) | 78 (86.7) | 0.208 |
| Renal remission | | | |
| At 6 months | 108 (81.2) | 46 (59.0) | **<0.0001** |
| Total | 123 (91.1) | 77 (85.6) | 0.194 |
| Complete remission | | | |
| At 6 months | 34 (27.0) | 12 (14.8) | **0.040** |
| Total | 82 (55.8) | 37 (35.6) | **0.001** |
| Relapse | | | |
| At 12 months | 23 (16.4) | 9 (9.7) | 0.470 |
| Total | 34 (23.1) | 19 (18.3) | 0.345 |
| Renal relapse | 27 (79.4) | 19 (100.0) | 0.169 |
| Death | | | |
| At 24 months | 10 (6.8) | 12 (11.5) | 0.191 |
| Total | 33 (22.4) | 29 (27.9) | 0.325 |
| **Renal, n (%)** | | | |
| ESRD | | | |
| At 24 months | 19 (12.9) | 40 (38.5) | **<0.0001** |
| Total | 31 (21.1) | 47 (45.2) | **<0.0001** |
| Dialysis within 4 weeks | 11 (7.5) | 31 (29.8) | **<0.0001** |
| Renal function recovery after 6 months to an eGFR > 30 mL/min/1.73m$^2$ | 53 (53.0) | 25 (41.7) | 0.165 |
| **Combined events of ESRD and/or death, n (%)** | | | |
| At 18 months ) | 24 (16.3) | 43 (41.3) | **<0.0001** |
| At 24 months | 26 (17.7) | 44 (42.3) | **<0.0001** |
| Total | 55 (37.4) | 60 (57.7) | **0.001** |

***p*-value < 0.05 is considered significant (Pearson $\chi^2$ test for categorical variables, t-test for continuous variables with normal distribution and Mann-Whitney U test for continuous variables with skewed distribution).**
**# - "Total" "** refers to the number of occurrence during all follow up time.

**Abbreviations:** AAV - antineutrophil cytoplasmic antibody associated vasculitis; ANCA - anti-neutrophil cytoplasmic antibody; BVAS/WG - Birmingham vasculitis activity score for Wegener Granulomatosis; eGFR – estimated glomerular filtration rate [**GFR is estimated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) method];** ELISA - enzyme linked immunosorbent assay; ESDR - end-stage renal disease; ESR - erythrocyte sedimentation rate; FU - follow-up; GPA - granulomatosis with polyangiitis; IQR - interquartile range; IV – intravenous; MPA - microscopic polyangiitis; MPO – myeloperoxidase; n- number; PLEX - plasma exchange; PR3 – proteinase 3; RPGN – rapidly progressive glomerulonephritis.

**Population follow up:**
6 months – No PLEX: n=172 vs. PLEX: n=45;
12 months – No PLEX: n=157 vs. PLEX: n=45;
18 months – No PLEX: n=147 vs. PLEX: n=43;
24 months – No PLEX: n=142 vs. PLEX: n=39.

Supplemental Table 6 - Analysis of the distribution of the variables included in the propensity score matching analysis in patients with AAV and active severe renal disease according with the status of treatment with plasma exchange (PLEX).

| *Variables included in the Propensity-Score Matching Analysis** | *Pre-Matching* | | | *Post-Matching** | | |
|---|---|---|---|---|---|---|
| | No PLEX n = 200 (79.7%) | PLEX n = 51 (20.3%) | ***Std. Diff. (%)* | No PLEX n = 45 (22.5%) | PLEX n = 45 (88.2%) | ***Std. Diff. (%)* |
| **Alveolar hemorrhage BVAS/WG at diagnosis, n (%)** | 25 (12.5) | 15 (29.4) | **42.4** | 9 (20.0) | 9 (20.0) | **0.0** |
| **eGFR at diagnosis of renal involvement < 15 mL/min/1.73m$^2$, n (%)** | 75 (37.5) | 29 (56.9) | **39.6** | 23 (51.1) | 23 (51.1) | **0.0** |
| **IV methylprednisolone at induction remission** | 111 (55.5) | 46 (90.2) | **84.7** | 40 (88.9) | 40 (88.9) | **0.0** |
| **Cyclophosphamide** | 124 (62.0) | 37 (72.5) | **22.5** | 31 (68.9) | 31 (68.9) | **0.0** |
| **Rituximab** | 50 (25.0) | 14 (27.5) | **5.7** | 14 (31.1) | 14 (31.1) | **0.0** |

*** The pairs used for the variables comparison after matching were obtained by analyzing the outcome of Combined events at 18 months. ** Standardized mean differences.**

**Abbreviations**: AAV - antineutrophil cytoplasmic antibody associated vasculitis; ANCA - anti-neutrophil cytoplasmic antibody; BVAS/WG - Birmingham vasculitis activity score for Wegener Granulomatosis; eGFR – estimated glomerular filtration rate [**GFR is estimated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) method**]; ELISA - enzyme linked immunosorbent assay; ESRD - end-stage renal disease; ESR - erythrocyte sedimentation rate; FU - follow-up; GPA - granulomatosis with polyangiitis; IQR - interquartile range; IV – intravenous; MPA - microscopic polyangiitis; MPO – myeloperoxidase; n- number; PLEX - plasma exchange; PR3 – proteinase 3; RPGN – rapidly progressive glomerulonephritis.

Supplemental Table 7 – Post propensity score matching outcomes comparison of patients with AAV and active severe renal disease according with the status of treatment with plasma exchange (PLEX).

| | No PLEX | PLEX | *p-value |
|---|---|---|---|
| **Outcomes** | | | |
| **Vasculitis activity** | | | |
| Remission – 6 months | | | |
| [No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%)] | 34 (75.6) | 30 (66.7) | 0.352 |
| Complete remission – 6 months | | | |
| [No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%)] | 6 (15.8) | 11 (26.8) | 0.233 |
| Relapse – 12 months | | | |
| [No PLEX n = 41/200 (20.5%) vs. PLEX n = 41/51 (80.4%)] | 4 (9.8) | 7 (17.1) | 0.331 |
| Death – 24 months | | | |
| [No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%)] | 7 (15.6) | 4 (8.9) | 0.334 |
| **Renal** | | | |
| ESRD - 24 months - No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%) | 13 (28.9) | 14 (31.1) | 0.818 |
| [No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%)] | | | |
| **Combined events of ESRD and/or death** | | | |
| 18 months | | | |
| [No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%)] | | | |
| 24 months | 15 (33.3) | 15 (33.3) | **1.000** |
| [No PLEX n = 45/200 (22.5%) vs. PLEX n = 45/51 (88.2%)] | 15 (33.3) | 15 (33.3) | **1.000** |

**Abbreviations**: AAV - antineutrophil cytoplasmic antibody associated vasculitis; ANCA - anti-neutrophil cytoplasmic antibody; BVAS/WG - Birmingham vasculitis activity score for Wegener Granulomatosis; eGFR – estimated glomerular filtration rate; ELISA - enzyme linked immunosorbent assay; ESRD - end-stage renal disease; ESR - erythrocyte sedimentation rate; FU - follow-up; GPA - granulomatosis with polyangiitis; IQR - interquartile range; IV – intravenous; MPA - microscopic polyangiitis; MPO – myeloperoxidase; n- number; PLEX - plasma exchange; PR3 – proteinase 3; RPGN – rapidly progressive glomerulonephritis. * The pairs resultant from the propensity score matching were obtained by the analysis of the outcome of Combined Events of ESRD and/or death at 18 months. ***p*-value < 0.05 is considered significant (Pearson $\chi^2$ test for categorical variables, t-test for continuous variables with normal distribution and Mann-Whitney U test for continuous variables with skewed distribution).

Supplemental Table 8 - Multivariable analysis of predictive factors for combined events of ESRD and/or Death at 18 months in patients with Anti-Neutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis (AAV) with active severe renal disease.

| | Multivariable Cox Regression | |
|---|---|---|
| | IRR (95% CI) | p-value |
| eGFR < 15 mL/min/1.73m$^2$ at diagnosis of severe renal involvement | 3.092 (1.493 – 6.401) | **0.002** |
| Renal function recovery for eGFR > 30 mL/min/1.73m$^2$ at 6 months | 0.274 (0.118 – 0.637) | **0.003** |
| Renal remission at 6 months | 0.402 (0.179 - 0.902) | **0.027** |

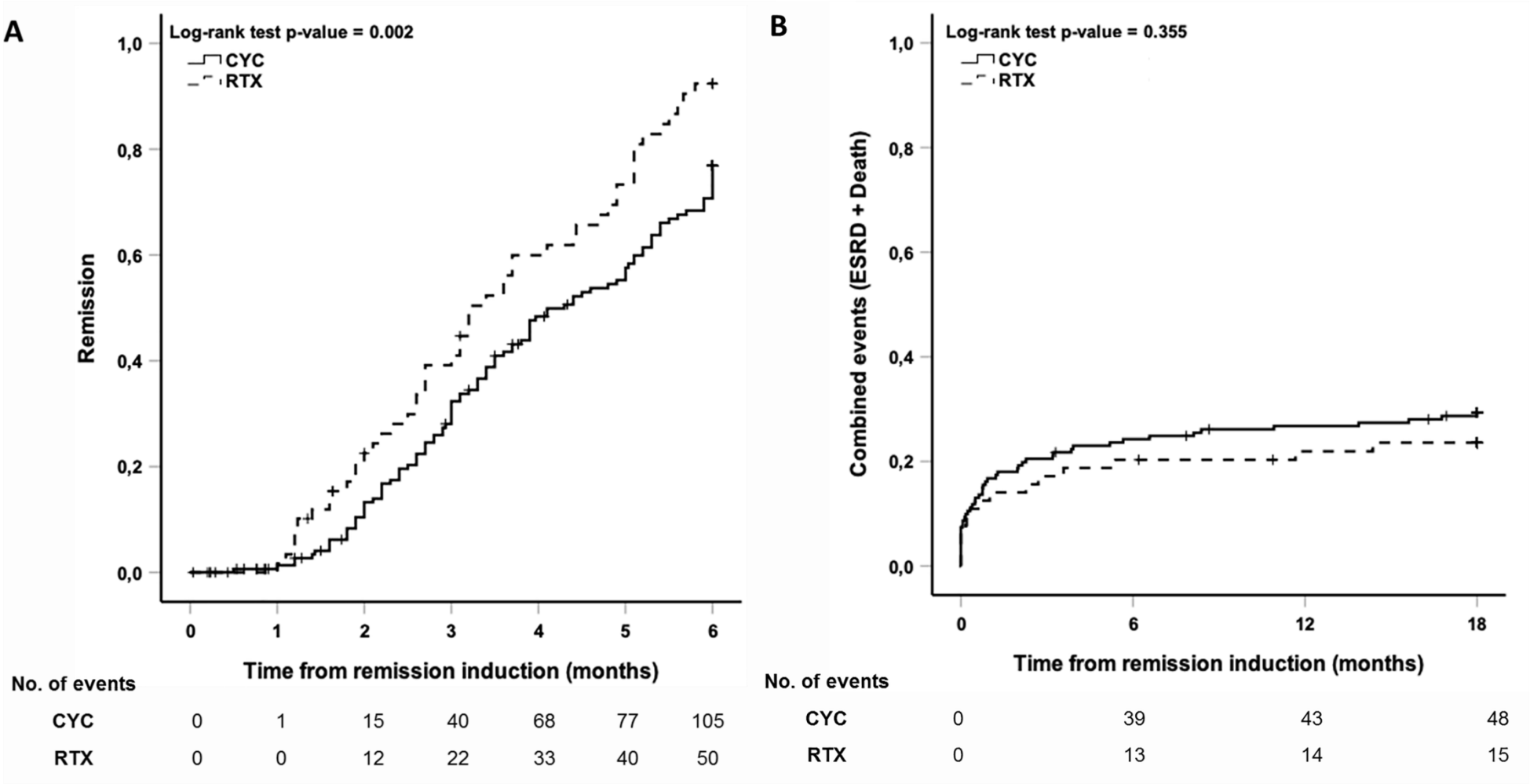
CI – confidence interval; eGFR – estimated glomerular filtration; IRR – incidence rate ratio. *p-value < 0.05 is considered significant (Uni - and Multivariable Cox Regression).

Supplemental Table 9 – Risk for the outcome stratified by treatment after propensity score matching analysis and adjusted per decade (1996-2005 vs. 2006-2015).

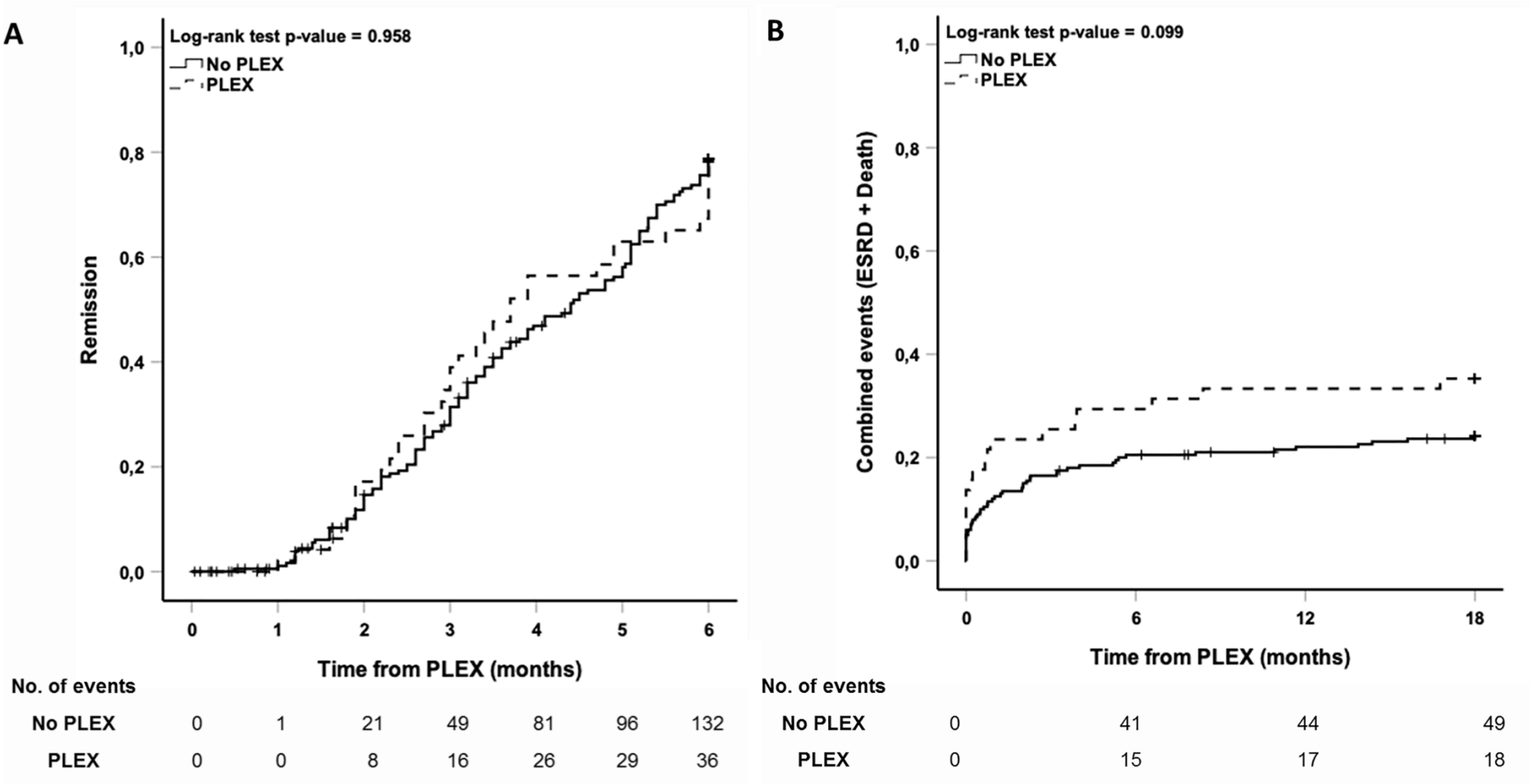
| | Post-Propensity Score Matching Analysis | | | |
|---|---|---|---|---|
| | Logistic regression | | Cox regression | |
| | OR (95% CI) | p-value | IRR (95% CI) | p-value |
| Remission at 6M | | | | |
| RTX vs. CYC | 1.210 (0.442 – 3.316) | 0.711 | 1.291 (0.799 – 2.086) | 0.297 |
| PLEX vs. No PLEX | 0.615 (0.240 – 1.575) | 0.311 | 0.691 (0.411 – 1.161) | 0.691 |
| Relapse at 12 months | | | | |
| RTX vs. CYC | 2.075 (0.599 – 7.192) | 0.096 | 2.112 (0.805 – 5.542) | 0.129 |
| PLEX vs. No PLEX | 2.118 (0.554 – 8.105) | 0.273 | 2.075 (0.599 – 7.192) | 0.250 |
| Combined events of ESRD and/or death at 18M | | | | |
| RTX vs. CYC | 1.429 (0.522 – 3.916) | 0.488 | 1.342 (0.569 – 3.166) | 0.502 |
| PLEX vs. No PLEX | 1.152 (0.469 – 2.831) | 0.758 | 1.074 (0.515 – 2.241) | 0.850 |
| Survival at 24 months | | | | |
| RTX vs. CYC | 1.839 (0.496 – 6.825) | 0.362 | 1.693 (0.496 – 5.776) | 0.401 |
| PLEX vs. No PLEX | 0.560 (0.146 – 2.147) | 0.398 | 0.573 (0.163 – 2.012) | 0.385 |
| ESRD at 24 months | | | | |
| RTX vs. CYC | 0.888 (0.327 – 2.414) | 0.816 | 0.904 (0.375 – 2.176) | 0.821 |
| PLEX vs. No PLEX | 1.240 (0.490 – 3.134) | 0.649 | 1.101 (0.516 – 2.350) | 0.804 |
| Combined events of ESRD and/or death at 24M | | | | |
| RTX vs. CYC | 0.853 (0.349 – 2.082) | 0.727 | 0.887 (0.411 – 1.915) | 0.761 |
| PLEX vs. No PLEX | 1.024 (0.421 – 2.491) | 0.958 | 0.999 (0.485 – 2.057) | 0.998 |

CI – confidence interval; CYC – cyclophosphamide; ESRD – end stage renal disease; IRR – incidence rate ratio; OR – odds ration; PLEX – Plasma Exchange; n- number; RTX - Rituximab. *$p$-value < 0.05 is considered significant.

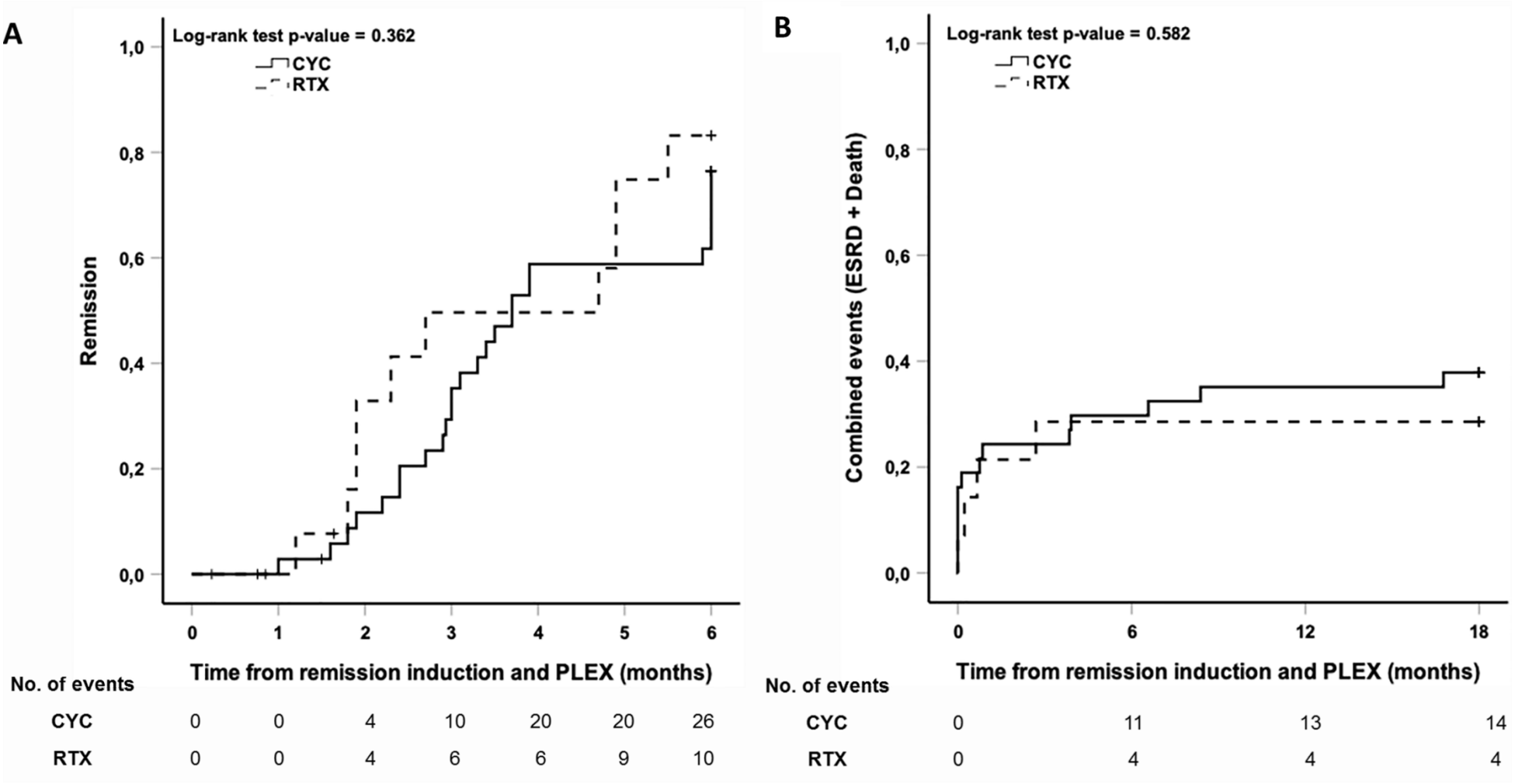
**Supplemental Fig. 1**



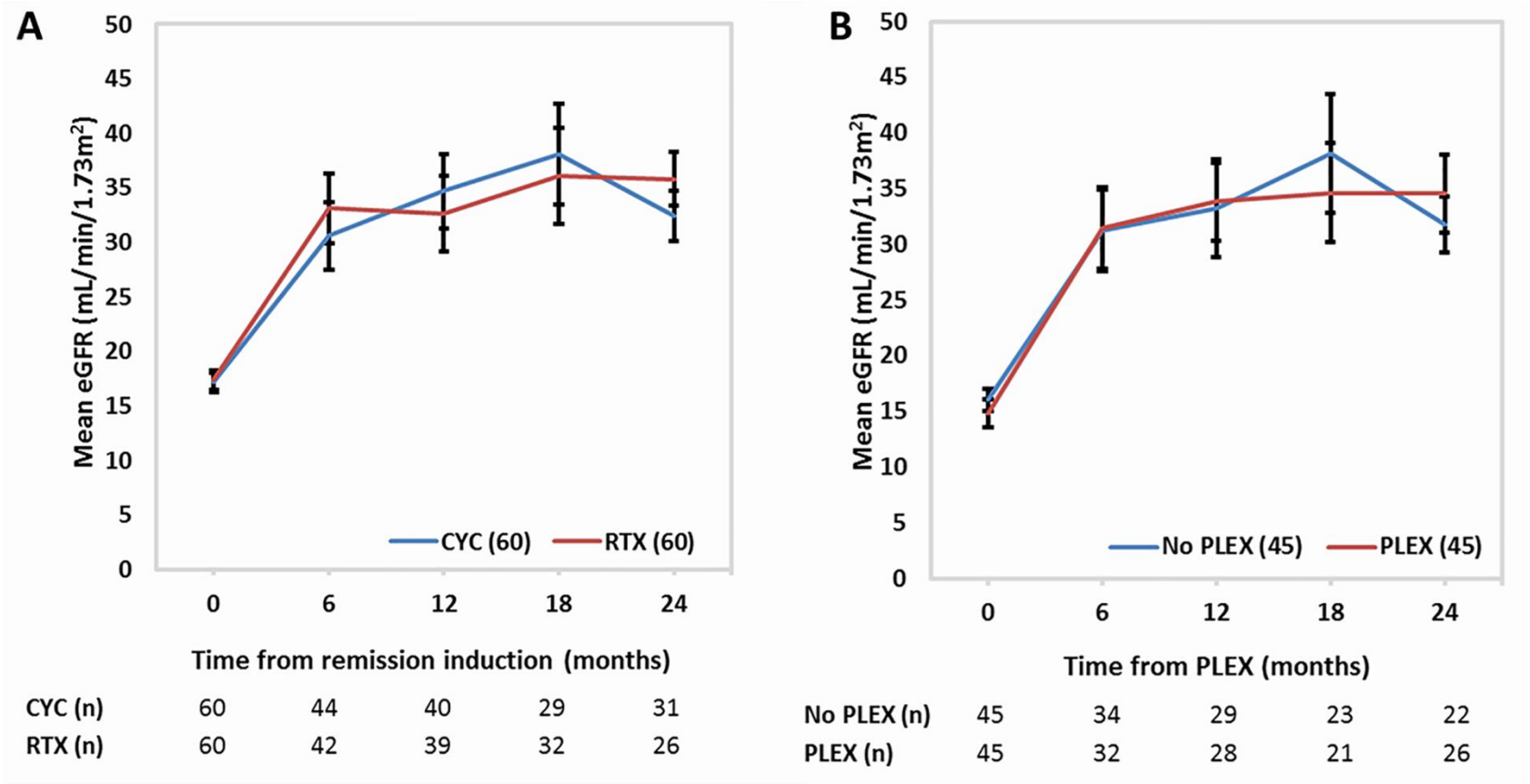
**Supplemental Fig. 2**



**Supplemental Fig. 3**



**Supplemental Fig. 4**



**Supplemental figures legends**

**Supplemental Fig. 1 -** Before propensity score matching Kaplan Meier plots of remission achieved over 6 months after initiating remission-induction therapy (1A), and combined events (ESRD and/or death) at 18 months (1B), according with the remission-induction immunosuppression - CYC vs. RTX and before propensity score matching analysis. (Abbreviations used: CYC - cyclophosphamide; ESRD – end-stage renal disease; RTX - rituximab).

**Supplemental Fig. 2 -** Before propensity score matching Kaplan Meier plots of remission achieved over 6 months after initiating remission-induction therapy (2A), and combined events (ESRD and/or death) at 18 months (2B), according with the status of treatment or no treatment with PLEX and before propensity score matching analysis. (Abbreviations used: ESRD – end-stage renal disease; PLEX - plasma exchange).

**Supplemental Fig. 3 –** Before propensity score matching Kaplan Meier plots of remission achieved over 6 months after initiating remission-induction therapy (3A), and combined events (ESRD and/or death) at 18 months (3B), for patients treated with PLEX stratified by remission-induction immunosuppression - CYC vs. RTX. (Abbreviations used: CYC - cyclophosphamide; ESRD – end-stage renal disease; PLEX - plasma Exchange; RTX - Rituximab).

**Supplemental Fig. 4 -** eGFR at baseline, and 6, 12, 18 and 24 months post-diagnosis for severe renal involvement in after PS matching. Estimates for the mean and SEM of eGFR (milliliters per minute per $1.73m^2$) at baseline and 6, 12 and 18 months after beginning of remission-induction therapy for each treatment group: 4A. CYC versus RTX (mean eGFR at baseline – 17.2 vs. 17.9 mL/min/$1.73m^2$, p = 0.556); 4B. PLEX versus No PLEX (mean eGFR at baseline - 14.9 vs. 16.1 mL/min/$1.73m^2$, p = 0.446). GFR is estimated using CKD-EPI method. (Abbreviations used: CKD-EPI - Chronic kidney disease epidemiology collaboration formula, CYC - cyclophosphamide, eGFR - estimated glomerular filtration rate, PLEX - plasma exchange, RTX - rituximab, SEM - standard error of the mean).