MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS: IS THERE A CORRELATION BETWEEN HISTOPATHOLOGY PATTERN AND TREATMENT OUTCOME? A SINGLE CENTER EXPERIENCE

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BACKGROUND

Membranoproliferative glomerulonephritis (MPGN) is a pattern of injury that has multiple aetiologies even in the setting of the same disease subtype. For this reason, a specific treatment protocol has never been compiled. We aimed to evaluate the effect of the most recent treatment options in terms of proteinuria reduction and renal function preservation. We also assessed the rate of adverse events associated with different therapeutic regimens and evaluated predictors of efficacy.

METHODS

We performed an observational, retrospective study evaluating all kidney biopsies performed in our center between 2002 and 2015 consistent with an histological MPGN diagnosis, either primary or secondary. We also evaluated biochemical and physical characteristics of the patients at the time of biopsy and at 30, 90 and 180 days after the beginning of the treatment. Complete remission was defined as a proteinuria value lower than 0.5 g/day.

Every histological specimen was evaluated for glomerular sclerosis and the resulting score correlated with biochemical parameters.
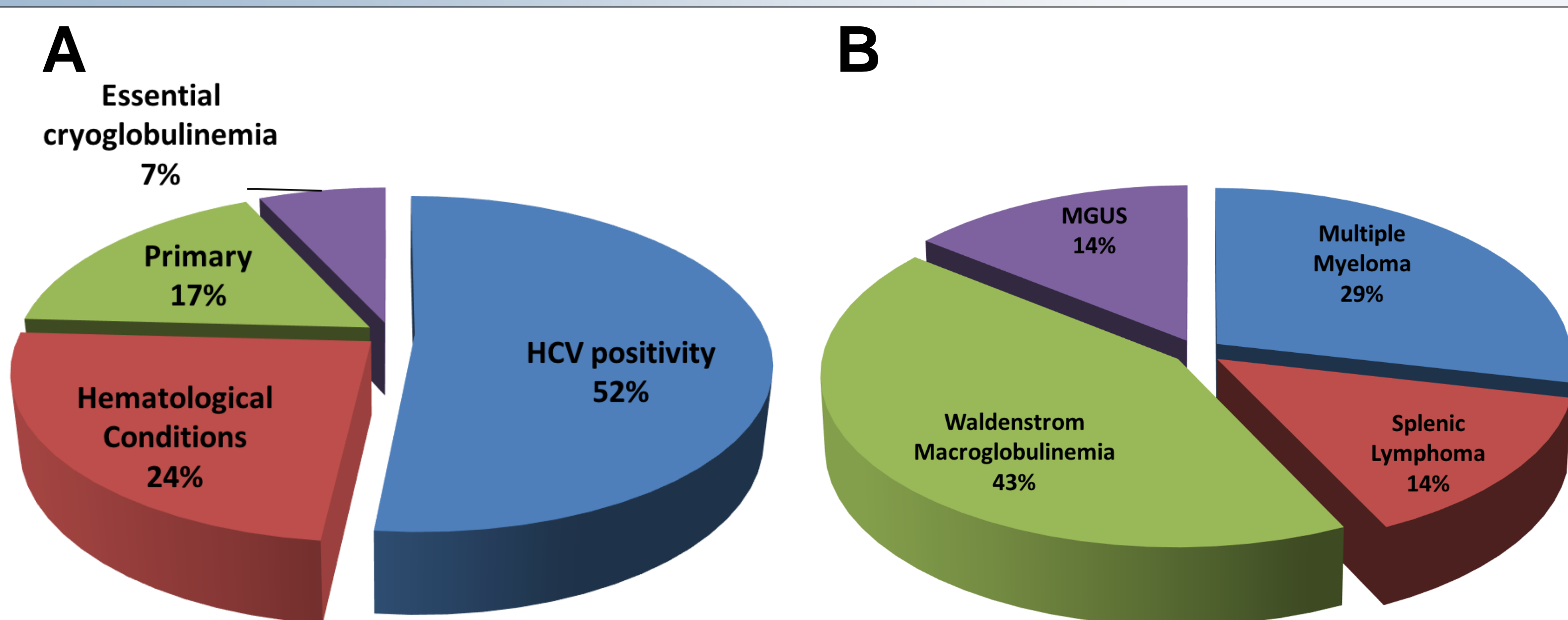
RESULTS

Figure 1. A. *Aetiology of MPGN in our cohort* **B.** *Detail of hematological conditions responsible for MPGN in our cohort.*

Number of patients	29
Male(%)	18(62%)
Female(%)	11(38%)
Age (years)	68,65±12,43
IgA (mg/dl)	756,40±2740,00
IgG (mg/dl)	5104,00±21155
IgM (mg/dl)	1337±5405
C3 (mg/dl)	87,84±25,12
C4 (mg/dl)	16,18±15,88
Serum creatinine at diagnosis (mg/dl)	2,26±1,18
Proteinuria at diagnosis (g/day)	4,46±4,25
CDK-epi eGRF at diagnosis (mL/min/1,73 m^2)	38,00±18,16
Blood cholesterol at diagnosis (mg/dl)	227,6±54,05
Systolic blood pressure at diagnosis (mmHg)	154,80±31,17
Diastolic blood pressure at diagnosis (mmHg)	79,35± 20,80
Glomerulosclerosis percentage (%)	44,40±17.07
Grade of glomerulosclerosis	2,29±0,78

Table 1. *Data collected at the time of diagnosis, considered concurrent to time of biopsy. Data are presented as mean±SD.*

	Rituximab	Other Therapies		
		Steroids/Steroids + Cyclophosphamide	Immunosuppressive Therapies (MMF, Tacrolimus)	Other
Number of patients	12	9	2	6
Partial Percentage (%)		31	7	21
Overall Percentage (%)	41	59		

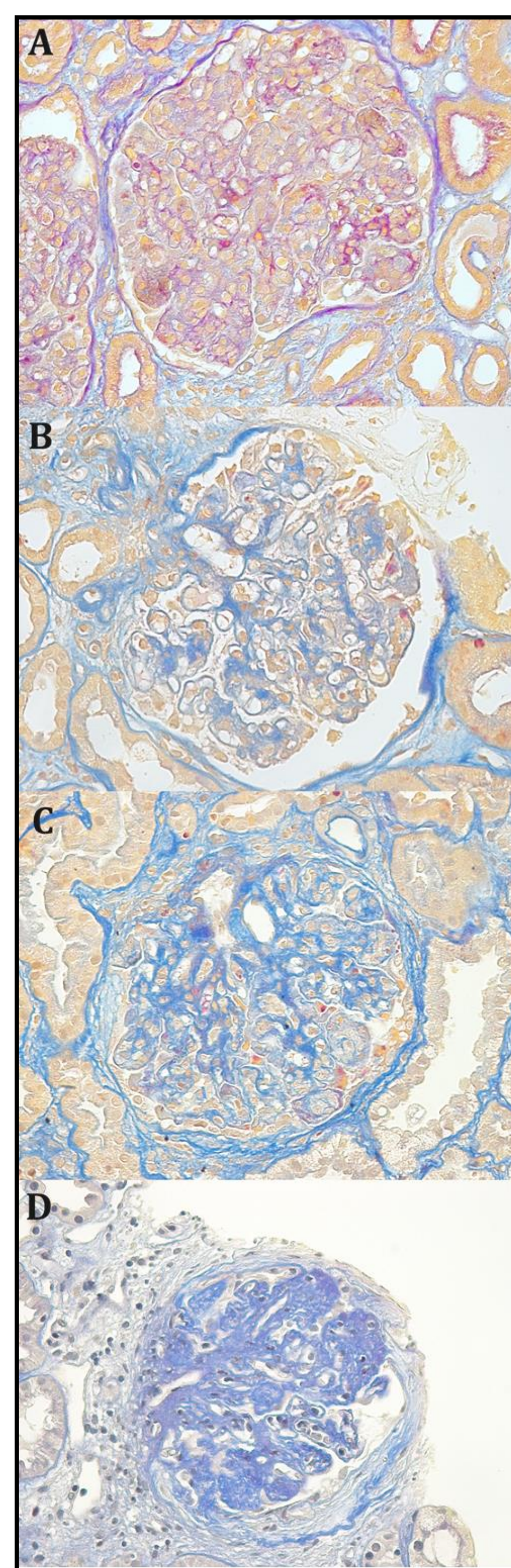**Table 2.** *Treatments performed in our population.*

Figure 2.
A. *Average glomerular appearance in Grade 1;*
B. *Average glomerular appearance in Grade 2*
C. *Average glomerular appearance in Grace 3*
D. *Typical appearance of very advanced glomerulosclerosis*

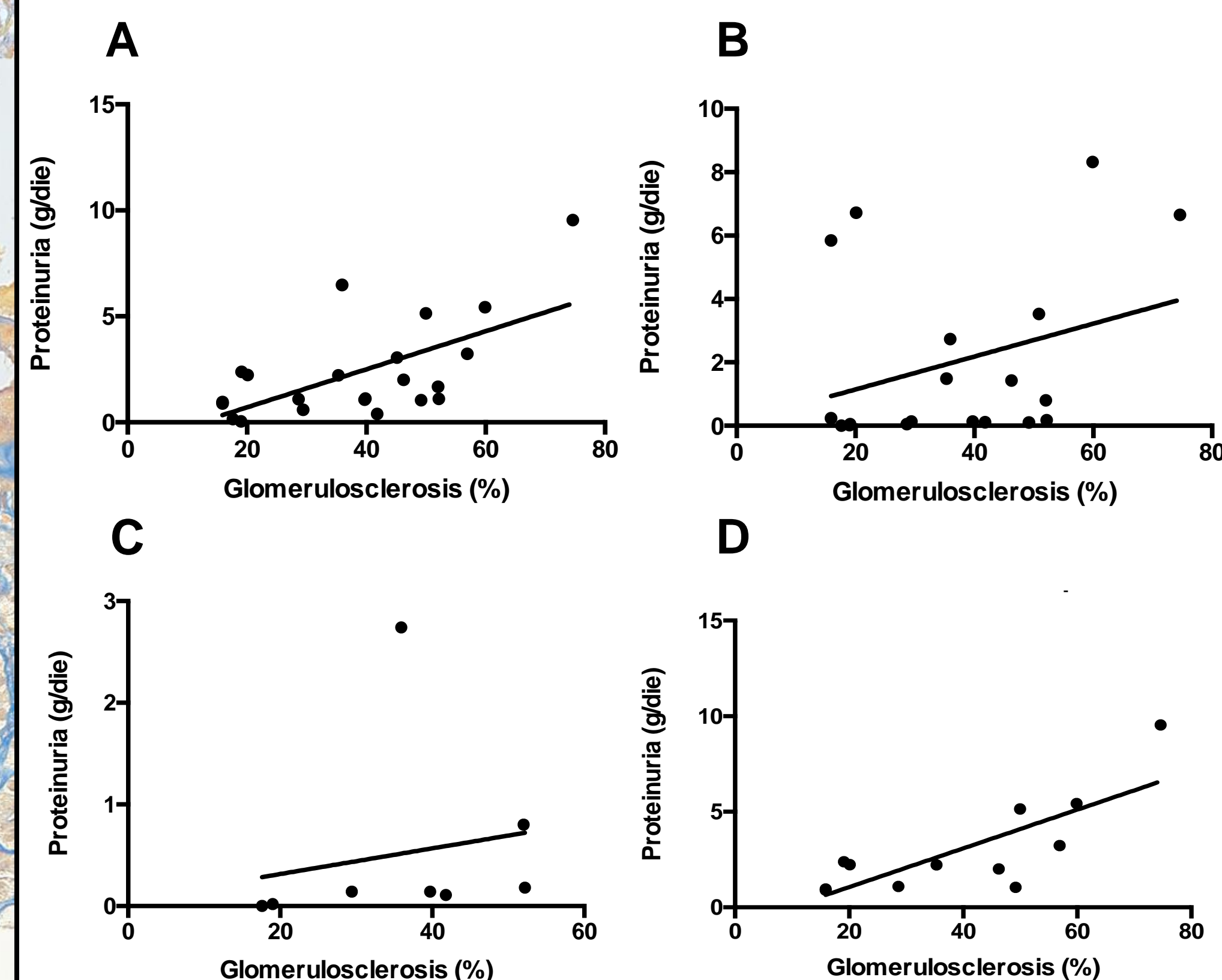**Figure 3.** *Correlations. Glomerulosclerosis and proteinuria at 30 days (A) and 180 days (B) from the beginning of treatment (p<0,05). Glomerulosclerosis and proteinuria in patients treated with Rituximab at 30 days (p=NS) (C). Glomerulosclerosis and proteinuria in patients treated with therapies other than Rituximab at 30 days (p<0,05) (D).*

Figure 4. *Complete remission of proteinuria in female patients compared to male ones at 180 days from the beginning of treatment, regardless of therapy (p<0,05).*
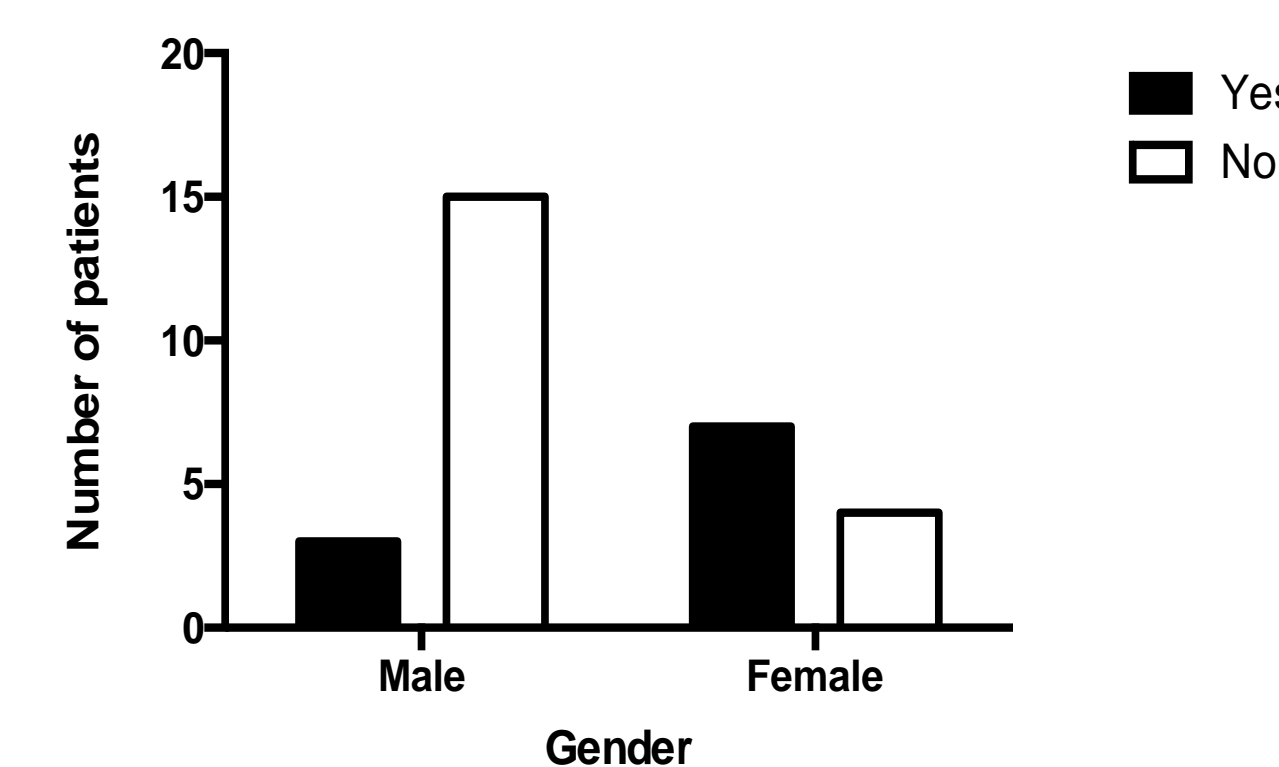
Figure 5. *Complete remission of proteinuria in patients treated with Rituximab compared with other treatment regimens at 30 days from the beginning of treatment (p<0,05).*
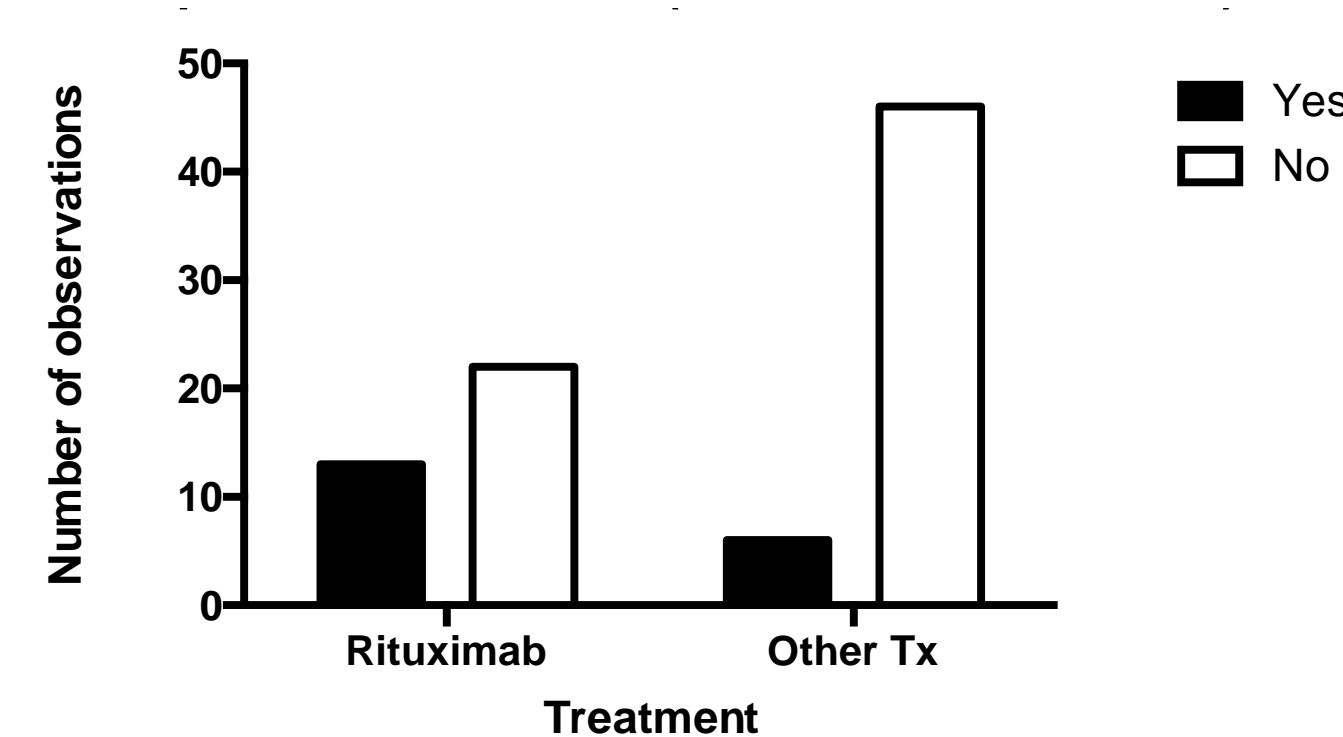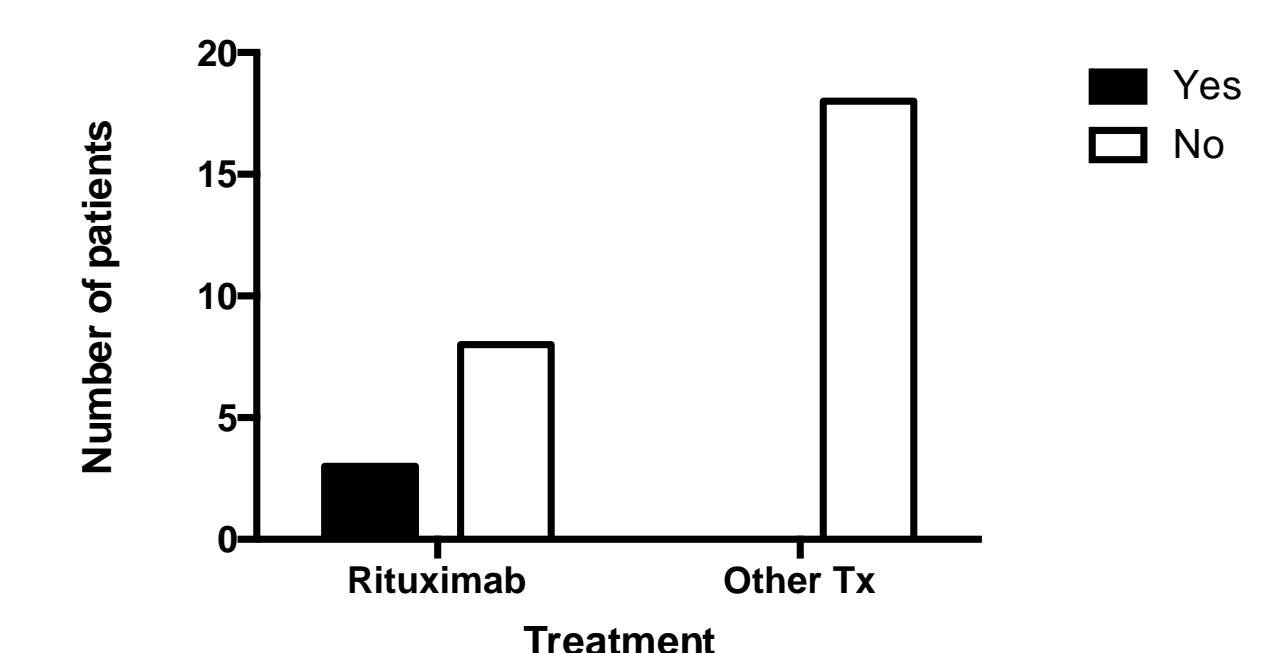

Figure 6. *Complete remission of proteinuria in patients treated with Rituximab compared with other treatment regimens during the study (p<0,05)*
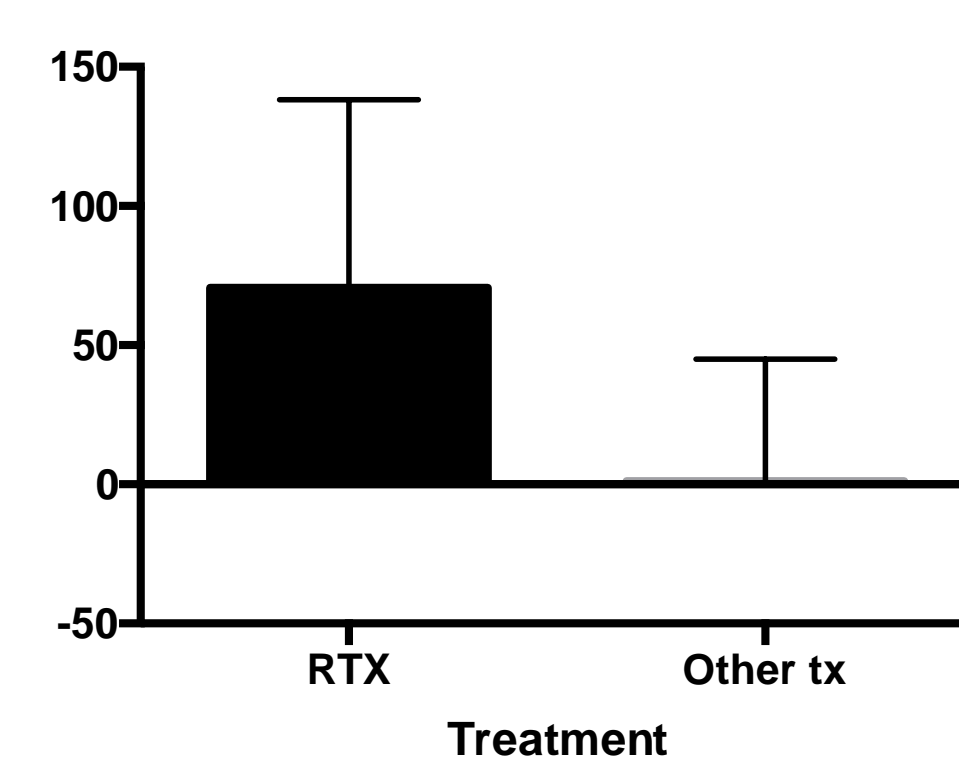
Figure 7. *Difference of eGFR compared to baseline values in patients treated with Rituximab or other treatment regimens at the end of the follow-up (p<0,05).*
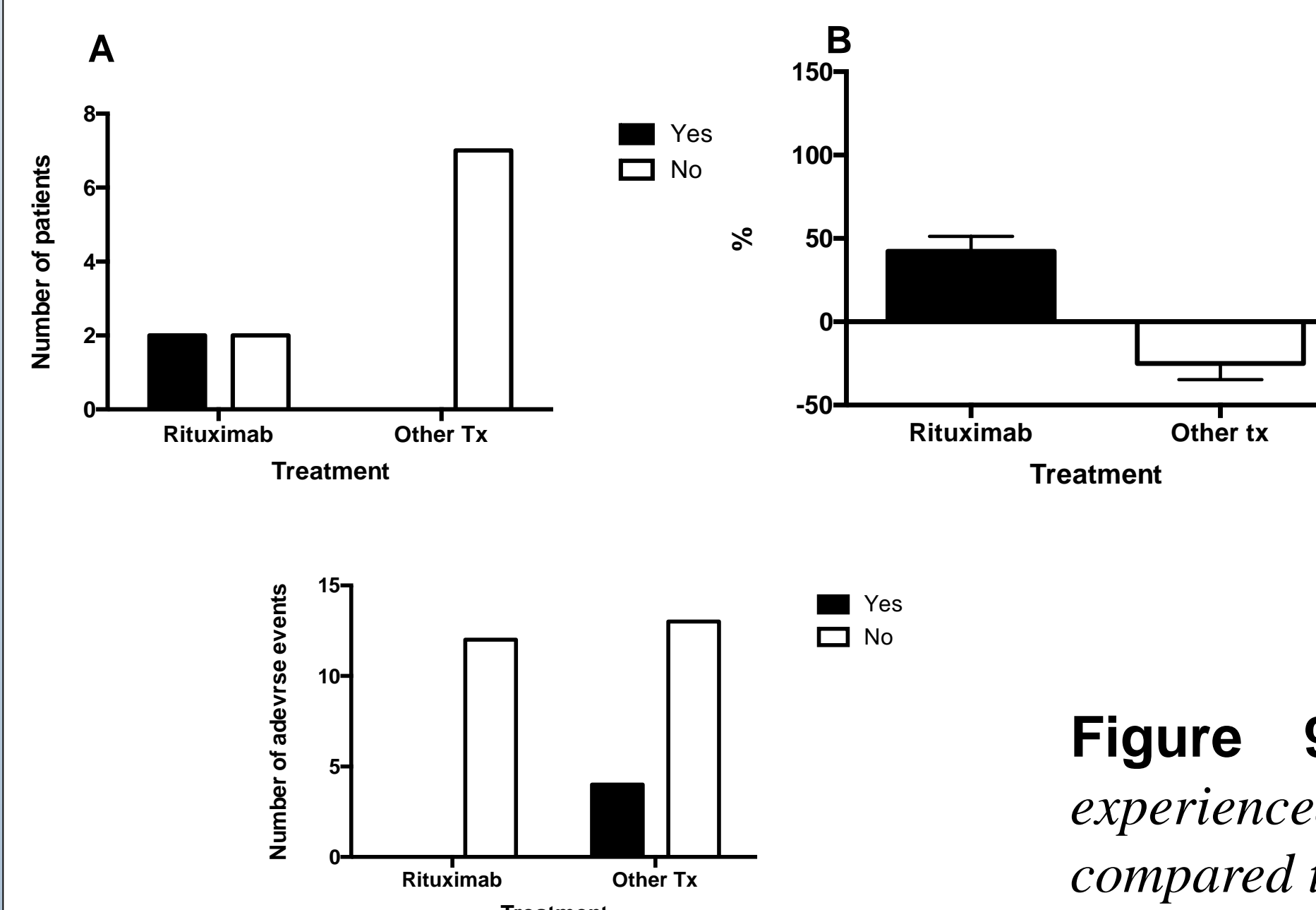
Figure 8. *A. Remission of proteinuria in patients presenting with glomerulosclerosis grade 3 treated with Rituximab compared to other treatment regimens (p=NS). B. Difference of eGFR compared to baseline values in patients presenting with glomerulosclerosis grade 3 treated with Rituximab compared to other treatment regimens (p=NS).*

Figure 9. *Number of adverse events experienced by patients treated with Rituximab compared to other treatment regimens (p=NS).*

CONCLUSIONS

Our study demonstrates that: the percentage of glomerulosclerosis at diagnosis positively correlates with proteinuria at 30 and 180 days after the beginning of treatment, independently of the therapy itself; females have a better response to therapy than males; Rtx treatment is associated with a faster reduction of proteinuria and a higher number of complete remissions; Rtx treatment is able to induce complete remission of proteinuria even in patients with the highest grade of glomerulosclerosis; Rtx preserves kidney function, is well tolerated and associated with less adverse events than other conventionally used therapies.