RITUXIMAB THERAPY IN PATIENTS WITH PRIMARY AND SECONDARY GLOMERULONEPHRITIS: RELATIONSHIP BETWEEN CLINICAL RESPONSE AND CD19+ TREND

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INTRODUCTION AND AIMS

Rituximab has been shown to be an effective therapy in a number of primary glomerulonephritis and in immune-mediated systemic disease with renal involvement. Once administered with the schedule used in lymphoma (i.e. 4 administrations, 375 mg/m^2), more recently it is administered as a single administration or using the rheumatologic dose regimen (2 administrations, 1 g).

It is still unclear whether a single administration obtaining complete CD 19$^+$ depletion may be enough to obtain a significant clinical response.

Little is known for how long CD19$^+$ depletion persists following one single administration.

METHODS

Single centre, retrospective analysis of 21 patients (10 M/ 11 F; mean age 58.94 $\pm$ 16.47 years), treated with Rituximab in single or multiple doses for a variety of conditions (Fig.1) between June 2009 and February 2014 (median follow up of 13 months, range 1 - 47.03 months).

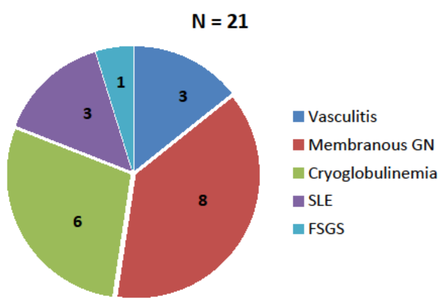

Figure 1: Underlying Nephropathy

CD 19$^+$ levels, serum creatinine, proteinuria and clinical manifestations of systemic disease were collected at baseline (first Rituximab administration) and during follow-up.

RESULTS

Rituximab therapy was decided because of refractory disease to more traditional therapies and absolute or relative contraindications. Patients received from one to four Rituximab infusions (mean 1.69) according to clinical needs and CD19+ trend over time. 4 patients received a rheumatologic dosing regimen. The mean dose for each Rituximab administration was 747 $\pm$ 185 mg with a mean cumulative dose of 1305 $\pm$ 934 mg (min 375 mg, max 3400 mg).

Complete CD19+ depletion (CD19+ < 5 cell/mm^3) was obtained in all the patients; CD19+ returned to values $\geq$ 5 cell/mm^3 in 16 patients after a mean of 8.72 $\pm$ 5.2 months (min 3.6, max 20.4 months). (Figure 2,3,4)

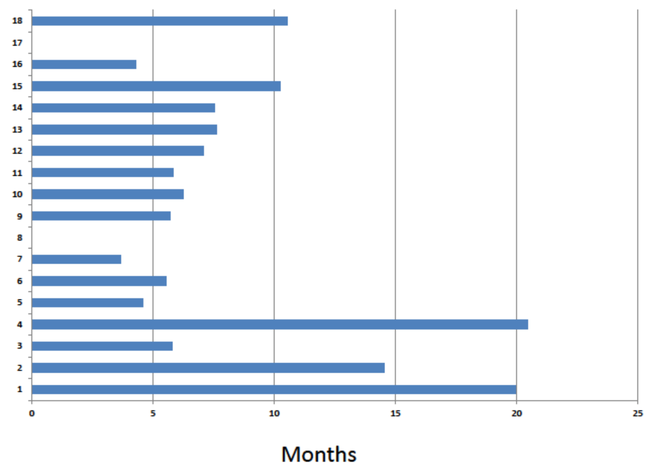

Figure 2: Time to CD19+ $\geq$ 5 cell/m^3

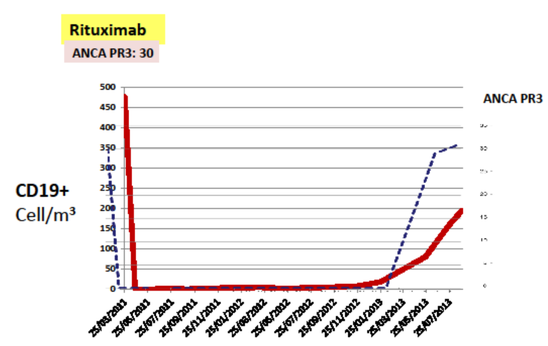

Figure 3: The trend of CD19+ in a patient with ANCA positive nephritis

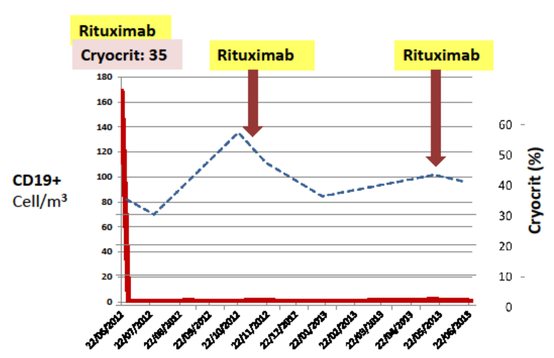

Figure 4: The trend of CD19+ in a patient with type 2 cryoglobulinemia

The trend of CD19+ was related to clinical manifestations in 4 out of 16 patients (five patients were excluded for inconclusive data or short follow-up). (Fig.5)

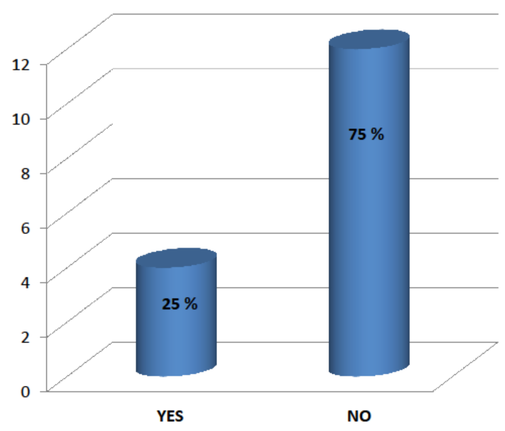

Figure 5: The relationship between the trend over time of CD19+ and clinical course

Treatment response (defined as significant improvement of clinical manifestations of the disease and/or proteinuria decrease and/or improvement in renal function) was obtained in 17 patients (4 partial remission, 13 full response) (Table 1)

Nephropathy	Treatment response
Membranous GN	3 partial remissions, 3 complete remissions, 2 no effect
SLE	Effective in all the three treated patients
Cryoglobulinemia	Effective in 4 pts, no effect in two pts (low dose, advanced CKD)
Vasculitis	Effective in all the three treated patients
FSGS	1 ts, no significant effect

Table 1: Rituximab efficacy according to renal disease

Drug administration was complicated by fever in one patient and atrial fibrillation in another one. 4 patients developed pneumonia following Rituximab administration and one patient had severe sepsis. One patient had a syncope two weeks after drug administration. (Table 2)

	N	Description	Comment	Drug correlation
Skin	3	rash		possible
Infections	4	Pneumoniae (n.4) Sepsis (n.1)	1 Pneumoniae months later	possible
Nervous system	1	Syncope	2 weeks after RTX	possible
Heart	1	Atrial Fibrillation	During RTX infusion	possible
Haematopoietic system	1	Autoimmune thrombocytopaenia	Months later	unlikely
Fever	1		During RTX infusion	Yes, likely
Death	1	Pulmonary edema		Not related

Table 2: Adverse reactions to Rituximab

CONCLUSIONS

Rituximab is an effective treatment option in adult patients with primary and secondary glomerulonephritis. According to our limited experience, CD19+ depletion cannot always predict patient response to Rituximab and/or disease relapses, even if in some patients increased CD19+ levels may anticipate disease relapses.

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