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# P391 -Long term outcomes of rituximab treatment in membranous nephropathy

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Background
The treatment of idiopathic membranous nephropathy (iMN) remains challenging. The recommended cyclical cyclophosphamide – steroid regimen is effective in inducing remission; however side effects are common. Rituximab is increasingly used as an alternative first line treatment as well as for relapsing disease, but there are few published data on long term outcomes.
Methods
In this retrospective, observational cohort study we report outcomes of 37 adult patients with biopsy proven iMN treated with rituximab between January 2008 and January 2018. The patients were followed up for a mean of 4 years (range 1-10years). Rituximab, 2 x 1 g doses at days 0 and 14, was administered for first line treatment (n=18), or for resistant or relapsing nephrotic syndrome (n=18), or for facilitating tacrolimus withdrawal in frequently relapsing patients (n=1). Complete remission (CR) was defined as urinary protein creatinine ratio UPCR <50mg/mmol, and partial remission (PR) as the reduction of UPCR by 50% and less than 350 mg/mmol.
Results
37 patients, 24 male and 13 female with mean age at diagnosis of iMN of 54 years (range 23-77 years) were identified. Patients with secondary membranous were excluded. PLA2R biopsy staining was positive in 19, negative in 12 and unavailable in 6. Mean UPCR of proteinuric patients at time of treatment was 999mg/mmol (range 207-2612) and mean GFR was 47 ml/min/1.73m² (9-120). At 1 year mean proteinuria had reduced to 426 mg/mmol (0-1654). Mean GFR at 1 and 3 years was 54 ml/min/1.73m² (range 9-10) and 57 ml/min/1.73m² (16 – 120) respectively excluding patients on haemodialysis (table 1).
Specifically remission (CR and PR), relapse, and dialysis (HD) rates were: at 6 months 7PR, 5CR and 2HD; at 1 year 12PR, 6CR, 2 relapse, 3HD ; at 3 years (n=26) 6PR, 11CR, 2 relapse, 6HD (figure 1). After 4 years and until the end of the follow up period all but one patients remained in sustained remission (CR/PR).
During the follow up period 7 patients required dialysis, one at the time of administration of rituximab. These patients had either low GFR at presentation or resistant disease previously treated with tacrolimus and/or cyclical cyclophosphamide with steroids.
3 patients died during the follow up period one from intracerebral haemorrhage, one from lung malignancy and one from a cardiac event.
Conclusion
Rituximab appears to be effective in treating iMN with reduction of proteinuria at 1 year, however remission can take considerably longer to achieve. In patients whose proteinuria responds to treatment, renal function was preserved over time, including in some patients with significant CKD (GFR<30ml/min/1.73m²). Relapse occurs in some patients but others maintain sustained remission. Differentiation of these groups will allow focussed retreatment for patients vulnerable to relapse.