Rituximab Treatment in Myasthenia Gravis: a window into one center experience

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Background: Myasthenia gravis (MG) is a chronic autoimmune disease affecting the neuromuscular junction. Up to 30% of patients do not respond to conventional treatments. Rituximab (RTX) is a chimeric mouse/human anti-CD20 monoclonal antibody that depletes B cells. While rituximab has been shown to be highly efficacious in MuSK-positive patients, its efficacy in AchR-positive patients is variable and debated.

Methods and materials: We conducted a retrospective review of all patients treated with rituximab at the neuromuscular centre at Ca' Foncello Hospital in Treviso. Efficacy was evaluated, as well as through the reduction of steroids or other immunosuppressive and safety was monitored.

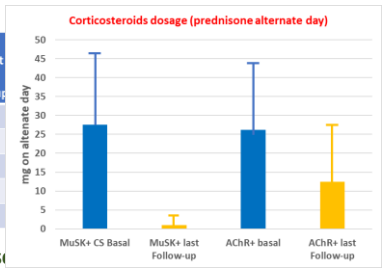
Results: we treated 16 pts with RTX. All had a history of refractory MG, classified as MGFA II-III. The five MuSK+ had an average age of 59 years (range 45–63). Four patients achieved RF after a mean of 30 months (range 11–42), and were able to reduce their CS dosage by 75%. The eleven AchR+ pts had an average age of 48 years (range 33–75). Six of these patients had one or more reinfusions after an average of 12 months. In terms of efficacy, at the end of follow-up (mean 17 months; range 4–53), three patients stopped using IVIG, five were in clinical remission, three in minimal manifestations. Two were non-responders. Corticosteroid dose decreased from a mean of 25 mg to 12.5 mg every other day.

MuSK+ Clinical characteristics

N°	Age (yrs)	Sex	Age at onset (yrs)	Previous therapies
1	54	F	34	CSA, AZA, MCF, MTX, regular weekly PE
2	64	F	59	AZA, PE, IVIG
3	53	F	44	AZA, MCF, PE, IVIG
4	63	F	42	-
5	60	F	31	AZA, PE, IVIg

MuSK+ RTX dose and response

N°	RTX Dose	Subsequent Infusion (months)	Follow up (months)	Clinical status at last follow up
1	375 mg x 4	Yes (11, 26, 38)	42	RF
2	375 mg x 4	Yes (12, 23)	38	RF
3	375 mg x 4	Yes (15, 28, 35)	36	RF
4	1000 mg x 2	No	11	MM
5	1000 mg x 2	NO	6	RF



AChR+ Clinical characteristics

N°	Age (yrs)	Sex	Age at onset (yrs)	Previous therapies
6	75	M	64	IVIg, MCF, AZA
7	36	F	23	
8	33	F	23	AZA, MCF, Chronic PE
9	60	F	56	AZA, MCF, PE, Chronic IVIg
10	51	M	28	AZA, MCF, PE and IVIg
11	45	F	31	AZA, MCF, Chronic PE
12	52	F	47	AZA
13	42	F	26	AZA, CSA, Chronic IVIg
14	70	M	67	AZA, IVIg for crisis
15	49	M	19	AZA, MCF
16	46	F	43	AZA, MCF, MTX

CS: corticosteroids, RTX Rituximab

AChR+ RTX dose and respons

N°	RTX Dose	Subsequent Infusion (months)	Follow up (months)	Clinical status at last follow up
6	1000 mg x 2	yes (6)	15	MM
7	1000 mg x 2	yes (16)	18	RF
8	1000 mg x 2	No	13	Non responder
9	1000 mg x 2	No	4	Initial response
10	1000 mg x 2	Yes (23)	53	RF
11	375 mg x 4	Yes (21)	40	Non responder
12	1000 mg x 2	No	10	RF
13	375 mg x 4	Yes (12)	20	MM
14	1000 mg x 2	No	9	RF
15	1000 mg x 2	No	12	RF
16	1000 mg x 2	Yes (11, 19)	19	MM

Three side effects were recorded (H Zoster, viral meningitis with hypoacusia and endocarditis and sepsis. This latter patient had uncontrolled diabetes and other severe comorbidities, and was lost at follow-up.

Conclusions and discussion: Despite the small size of our sample, our study increases the existing experience. Rituximab seems a valid treatment option. It was effective in reducing the burden of refractory MG and corticosteroids dose in 100% and 80% of anti-Musk and anti-AChR patient respectively. Further studies are needed to determine the position of rituximab in the treatment of MG as well as the optimal long-term infusion protocol.