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Treatment

Poster ID 71

Rituximab in Multiple Sclerosis: B-lymphocyte population study and its relationship with dosing regimen

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Introduction

The involvement of B-lymphocytes in the pathophysiology of Multiple Sclerosis (MS) is being increasingly studied.

Rituximab is an anti-CD20 monoclonal antibody used as an off-label treatment in MS.

CD20-depleting strategies have a variable effect in the different B-cell subpopulations.

Many questions about the role of B-cells in MS remain still unanswered, ranging from the role of specific B-cell subsets to the optimal treatment regimen and monitoring strategies.

Aim

To study the effectiveness of rituximab in MS patients and their relationship with treatment regimen and B-lymphocyte population study

Methods

Retrospective observational single-center study of MS patients treated with rituximab for ≥6 months

- Characterization of demographic, clinical [relapse incidence, Expanded Disability Status Scale (EDSS), duration of treatment and dosing regimen] and laboratorial (B-lymphocyte population study in peripheral blood) variable
- **Disability progression** was defined by 1 point EDSS change (0,5 point if baseline EDSS was >5,0)
- **Responders** were defined by the absence of relapses and disability progression or physician perception of therapeutic benefit during follow-up period
- 2 groups of treatment regimen (TR) were determined: the 500mg biannual and the others TR (annual dosage < 1000mg and > two times)
- Descriptive and comparative statistical analysis (p<0.05 as statistically significant)

References: Salzer J, Svenningsson R, Alping P, et al. Rituximab in multiple sclerosis: A retrospective observational study on safety and efficacy. Neurology. 2016 Nov 15;87(20):2074-2081. Klein da Costa B, Brant de Souza Melo R, Passos GRD, et al. Unraveling B lymphocytes in CNS inflammatory diseases: Distinct mechanisms and treatment targets. Neurology. 2020 Oct 20;95(16):733-744. Bittner S, Ruck T, Wiendl H, et al. Targeting B cells in relapsing-remitting multiple sclerosis: from pathophysiology to optimal clinical management. Ther Adv Neurol Disord. 2017 Jan;10(1):51-66. Barra ME, Soni D, Vo KH, et al. Experience with long-term rituximab use in a multiple sclerosis clinic. Mult Scler J Exp Transl Clin. 2016 Oct 9;2:205-12. Lehmann-Horn K, Kinzel S, Weber MS. Deciphering the Role of B Cells in Multiple Sclerosis-Towards Specific Targeting of Pathogenic Function. Int J Mol Sci. 2017 Sep 23;18(10). Salzer J, Svenningsson R, Alping P, et al. Rituximab in multiple sclerosis: A retrospective observational study on safety and efficacy. Neurology. 2016 Nov 15;87(20):2074-2081.

Conclusion

- The B lymphocyte population study may help in therapeutic decision.
- Patients with higher percentage of immature and naïve cells, reflecting a higher B-lymphocyte turnover, had a good outcome.
- Patients with a higher percentage of plasmablasts had a worse clinical response, in possible association with antibody production and promotion of the differentiation of autoreactive T-cells.
- The 500mg biannual regimen is related to a better immunological profile in both MS forms.

Results

	Total population (n = 80)
Age (y), mean (SD)	49,49 (11,62)
Female, n (%)	53 (66,3)
Progressive MS, n (%)	42 (52,5)
Disease duration (y), mean (SD)	16,19 (7,27)
Follow-up period (y), mean (SD)	2,96 (1,41)

Table 1. Characterization of the total population.

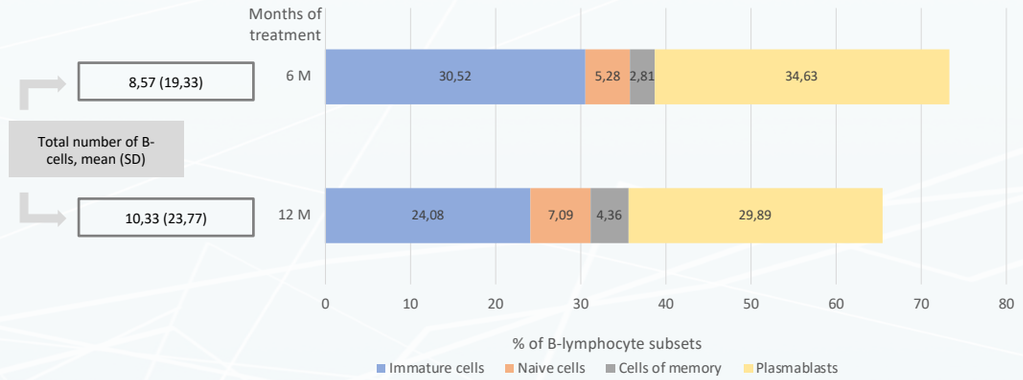

Figure 1. B-lymphocyte population study at 6 and 12 months of treatment.

B-lymphocyte population study	6 M Responders (n=33)	6 M Non-responders (n=14)	12 M Responders (n=41)	12 M Non-responders (n=23)
Total number of B cells, mean (SD)	12,31 (22,68)	0,77 (1,34)	14,58 (28,45)	3,65 (11,16)
B-lymphocyte population				
Immature cells %, mean (SD)	37,96 (41,99)	12,43 (27,38)	31,39 (41,67)	3,65 (11,16)
Naïve cells %, mean (SD)	7,21 (19,12)	0,71 (2,67)	11,07(25,79)	11,04 (30,10)
Cells of memory %, mean (SD)	3,72 (8,48)	0,64 (2,40)	4,54 (16,35)	0,00 (0,00)
Plasmablasts %, mean (SD)	30,93 (41,54)	43,35 (46,50)	28,29 (42,52)	32,73 (46,38)

Responders had a higher % of immature cells at 6 and 12 months (p=0.018 and 0.028, respectively)

Table 2. Comparison of B-lymphocyte population study between responders and non-responders at 6 and 12 months of treatment.

There is a negative correlation between the final EDSS and the percentage of immature cells at 12 months (r=-0.36 p=0.003)

B-lymphocyte population study at 12 M	With disability progression (n=21)	No disability progression (n=43)	500mg biannual (n=26)	Others TR (n=38)
Total number of B cells, mean (SD)	2,91 (10,65)	14,36 (27,80)	13,25 (26,64)	8,62 (22,14)
B-lymphocyte population				
Immature cells %, mean (SD)	5,81 (21,93)	33,00 (42,38)	37,49 (45,27)	14,89 (31,34)
Naïve cells %, mean (SD)	0,81 (3,71)	10,16 (25,31)	6,72 (19,64)	7,34 (22,53)
Cells of memory %, mean (SD)	0,81 (21,93)	3,56 (15,35)	0,85 (2,02)	6,76 (22,25)
Plasmablasts %, mean (SD)	44,57 (49,55)	22,73 (39,01)	23,86 (41,91)	34,02 (44,85)

Patients with no progression had higher % of immature (p=0.001 and 0.022, respectively) and naïve cells and lower % of plasmablasts (p=0.086)

The 500mg biannual regimen was related to the highest % of immature cells at 12 M (p=0.033)

Table 3. Comparison of B-lymphocyte population study between patients with disability progression and patients with no disability progression, and between the 500mg biannual regimen and others treatment regimens (TR).