Rituximab in Multiple Sclerosis: importance of the dosing regimen

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Introduction

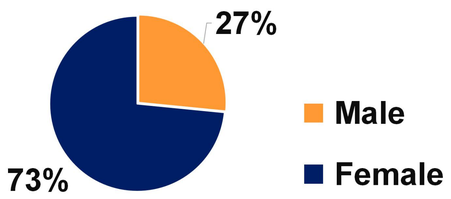
- The involvement of B-lymphocytesin the pathophysiology of Multiple Sclerosis (MS) is being increasingly studied.
- Rituximab, a monoclonal antibody directed at CD20 positive B-lymphocytes, is used as an off-label treatment in MS, with good efficacy and safety profile.
- CD20-depleting strategies have a variable effect in the different B-cell subpopulations and the recovery after depletion determines therapeutic and safety profiles, as well as treatment schedules.
- It is essential to improve the knowledge regarding dosage, treatment intervals and monitoring strategies.
- Our aim was to study the effectiveness and safety of rituximab in MS patients and their relationship with treatment regimen and B lymphocyte population study.

Methods

- Retrospective longitudinal observational single-center study.
- MS patients treated with Rituximab for ≥6 months.
- The following data was collected and analyzed:
  - Baseline demographic information;
  - Duration of treatment and dosing regimen;
  - Adverse events;
  - B lymphocyte population study in peripheral blood
    - 6 months after treatment start;
    - 12 months after treatment start.
  - Relapse incidence, MRI data and Expanded Disability Status Scale variation at 12 months.
  - Responders were defined by the absence of relapses, new lesions on follow-up brain imaging and disability progression.
- **Statistical analysis:** descriptive and mean comparison with Student´s t-test.

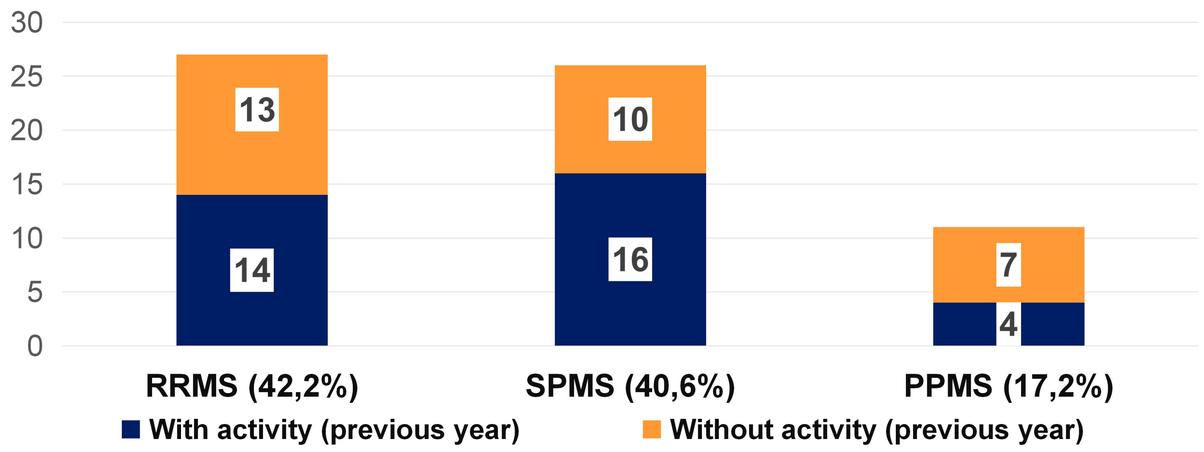
Results

Demographics



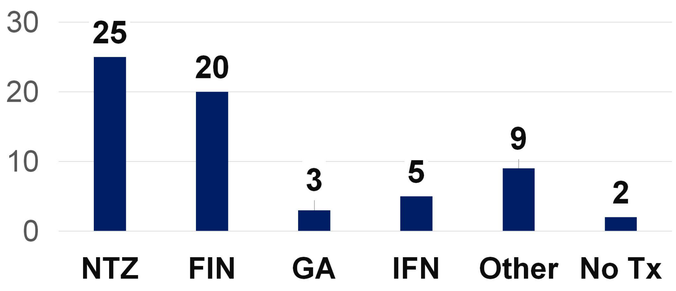
Mean age:
46.95 ± 11.10 years

Mean disease duration:
14.16 ± 7.05 years

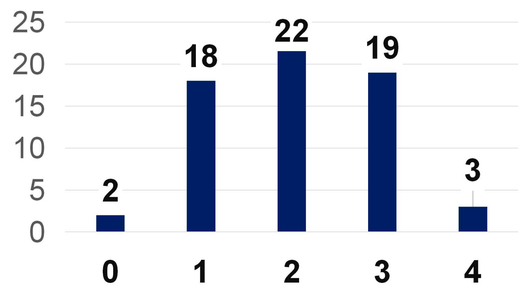


Previous treatment

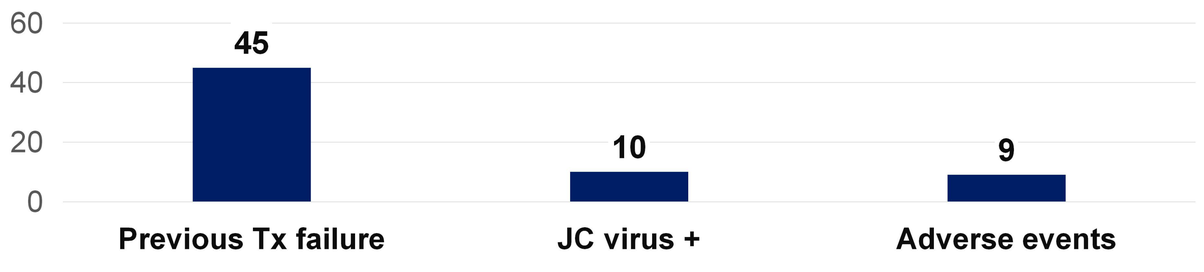
Last disease modifying therapy (DMT)



Number of previous DMT

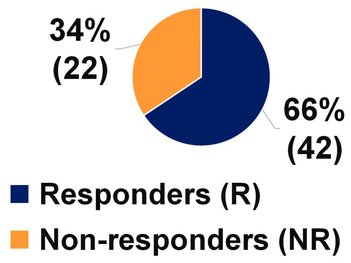


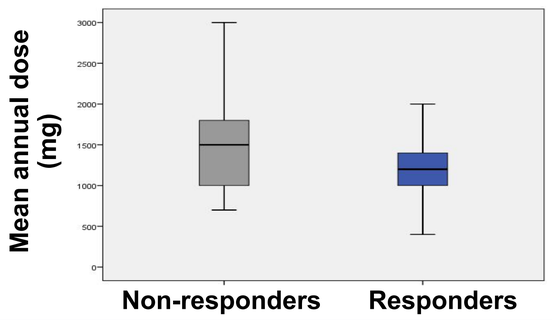
Reason for changing to Rituximab



Rituximab effectiveness

Mean treatment duration: 20.16 ± 7.60 months.
Mean annual dose: 1305.47 ± 447.67mg (variation 400-3000mg).
Interval between doses: variation from 2-2 to 6-6 months.
Most frequent dosing regimen: 500mg 6-6 months (n – 23).

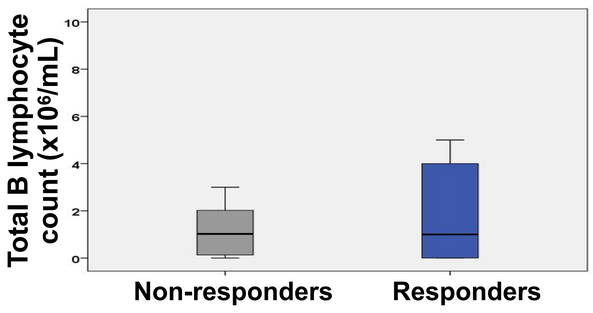




Comparison of mean annual dose between responders and non-responders

- The responders group had statistically significant lower mean annual dose (p=0.032);
- This difference was also found in the comparison between mean dose at 12 months (p=0.040).

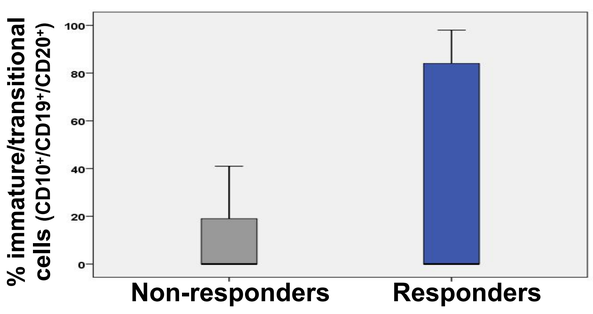
B lymphocyte population study at 6 months

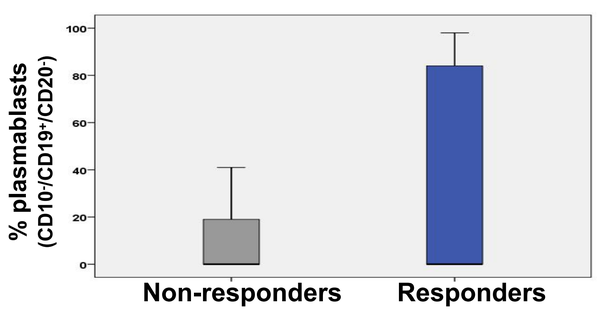


Comparison of total B lymphocyte count between responders and non-responders

- There were no significant differences;

There were no significant differences in any B lymphocyte population study parameters at 12 months



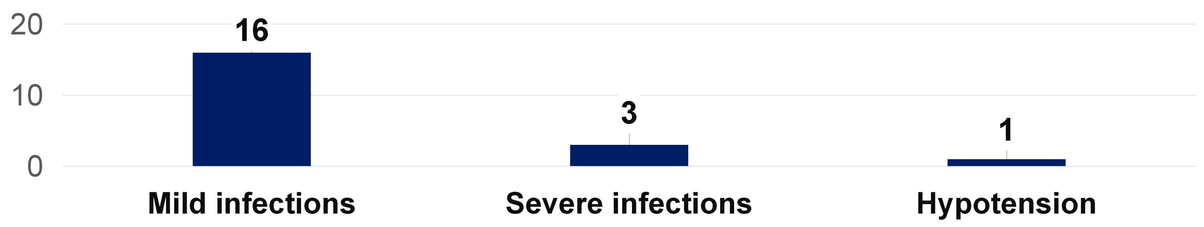


Comparison of immature/transitional cells and plasmablasts percentages between responders and non-responders

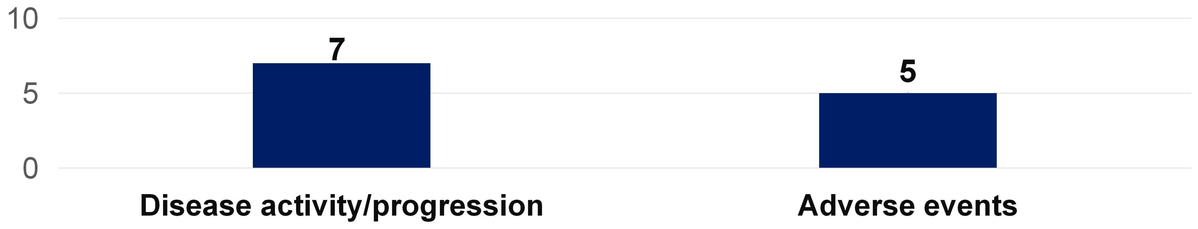
- There was a trend for higher immature/transitional cells and lower plasmablasts percentages in the responders group, without statistical significance (p=0.068 and p=0.070, respectively).

Safety profile

Adverse events (n - 20)



Rituximab discontinuation (n - 12)



Discussion

- In our cohort, Rituximab showed efficacy in stabilizing the disease, with a good safety profile.
- Responders had a lower mean annual dose, which is in accordance with the existing literature and supports the need for a personalized treatment regimen.
- 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.
- Also, patients with lower percentage of immature/transitional cells, reflecting a lower B lymphocyte turnover, had a worse clinical response.
- This could be explained by a high number of remaining plasmablasts/memory cells and an lower production of immunosupressive regulatory B cells.
- A better understanding of the role of B lymphocytes in MS is still needed in order to fully understand the therapeutic effects of Rituximab and other CD20-depleting therapies.

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