Rituximab in Multiple Sclerosis: importance of the dosing regimen

João Durães1, Miguel Tábuas-Pereira1, Ana Margarida Novo1, Inês Correia1, Isabel Campelo2, Isabel Silva2, Sandra Silva3
Artur Paiva3, Sónia Batista1, Carla Nunes1, Lívia Sousa1, Maria Carmo Macário1
1 – Neurology Department, Centro Hospitalar e Universitário de Coimbra, Portugal
2 – Pharmacy Department, Centro Hospitalar e Universitário de Coimbra, Portugal
3 – UGOC, Clinical Pathology Department, Centro Hospitalar e Universitário de Coimbra, Portugal

Introduction

- The involvement of B-lymphocytes in 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 36 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

<table>
<thead>
<tr>
<th>Mean age: 46.95 ± 11.10 years</th>
<th>Male (27%)</th>
<th>Female (73%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean disease duration: 14.16 ± 7.05 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B lymphocyte population study at 6 months

- 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.
- Statistical difference was found in the comparison between mean dose at 12 months (p=0.040).

Safety profile

- 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 immunosuppressive 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.

Discussion

- Adverse events (n - 20)
  - Mild infections: 16
  - Severe infections: 3
  - Hypotension: 1

Rituximab discontinuation (n - 12)

<table>
<thead>
<tr>
<th>Disease activity/progression</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>

References

- Joao Durães, Miguel Tábuas-Pereira, Ana Margarida Novo, Inês Correia, Isabel Campelo, Isabel Silva, Sandra Silva. Rituximab effectiveness and safety profiles, as well as treatment schedules.