**INTRODUCTION**

- Multiple sclerosis (MS) is a progressive inflammatory disease of the central nervous system that represents a burden for approximately 2.2 million people all over the world.

- Prevalence in Brazil varies from 1.36 to 2.15 cases per 100,000 inhabitants. 

- Relapsing remitting multiple sclerosis (RRMS) is the most common clinical course, occurring in 88% of all cases, 4.

- First line of treatment for RRMS is based on disease-modifying agents including glatiramer acetate and interferon-β. 5

- Currently, there are three types of recombinant interferon-β available in Brazil: subcutaneous interferon-β 1b (Betaferon®, Bayer); subcutaneous interferon-β 1a (Rebif®, Merck); and intramuscular interferon-β 1a (Avonex®, Biogen-Idec). 6

**OBJECTIVES**

- Brazilian Health Ministry recommends the use of interferon-β as a reference treatment. However, the recommendation is overall and does not distinguish among different preparation of interferon-β. 

- Considering the lack of evidence and tools to support the decision-making process we performed a SRMA to compare the clinical outcomes of different therapeutic options of interferon-β available in Brazil for the treatment of RRMS.

**METHODOLOGY**

- MEDLINE (PubMed), Cochrane Library, CENTRAL and LILACS databases were searched up to April 2016 for RCT, placebo-controlled studies comparing different options of interferon-β in patients. Systematic reviews evaluating RRMS treatment were also identified during the search.

- MESH terms used in the Medline search were “multiple sclerosis AND interferon AND (randomized trials OR meta-analysis)”; to the other database search, the combination of terms “multiple sclerosis” and “interferon” was used.

- Eligibility criteria: studies evaluating interferon-β or other drugs unavailable in Brazil, or with outcomes not directly related to clinical benefit. Trials evaluating different types of MS were included; however, analyses were performed only for subgroup of RRMS patients.

- Outcomes evaluated: weekly intramuscular 30 mcg of interferon-β 1a (Avonex®, Merck) and weekly in alternate days (q.o.d) 250mcg of interferon-β 1b (Betaferon®, Bayer). 7

- Endpoints: 
  
  - Clinical relapse: proportion of participants experiencing new relapses over 32 and 24 month follow-up, as well as exploratory analysis on relapses beyond these periods (8).
  
  - Disability progression: defined as increase of at least one point in the Expanded Disability Status Scale (EDSS) compared to baseline and sustained for at least 6 months, or the EDSS at 24 month after initiating therapy (9).
  
- Meta-analysis: fixed effect model using Review Manager software (version 4.1); relative risk (RR) with 95% Confidence Interval (CI) used as measure of association. Pooling was done in all studies to show differences according to the type of interferon-β.

**RESULTS**

- We identified 405 articles, of which 9 fit the inclusion criteria (5 placebo-controlled and 4 head-to-head trials).

**Table 1: Study design of the placebo-controlled trials evaluating different interferon-β**

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Experimental arm</th>
<th>Placebo arm</th>
<th>Sample Size</th>
<th>Binding</th>
<th>Primary Outcome</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>OWSM (1999)</td>
<td>SC interferon-β 1a (Rebif®)</td>
<td>293</td>
<td>Double-blind</td>
<td>Relapse rate at 12 and 24 months, progression of disability at 24 months</td>
<td>Relapse rate at 24 months, progression of disability at 24 months</td>
<td></td>
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<tr>
<td>PRISMS (1998)</td>
<td>Intramuscular interferon-β 1a (Avonex®)</td>
<td>560</td>
<td>Double-blind</td>
<td>Relapse rate at 12 and 24 months, progression of disability at 24 months</td>
<td>Relapse rate at 12 and 24 months, progression of disability at 24 months</td>
<td></td>
</tr>
<tr>
<td>MSCG (1995)</td>
<td>IM interferon-β 1a (Betaferon®)</td>
<td>301</td>
<td>Double-blind</td>
<td>Relapse rate at 12 and 24 months, progression of disability at 24 months</td>
<td>Relapse rate at 12 and 24 months, progression of disability at 24 months</td>
<td></td>
</tr>
<tr>
<td>Kobusler (1996)</td>
<td>IM interferon-β 1b (Betaferon®)</td>
<td>12</td>
<td>Double-blind</td>
<td>Relapse rate at 12 months</td>
<td>Relapse rate at 12 months</td>
<td></td>
</tr>
<tr>
<td>IFNM (1998)</td>
<td>IM interferon-β 1a (Avonex®)</td>
<td>372</td>
<td>Double-blind</td>
<td>Relapse rate at 12 months, progression of disability at 24 months</td>
<td>Relapse rate at 12 months, progression of disability at 24 months</td>
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</tbody>
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**Figure 1: Prime of the meta-analysis comparing interferon-β versus placebo.**

**Figure 2: Flow chart of the meta-analysis comparing interferon-β versus placebo.**

**Figure 3: Flow chart of the meta-analysis comparing interferon-β versus placebo.**

**Figure 4: Flow chart of the meta-analysis comparing interferon-β versus placebo.**

**References**