ISPOR 23rd Annual International Meeting - **PND12**

IMMUNOMODULATORS AND IMMUNOSUPPRESSANTS FOR PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS: A NETWORK META-ANALYSIS

Lucchetta RC [1], Tonin FS [1], Borba HHL [1], Leonart LP [1], Ferreira VL [1], Bonetti AF [1], Riveros BS [1], Becker J [2], Pontarolo R [1], Fernandez-Llimós F [3], Wiens A [1]

[1] Federal University of Parana, Curitiba, Brazil, [2] Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil, [3] Research Institute for Medicines (iMed.ULisboa), Lisboa, Portugal.

Objectives

- The aim of this study was to synthesize the evidence of clinical outcomes for alemtuzumab, cladribine, daclizumab, dimethyl fumarate, fingolimod, glatiramer acetate, interferons, natalizumab, ocrelizumab, peginterferon and teriflunomide in adults with relapsing-remitting multiple sclerosis.

Methods

- A systematic review was performed by Medline, Scopus and manual search (May 2017);
- Bayesian network meta-analyzes were conducted, of randomized clinical trials that evaluated any of the disease modifying therapies head-to-head or against placebo;
- For efficacy, the annualized relapse rate was considered, whereas safety was evaluated through discontinuation due to adverse events in 96 weeks;
- Surface Under the Cumulative Ranking analysis (SUCRA), Cochrane tool for risk of bias (v2.0) [1] and GRADE [2] were used to ranking therapies, assess methodological bias, and quality of general evidence, respectively;
- Statistical analyses were performed using software R v. 3.4.1/R studio 1.0.153 [3].

Results

Thirty-three studies were included in the meta-analyzes (Figure 1 and 2). All therapies were most effective than placebo. The highest rates, considering the outcome annualized relapse rate were alemtuzumab, natalizumab, and ocrelizumab [Hazard Ratio versus placebo, of 0.31 (95% Credibility Interval (CrI) 0.26, 0.38), 0.31 (95% CrI 0.27, 0.36) and 0.37 (95%CrI 0.31, 0.36), respectively] (Figure 3), without significant differences between these three therapies. Discontinuation due to adverse events (96-weeks) revealed similarity across all therapies compared to placebo (Figure 4).

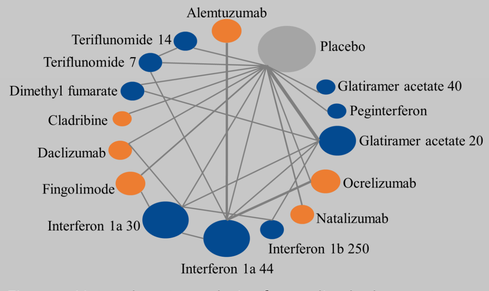

Figure 1. Network meta-analysis of annualized relapse rate.

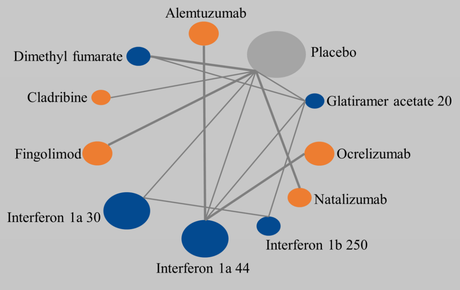

Figure 2. Network meta-analysis of discontinuaton due to adverse events in 96 weeks.

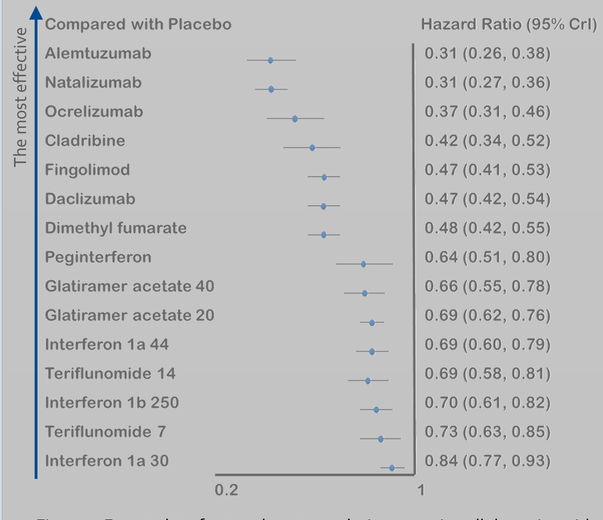

Figure 3. Forest plot of network meta-analysis comparing all therapies with placebo for annualized relapse rate, ranked by SUCRA.

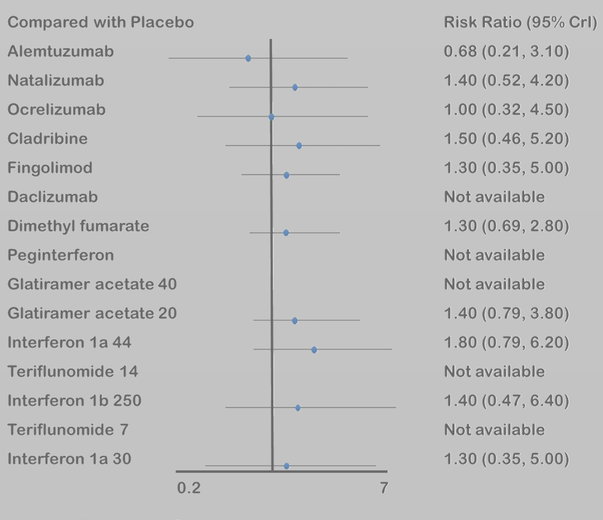

Figure 4. Forest plot of network meta-analysis comparing all therapies with placebo for discontinuation due to adverse events in 96 weeks.

Conclusions

Alemtuzumab, natalizumab, and ocrelizumab are the best choices considering clinical efficacy without compromising patient's safety (high quality evidence).

References

1 - Higgins J et al. Cochrane Methods Cochrane Database Syst Rev 2016; : Suppl.1.

2 - GRADE Working Group. BMJ 2004; **328**: 1490–0;

3 - Team RC. R: https://www.r-project.org/

Support

Institutional Development Support Program of the National Health System (Proadi-SUS) and Hospital Alemão Oswaldo Cruz (n. 01/2017).

Contact the Corresponding Authors

Rosa Lucchetta
Phone Number: +55 41 99280 3307
Email Address: rc.lucch@yahoo.com.br

Astrid Wiens
Phone Number: +55 41 3360 4161
Email Address: astrid@ufpr.br