A Network Meta-Analysis of Brazilian Relapsing-Remitting Multiple Sclerosis Drugs in an Early Highly Effective Approach.

Poster Code
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BACKGROUND:

- In Brazil, the treatment of relapsing-remitting multiple sclerosis (RRMS) involves the use of several drugs, with different efficacies, safety profiles and cost-effectiveness ratios.
- The use of early highly effective treatment at the beginning of the disease, rather than escalation in therapeutic lines, has been a currently recommended approach.
- The objective of this study is to conduct a network meta-analysis (NMA) that compares the efficacy of all disease modifying therapies (DMTs) approved in Brazil, regardless of the severity of the disease or previous treatments.

METHODS:

- A systematic review of the literature was conducted, searching for randomized controlled trials (RCTs) for the treatment of RRMS.
- A frequentist NMA was performed comparing the outcomes of annualized relapse rate (ARR) and six-month confirmed disability progression (CDP6).
- Scenario analysis were carried out by removing studies considered to be at high risk of bias or heterogeneity.

RESULTS:

- The base case includes 33 RCTs (Figure 1), only three of which were deemed to be at high risk of bias.
- Alemtuzumab (ALE), ofatumumab (OFA), and natalizumab (NAT) demonstrated the best efficacy in reducing ARR (Figure 2A).
- For CDP6, ALE, NAT, and ocrelizumab (OCRE) presented the highest efficacy (Figure 2B).
- The p-score analysis indicated that ALE was probably the best option for both outcomes (GRADE NMA, Table 1).
- The findings, excluding studies deemed to have a high risk of bias or heterogeneity, were in line with the results of the base case analysis.

Based on the NMA results, alemtuzumab demonstrated superior efficacy in reducing ARR and CDP6. This data, considering early intensive treatment approach for RRMS, can support future assessments of cost-effectiveness and budgetary implications in Brazil.

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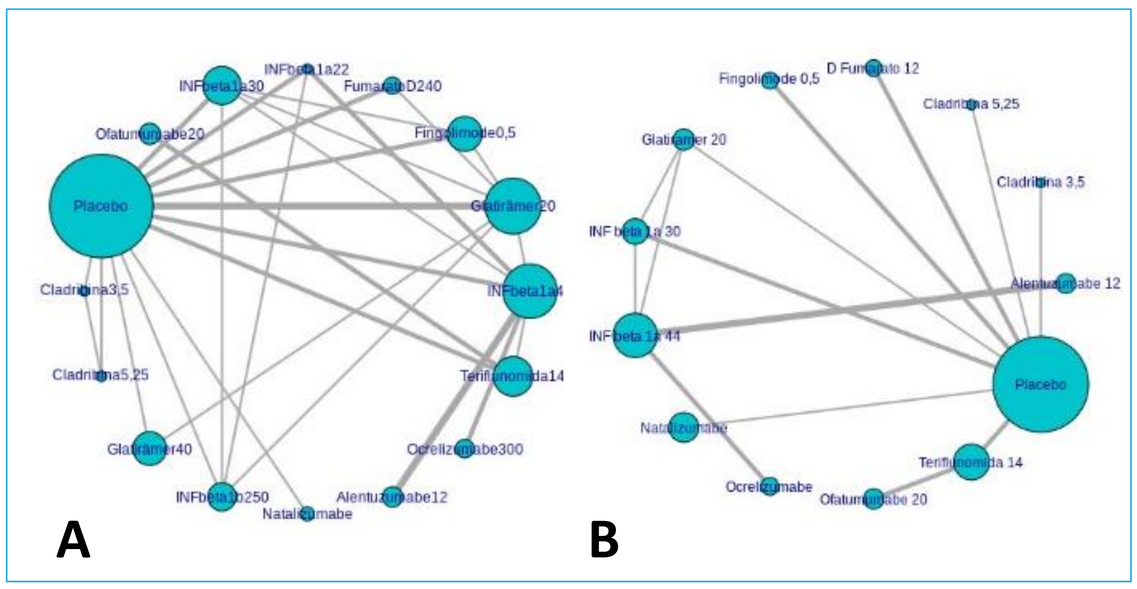


Figure 1. Network meta-analysis diagram of (A) annualized relapse rate and (B) sustained disability progression for relapsing-remitting multiple sclerosis.

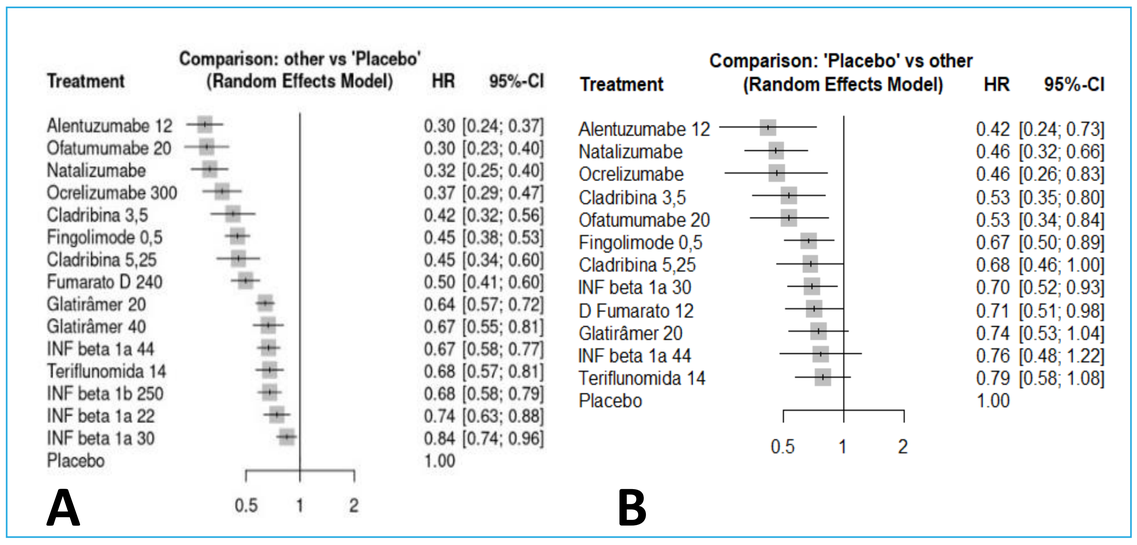


Figure 2. Base case forest plot of disease-modifying therepies versus placebo for (A) annualized relapse rate and (B) sustained disability progression

BENEFITS

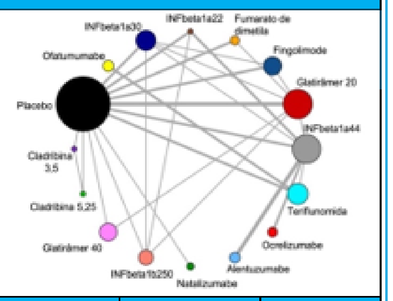
Estimate of effects. confidence intervals. and certainty of the body of evidence for disease-modifying drug therapy for patients with relapsing-remitting multiple sclerosis.

Patient or Population: Adult patients with relapsing-remitting multiple sclerosis.

Intervention: Disease-modifying therapies.

Comparator (reference): Placebo.

Outcome: Annualized relapse rate.



Total studies 33 RTC Total participants: 22.834		Relative effect HR (95% CI)	Anticipated absolute effect (95% IC)			Certainty of evidence	Ranking* (P-score)
			Without intervention	With intervention	Difference		
	Alemtuzumab	0.30 (0.24 to 0.37)	1.35 relapse/year	0.40 relapse/year	0.95 fewer (0.85 fewer to 1.03 fewer)	⊕⊕◯◯ Low ♦#	0.940
	Ofatumumab	0.30 (0.23 to 0.40)	1.35 relapse/year	0.41 relapse/year	0.94 fewer (0.81 fewer to 1.04 fewer)	⊕⊕⊕◯ Moderate #	0.920
	Natalizumab	0.32 (0.25 to 0.40)	1.35 relapse/year	0.43 relapse/year	0.92 fewer (0.81 fewer to 1.01 fewer)	⊕⊕⊕◯ Moderate!	0.900
	Ocrelizumab	0.37 (0.29 to 0.47)	1.35 relapse/year	0.50 relapse/year	0.85 fewer (0.71 fewer to 0.96 fewer)	⊕⊕◯◯ Low ♦#	0.793
	Cladribine 3.5	0.42 (0.32 to 0.56)	1.35 relapse/year	0.57 relapse/year	0.78 fewer (0.59 fewer to 0.92 fewer)	⊕⊕⊕⊕ High	0.699
	Fingolimod	0.45 (0.38 to 0.53)	1.35 relapse/year	0.61 relapse/year	0.74 fewer (0.64 fewer to 0.83 fewer)	⊕⊕⊕⊕ High	0.653
	Cladribine 5.25	0.45 (0.34 to 0.60)	1.35 relapse/year	0.61 relapse/year	0.74 fewer (0.54 fewer to 0.88 fewer)	⊕⊕⊕⊕ High	0.643
	Dimethyl fumarate	0.50 (0.41 to 0.60)	1.35 relapse/year	0.67 relapse/year	0.68 fewer (0.54 fewer to 0.79 fewer)	⊕⊕⊕⊕ High	0.577
	Glatiramer 20	0.64 (0.57 to 0.72)	1.35 relapse/year	0.86 relapse/year	0.49 fewer (0.38 fewer to 0.58 fewer)	⊕⊕⊕◯ Moderate ♦	0.386
	Glatiramer 40	0.67 (0.55 to 0.81)	1.35 relapse/year	0.90 relapse/year	0.45 fewer (0.26 fewer to 0.61 fewer)	⊕◯◯◯ Very low ♦!§	0.319
	INFB-1a 44	0.67 (0.58 to 0.77)	1.35 relapse/year	0.90 relapse/year	0.45 fewer (0.31 fewer to 057 fewer)	⊕⊕⊕◯ Moderate ♦	0.318
	Teriflunomide	0.68 (0.57 to 0.81)	1.35 relapse/year	0.91 relapse/year	0.44 fewer (0.26 fewer to 0.58 fewer)	⊕⊕⊕◯ Moderate §	0.299
	INFB-1b 250	0.68 (0.58 to 0.79)	1.35 relapse/year o	0.92 relapse/year	0.43 fewer (0.29 fewer to 0.56 fewer)	⊕◯◯◯ Very low ♦!¶	0.298
	INFB-1a 22	0.74 (0.63 to 0.88)	1.35 relapse/year	1.00 relapse/year	0.35 fewer (0.16 fewer to 0.50 fewer)	⊕◯◯◯ Very low ♦!§	0.178
	INFB-1a 30	0.84 (0.74 to 0.96)	1.35 relapse/year	1.14 relapse/year	0.21 fewer (0.05 fewer to 0.35 fewer)	⊕◯◯◯ Very low ♦!§	0.077
	Placebo	Reference	No estimable	No estimable	No estimable	Reference	0.000

HR: hazard ratio; CI: confidence interval; INFB: interferon beta.
In the network geometry, the lines represent direct comparisons.
* Classification result presented by the P-score in the random effect model.
♦Risk of bias; ! Indirectness; ¶ Inconsistency; # Intransitivity; § Imprecision.

GRADE Working Group Evidence Grades (or Certainty in Evidence).
High quality: We are very confident that the true effect is close to the effect estimate.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the effect estimate, but there is a possibility that it may be substantially different.
Low quality: We have limited confidence in the effect estimate: The true effect may be substantially different from the effect estimate.
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the effect estimate

Table 1. Summary of Results of Frequentist Network Meta-Analysis for Annualized Relapse Rate.

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