Second line therapies in relapsing-remitting multiple sclerosis: a head-to-head retrospective study

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Background

Relapsing-Remitting Multiple Sclerosis (RR-MS) patients are usually treated with a first-line therapies. However clinicians often have to switch or start directly a second-line therapies due to high MS activity. Fingolimod and natalizumab are both second-line treatments [1], but there is a general belief of natalizumab superiority. No prospective head-to-head studies have been performed so far, to compare their effectiveness and only few retrospective studies have been reported[2].

Patients & Methods

We retrospectively evaluated all RRMS patients treated with natalizumab (group 0) or fingolimod (group1) for 24 months at our MS centre. Baseline gender, naïve status, EDSS, disease duration (DD), age at disease onset and treatment start, number of relapse 1-year (1yR) and 2-years (2yR) pre-therapy, Annualized Relapse Rate (ARR-PT) pre-therapy were evaluated. We assessed EDSS, ARR-post therapy, relapse occurrence and time-to-first relapse after 24 months. Propensity score matching (PSM) was used in order to minimize the baseline differences.

Results

We included 179 MS patients (group 0= 101; group 1= 78). At baseline, groups were not different for gender, age at onset and EDSS. Group 0 patients had a lower age at treatment start (33.89 ±10.05 vs 40.70 ±10.73; p<0,001), a shorter DD (92.9 ± 78.22 vs 141.5 ±104.67; p<0,001), a higher 1yR (1.40 ±1.19 vs 0.85±0.92; p=0,001), 2yR (2.31 ±1.738 vs 1.45 ±1.29; p<0,001), ARR-PT (1.90 ±3.19 vs 0.66 ±0.68; p=0,002) and a higher percentage of naive patients (44.4% vs 21,1 %; p=0,001) (Table 1). A significant decrease of ARR was experienced in both groups (1.89±3.14 vs 0.22±0.47, p<0,001; 0.72±0,52 vs 0.22±0.54, p<0,001). Matching for PS, ARR decrease, risk of relapses and time to first relapse during therapy were not different between groups . In group 0 no significant variation of EDSS was observed (3.34±1.02 vs 3.40±1.08) while in group 1 we observed a significant increase of EDSS (3.54±1.09 vs 3.89±1.21; p<0,001), however, the variation of EDSS, matching for PS, was not different between groups (0.13 vs 0.24; p=0.321).

Conclusion

In our clinical practice, MS patients with higher disease activity (higher 1yR, 2yR and ARR-PT) are more likely to be treated with natalizumab. However, using PSM, natalizumab and fingolimod revealed the same efficacy in a 2-year follow-up in terms of delta-ARR, EDSS, occurrence of relapse and time to first relapse. Therefore, the general opinion of natalizumab superiority might derive from a bias in patients "selection" in clinical practice.

Table 1

Baseline characteristics			
	Treatment 0 (n=108)	Treatment 1 (n=71)	p-value
Age treatment start (years) Mean (SD) Median Min - max	33.89 (±10.046) 33.60 9.25 − 58.97	40.70 (±10.728) 41.59 18.09 − 62.83	<0.001[1]
Age onset (years) Mean (SD) Median Min - max	26.13 (±9.057) 24.48 6.42 − 53.63	28.88 (±9.026) 27.55 12.95 − 51.82	0.048[1]
Gender (female)	70 (64.8%)	48 (67.6%)	0.700[2]
Naïve (yes)	48 (44.4%)	15 (21.1%)	0.001[2]
Disease duration (months) Mean (SD) Median Min - max	92.9 (78.22) 66.0 0.0 − 349	141.5 (104.67) 122.0 9 − 537	<0.001[1]
EDSS	3.3 (±1.03)	3.5 (±1.09)	0.232[1]
Relapse (1 year pre-treatment)	1.40 (±1.196)	0.85 (±0.920)	0.001[1]
Relapse (2 years pre-treatment)	2.31 (±1.738)	1.45 (±1.296)	<0.001[1]
Total relapse	6.20 (±5.573)	6.20 (±3.905)	0.993[1]
ARR pre-treatment	1.90 (±3.186)	0.66 (±0.675)	0.002[1]

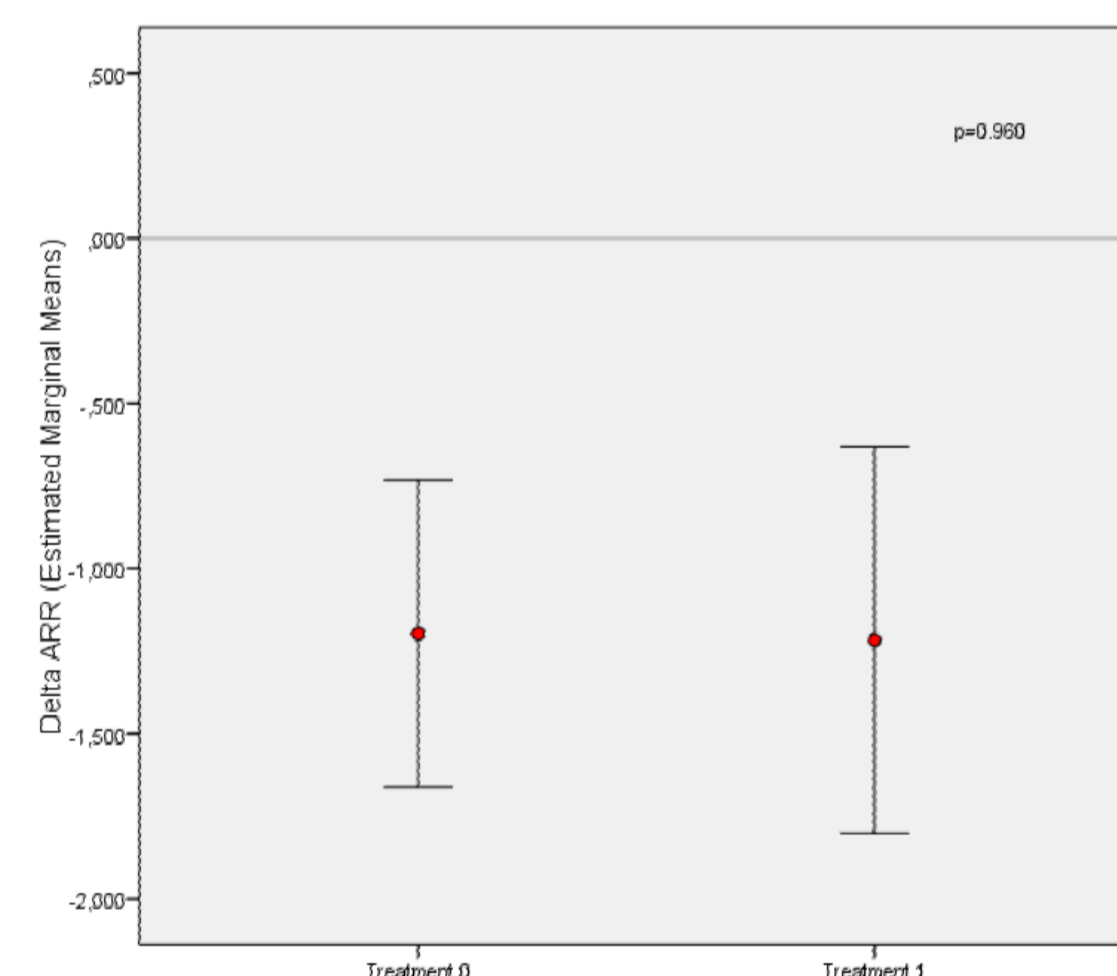[1] t-Student's test
[2] χ^2 test

Figure 1

Variation of the ARR corrected for the propensity score by treatment.
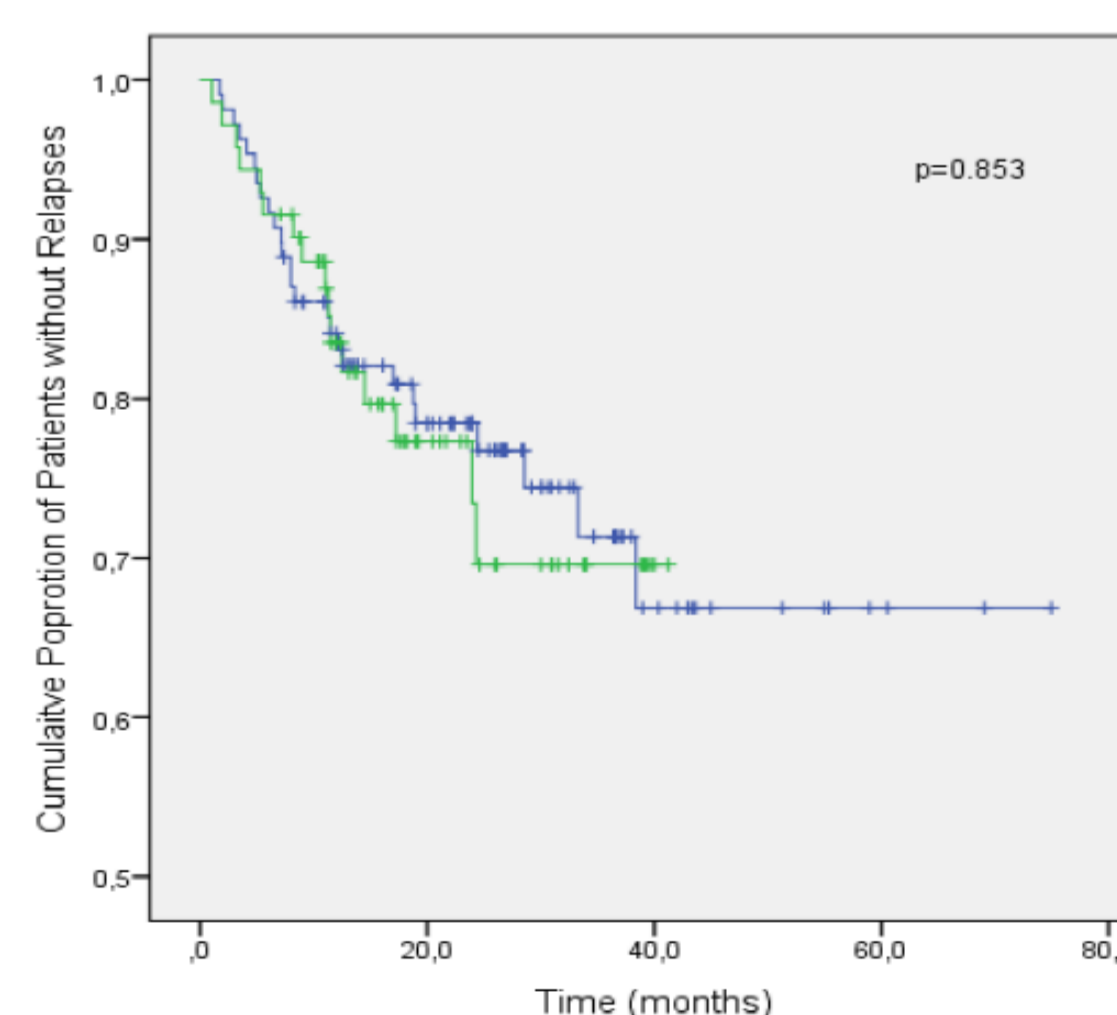

Figure 2

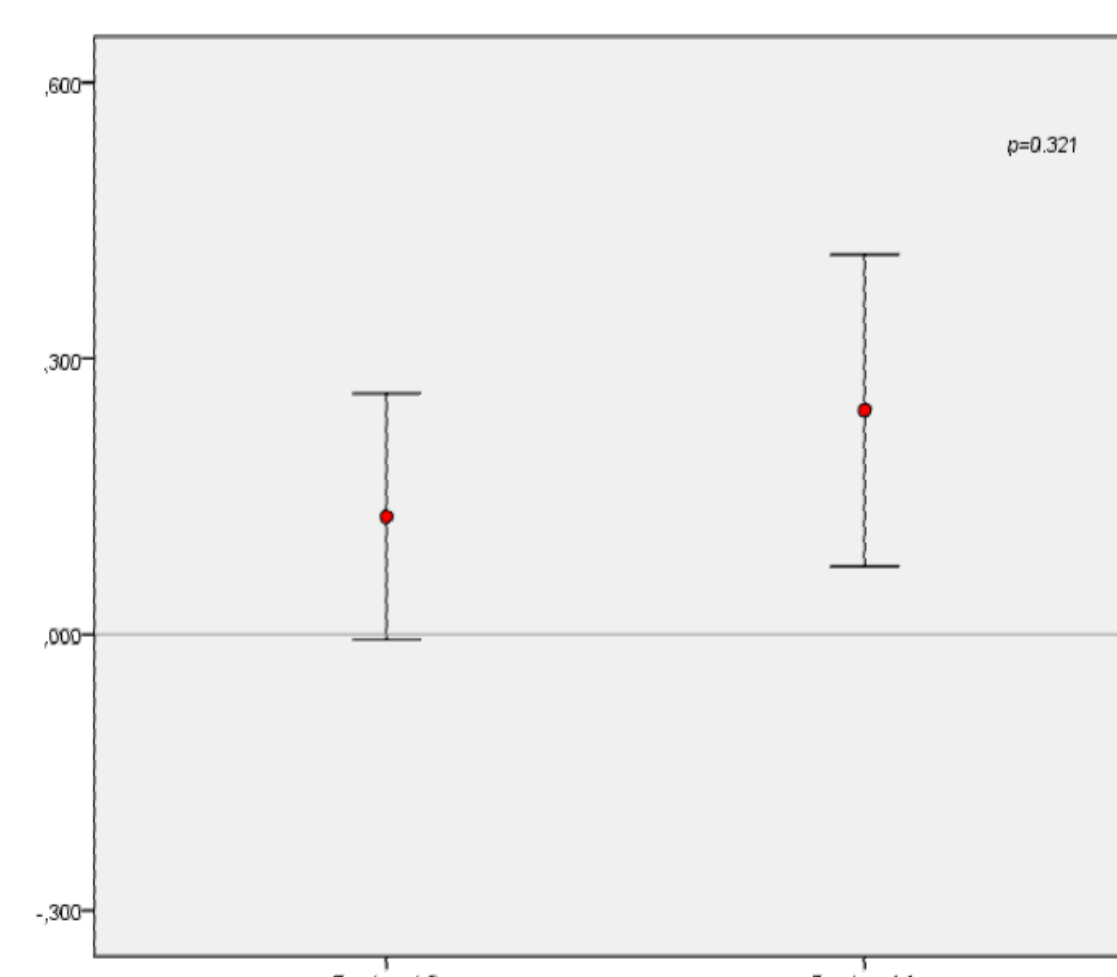Analysis of time to relapse: Kaplan Meier curves .

Figure 3

Variation of the EDSS corrected for the propensity score by treatment

References

•1.   Rudick, R.A., et al., *Natalizumab plus interferon beta-1a for relapsing multiple sclerosis*. N Engl J Med, 2006. **354**(9): p. 911-23.

•2.   Kalincik, T., et al., *Switch to natalizumab versus fingolimod in active relapsing-remitting multiple sclerosis*. Ann Neurol, 2015. **77**(3): p. 425-35.