FINGOLIMOD VERSUS NATALIZUMAB COMPARISON OF TREATMENT EFFECT ON COGNITIVE FUNCTIONS IN RELAPSING MULTIPLE SCLEROSIS

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BACKGROUND

Natalizumab (NTZ) exerts a positive impact on cognitive functions in Relapsing Multiple Sclerosis (RRMS).[1-3] Little is known about the effect of fingolimod (FIN) on these functions.

OBJECTIVES

To compare the effect on cognitive functions of 1-year treatment with FIN or NTZ.

METHODS

- All consecutive RRMS scheduled for treatment with NTZ or FIN underwent neuropsychological evaluation using the Brief Repeatable Battery, Stroop Test, Fatigue Severity Scale (FSS) and Beck Depression Inventory (BDI) at baseline and every 12 months.

- The Cognitive Impairment Index (CII) as a measure of global cognitive function was calculated for each patient.

- The annualized-relapse-rate (ARR) was recorded for each patient, before and during the treatment.

- Propensity score (PS)-matching (1:1) at the time of treatment start was used to compare effectiveness on cognitive functions between the two treatments. Covariates in the model: sex, age, prior DMD exposure, relapses prior the treatment, school education, and BDI score.

- The relapse risk during the treatment was estimated through a Poisson regression model with adjustment for overdispersion.

- A generalized linear mixed model (GLM) for repeated measures was applied to evaluate changes in CII, mean number of cognitive tests failed and FSS score after 1 year treatment.

RESULTS

We have included 100 patients treated with NTZ and 38 patients treated wih FIN. The effect of treatment on cognitive functions was evaluated in 62 matched RRMS patients receiving NTZ (n=31) or FIN (n=31). The characteristics before and after the PS matching are presented in table 1. The relapse incidence was not significant different between the treatments (FIN vs NTZ: Incidence rate ratio = 0.71, p = 0.57). The estimated mean±Standard Error (SE) number of cognitive tests failed was significantly reduced only in FIN treated patients (2.8±2.2 vs 1.7±1.8, p = 0.0014). (Fig. 1).

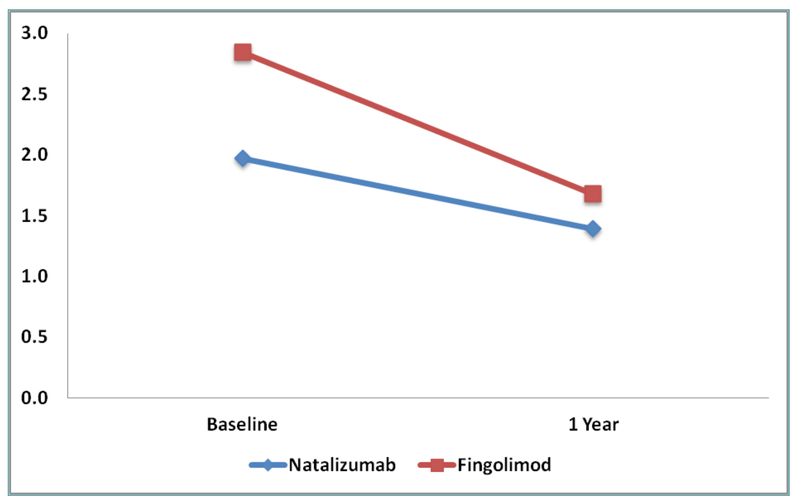
RESULTS

Table 1. Characteristics before and after the PS matching

	Before PS matching			After PS matching		
Variable	NTZ (100)	FIN (38)	SSD	NTZ (31)	FIN (31)	SSD
DMD esposure prior treatment	96 (96.00)	38 (100.00)	-28.8675	31 (100.00)	31 (100.00)	0
School education < 14 years	75 (75.00)	32 (84.21)	23.0096	25 (80.65)	25 (80.65)	0
Age at treatment start, years	34.55 (9.25)	33.72 (10.03)	-8.5986	34.36 (9.37)	34.96 (10.17)	6.0881
BDI score	10.36 (6.94)	8.87 (7.26)	-15.4849	8.58 (6.28)	9.52 (7.64)	12.8762
Total number of relapses prior treatment	8.71 (5.68)	5.89 (3.67)	-58.8839	6.90 (3.23)	6.55 (3.76)	-10.1287
Female sex	72 (72.00)	33 (86.84)	37.3473	27 (87.10)	26 (83.87)	-9.167

Figure 1. GLM for repeated measures – Number of cognitive tests failed before and after 1 year treatment

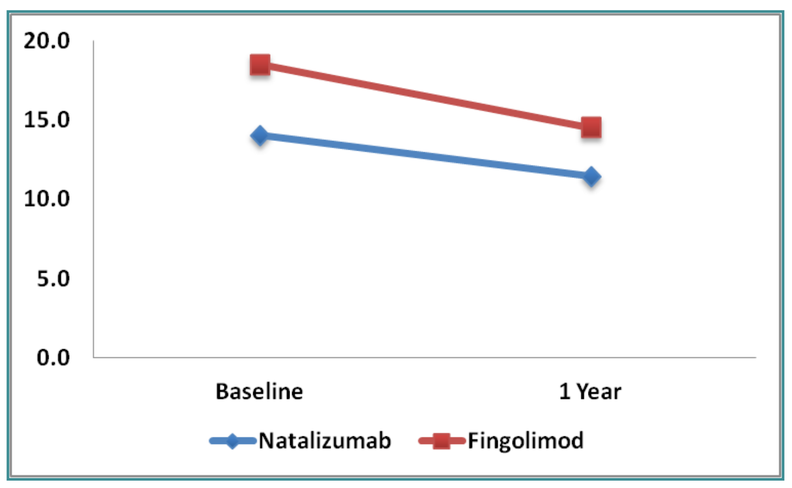
- Group x time interaction, p = 0.2412
- 1 Year vs Baseline FIN, P = 0.0014
- 1 Year vs Baseline NTZ, P = 0.0993



The CII significantly improved in both groups (NTZ 18.5±6.1 vs 14.5±6.1, p=0.0075; FIN 14.0±7.3 vs 11.5±7.5, p<0.0001), but there was not a significant interaction between the groups over time. (Fig. 2) The FSS was unchanged in both groups.

Figure 2. GLM for repeated measures – CII before and after 1 year treatment

- Group x time interaction, p = 0.2967
- 1 Year vs Baseline FIN, P < 0.0001
- 1 Year vs Baseline NTZ, P = 0.0075



Conclusions

Our results indicate that both NTZ and FIN treatments significantly ameliorate cognitive functions in RRMS. Moreover, the effect on the number of tests failed suggests that FIN could have a greater impact on cognition than NTZ. The improvement of cognitive functions goes in parallel with the reduction of the relapse rate. This latter finding supports the hypothesis that in the short-term, NTZ and FIN exert a positive impact on cognition likely by means of their anti-inflammatory properties.

REFERENCES

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