Fingolimod may prevent axonal degeneration at retinal level in multiple sclerosis when compared to first-line injectable treatments.

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Introduction

In recent years, thanks to technological innovations, the visual pathway is receiving increasing attentions as a reliable model to study central nervous system damage in vivo and in a non-invasive way [1]. Optical coherence tomography (OCT) in particular is used in multiple sclerosis (MS) to measure retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCL-IPL) thickness as a marker of axonal and neuronal loss, allowing to detect neurodegeneration [2]. A recent study suggested a protective role for Natalizumab (NAT) on neuroretinal damage [3], with the present work we wanted to explore the possible role of Fingolimod (FTY) in this field. A MRI study infact suggested FTY to have some impact on brain volume measures over time independently from the presence of Gadolinium enhancing lesions [4], and more recently some potential mechanisms of this neuroprotective effect have been also hypothesized, as for example the modulation of the RAGE axis [5].

Methods

Ninety MS patients, 45 receiving FTY (***FTY group***) and 45 Interferon (IFN - n.24) or Glatiramer acetate (GA - n.21), underwent OCT with RNFL and GCL-IPL thickness measurement, with 1 year follow-up. Clinical records were collected since 1 year before baseline assessment. Patients with ocular comorbidities, including severe refraction defects (i.e. greater than ± 6.00 diopters), and patients with recent ON (< 6 monhts) were not enrolled in the study. OCT was performed using a high-resolution spectral-domain device (Heidelberg Spectralis OCT: Spectralis; Heidelberg Engineering, Heidelberg, Germany); RNFL was measured with a 3.5 mm standard circle scan protocol centered on the optic disc, inner and outer boundaries were automatically identified by a segmentation algorhythm provided by the constructor. Mean GCL-IPL thickness was measured using a built-in Fast Macular Volume protocol consisting in 25 B-scans vertically crossing the macula. Follow-up scans were acquired using AutoRescan™ software. Since no significant difference was found between Interferon and GA patients, these two subgroups were unified for further analysis (***IFN-GA group***); enrolled patients and clinical - demographic data are reported in ***Figure 1*** and ***Table 1.***

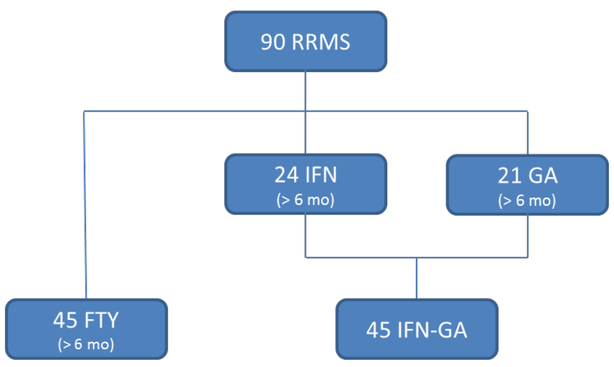


Figure 1. ***Enrolled patients***

	FTY (n.45)	IFN-GA (n.45)	Sig.
Age (mean)	41.4±9.4 years	41.4±10.0 years	p=0.820
Sex (Female/Male)	30/15	23/22	p=0.131
Disease Duration (mean)	13.3±7.3 years	9.9±6.4 years	p=0.024
EDSS (median)	2.0 (1.0-6.0)	1. 5 (1.0-6.0)	p=0.012
ON eyes	29/90 (4 bilateral)	26/90 (3 bilateral)	p=0.676
Treatment duration	2.59±1.2 years	4.19±3.6 years	p=0.006
Disease activity (1 year before baseline)	Relapse 6/45 MRI activity* 11/45	Relapse 5/45 MRI activity* 7/45	p=0.642
Disease activity (follow-up)	Relapse 0/45 MRI activity* 5/45	Relapse 6/45# MRI activity* 2/45	p=0.568

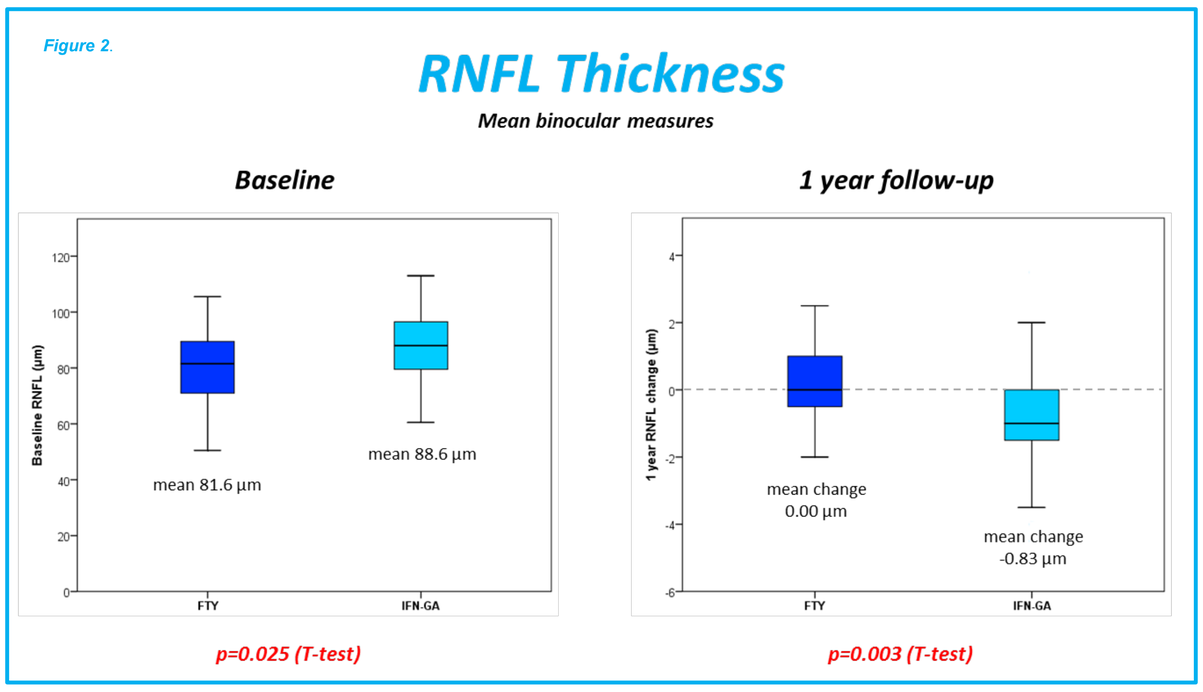
Table 1. ***Clinical and Demographic data. *New T2-FLAIR lesions or GD-enhancing lesions. #New symptoms and steroid administration in 4/6, but non evidence of MRI activity***

Results

Study population data [*Table 1*] showed FTY and IFN-GA groups to be similar in terms of sex and age distribution, while as expectable disease duration was longer in the FTY group. Furthermore, no significant difference was observed in terms of optic neuritis prevalence and disease activity.

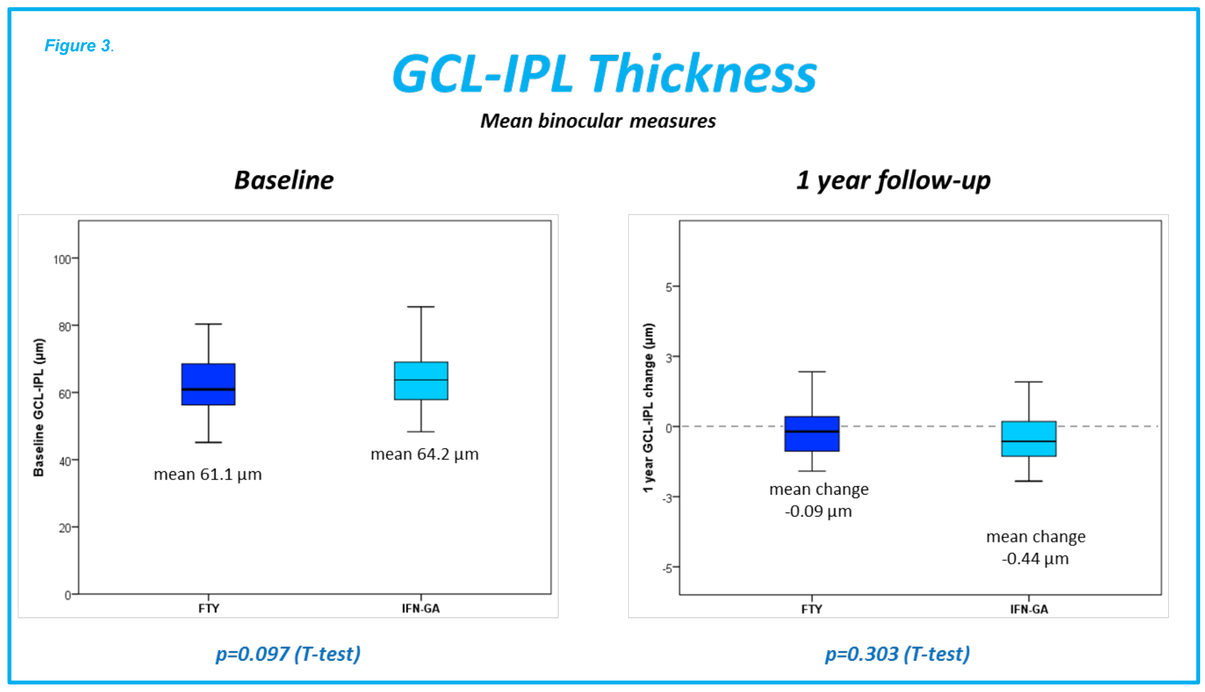
Over one year, patients under FTY had significantly lower ***RNFL*** thinning compared to IFN-GA group (0.00 ± 0.16 µm vs -0.83 ± 0.23µm; p=0.003), despite significantly lower baseline values (81.6 ± 15.2 µm vs 88.6 ± 13.9µm; p=0.025) [*Figure 2*]. ***GCL-IPL*** thickness did not significantly differ between the two groups, both at baseline (IFN-GA 64.2 ± 8.6 µm vs FTY 61.1 ± 9.7 µm; p=0.097) and over time (-0.44 ± 1.1 µm for IFN-GA vs -0.09 ± 1.3µm for FTY; p=0.303) [*Figure 3*]. Similar rates of disease activity (new relapses or new T2/Gd enhancing lesion at brain MRI) were found both in the year before baseline (24.3% for IFN-GA vs 28.8% for FTY; p=0.642) and during follow-up (15.3% for IFN-GA vs 13.3% for FTY; p=0.790). Interestingly these results were also confirmed when ***excluding EDA patients*** from analysis.

Figure 2.



p=0.025 (T-test) *p=0.003 (T-test)*

Figure 3.



p=0.097 (T-test) *p=0.303 (T-test)*

Discussion and Conclusions

Our results suggest ***FTY*** to ***prevent axonal loss at retinal level*** independently from clinical and neuroradiological evidence of inflammatory disease activity. Although a longer follow-up is warranted to confirm these observations, our findings of a potential neuroprotective effect at retinal level appear to be consistent with previous experiences reporting a reduction of brain volume loss in patients receiving FTY [4].

Bibliography and Acknowledgements

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