Fingolimod reduces the clinical expression of active demyelinating lesions in MS

Signoriello E.[1], Landi D.[2], Monteleone F.[2], Albanese M.[2], Buttari F.[2], Sica F.[2], Mataluni G.[2], Mori F.[2], Nicoletti C.G.[2], Boffa L.[2], Marfia G.A.[2], Lus G.[1], Centonze D.[2,3]

[1] *Multiple Sclerosis Center, II Division of Neurology, Second University of Naples, Italy.*
[2] *Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Tor Vergata University, 00133 Rome, Italy*
[3] *IRCCS Istituto Neurologico Mediterraneo (INM) Neuromed, 86077 Pozzilli (Is), Italy*

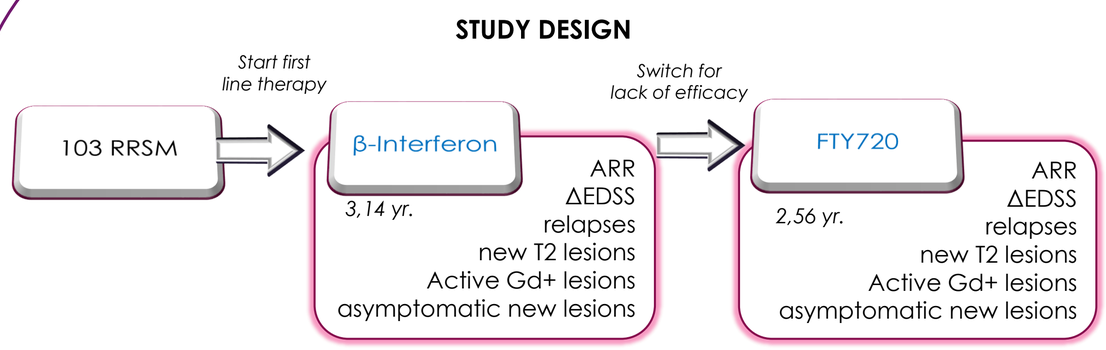
Background

New demyelinating lesions may or may not be associated with clinical symptoms depending on inflammation extent and individual network plasticity properties. In animal models and remitting MS Fingolimod (FTY720) has been proved to reduce neuroinflammation and modulate glutamate-mediated neurotransmission by enhancing synaptic plasticity and compensation for demyelinating damage. This study aimed to retrospectively observe whether treatment with FTY720 is able to amend the clinical expression of new lesions as detected by MRI.

Materials

103 patients with relapsing-remitting MS switching for inefficacy from first line injectables (FL), namely β-IFN, to FTY720 and treated for at least 12 months were included. For each patient the occurrence of new Gadolinium (Gd+) enhancing lesions was evaluated during FL and FTY720 treatment. The number of asymptomatic active lesions was compared between the two conditions (FL/FTY720 treatment). Annualized relapse rate (ARR), clinical recovery from relapse, EDSS and total new T2 lesions number were also collected in both conditions.

Results



Baseline characteristics of the included population are reported in Tab.1. Treatment with FTY720 was associated with significantly lower number of Gd+ lesions (p=0,01) and higher rate of asymptomatic lesions compared with FL therapy (88% vs 30,9%, p=< 0.025) (Fig. 1 and 2).
ARR, disability progression measured by EDSS and total number of new T2 lesions were also significantly reduced (p<0.001) (Tab. 2); higher rate of full recovery from relapse was achieved (p= 0,01). Assuming a linear trend between T2/active lesions accrual and ARR, we found that treatment with FTY720 was associated with an increase of 0,04 of the ARR for each new T2 lesion and of 0.06 for each new active lesion against treatment with β-IFN which was associated with an increase of 0.29 and 0.33 respectively (Fig. 3 and 4).

Tab. 1 Baseline characteristics of the included population

Age (mean, SD)	36,64 (8,85)
Gender (Female) %	61(60,4%)
Disease Duration (mean, SD)	10,12 (5,71)
Total relapses (mean, SD)	3,34 (2,04)
Total ARR (mean, SD)	0,41(0,32)
Baseline EDSS β-IFN (mean, SD)	1,79 (1,17)
Baseline EDSS FTY720 (mean, SD)	1,99 (1,32)
Basaline Gd+ lesions (mean, SD)	1,14 (1,79)

Tab. 2 Clinical outcomes in patients treated with β-IFN and FTY720

	β-interferon	FTY720	p
Progressed patients (n. %)	15(14,5%)	4(3,8%)	< 0,01
Baseline EDSS (mean, SD)	1,79 (1,17)	1,99 (1,32)	
End of Treatment EDSS (mean, SD)	1,86 (1,18)	1,80 (1,29)	
Delta EDSS	0,07 (0,61)	-0,12 (1,07)	0,112
Gd + lesions (mean, SD)	1,12 (1,23)	0,66 (1,67)	0,01
Relapses (mean, SD)	1,02 (1,18)	0,10 (0,39)	< 0,0001
ARR (mean,SD)	0,37 (0,42)	0,04 (0,17)	< 0,0001
New T2 lesions (mean,DS)	1,69 (1,36)	1,07 (1,88)	0,001

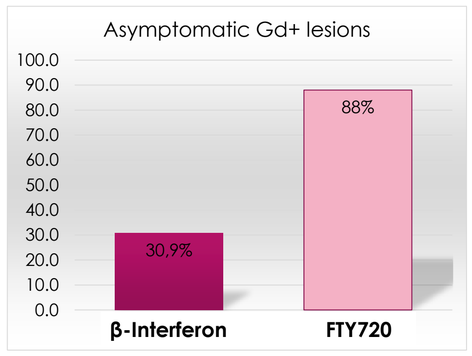


Fig.1 Reduction of active lesions during FTY720 therapy

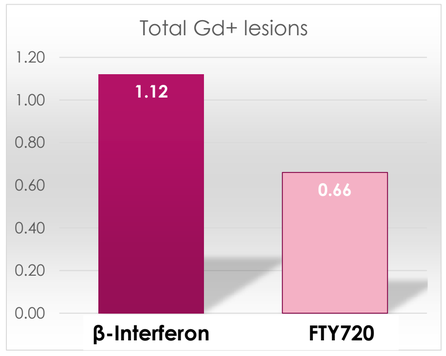


Fig.2 Higher rate of asymptomatic lesions during FTY720 therapy

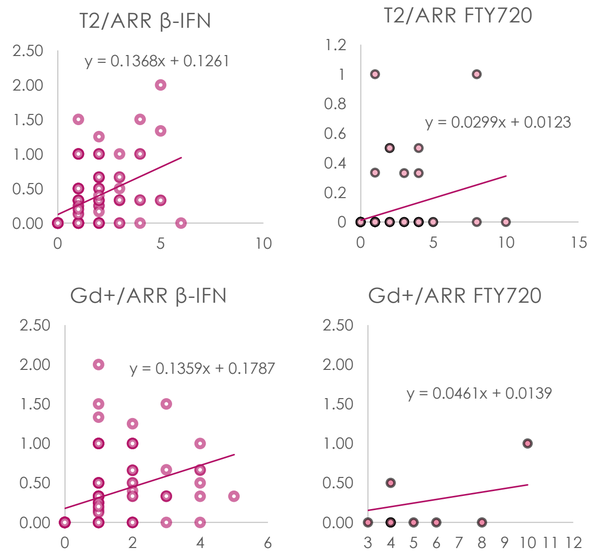


***Fig.*3 Reduction in ratio of T2 lesions increase and ARR during therapy with β-IFN and during therapy with FTY720(p <0.01)**

Fig.4 Reduction in ratio of Gd+ lesions increase and ARR during therapy with β-IFN and during therapy with FTY720 (p <0.01)

Discussion and conclusions

FTY720 is able to limit the clinical expression of new Gd+ enhancing lesions, eventually modulating brain network plasticity in patients with suboptimal response to prior immunomodulating treatments, besides an overall reduction of neuroinflammation.

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