NO EVIDENCE FOR SKIN MALIGNANCIES DURING FINGOLIMOD IN MULTIPLE SCLEROSIS: DATA FROM REAL LIFE

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Objective: To date definitive conclusions on any potential long-term risk for skin malignancy during Fingolimod (FTY) treatment cannot be drawn, especially for exposure greater than 2 years. We aimed to assess dermatological safety in a real life setting of relapsing remitting Multiple Sclerosis (RRMS) FTY-treated patients

Materials and Methods: All patients who started FTY treatment underwent a standardized clinical and dermoscopic examination at baseline and every six months thereafter. Simple and multivariate logistic regression models were performed to assess baseline factors (age at FTY, sex, skin phototype, history of sunburns and familiar skin cancers, number of naevi) that could predict the occurrence of atypical skin lesions .

Results: One-hundred and ninety eight patients (**Table1**) were followed-up for a mean period of 26± 8 months. Thirty one (15.6 %) had comorbidities. Eleven (5.9%) showed atypical skin lesions up to 1 year of therapy and were biopsied. None of these lesions resulted to be malignant. The only predictive factor for the incidence of atypical melanocytic naevi was the presence at baseline of a higher number of naevi (p=0.03, OR=1.62 95%CI=0.98-1) (**Table 2**). Patients showing atypical naevi had, from the third month of therapy, a lower number of CD3+ cells (296±100 vs 415.8±130,6, p =0.05). Two female patients experienced a basal cell carcinoma, after 30 and 22 month of treatment. They did not have previous exposure to immunosuppressant and reported histories of sunburns. Both patients showed, from the third month, a higher number of CD3+ (470 and 452) and a lower number of CD8+ (115 and 118) and CD16+/CD56+ cells (134 and 152) compared to the mean of other FTY treated patients in our cohort (mean CD3+: 392.5 ± 87.4, CD8+: 226.3 ± 97.8 and CD16/CD56+: 216.8± 102.3). (**Figure 1**) Both patients discontinued FTY for skin biopsy, and they re-started the same therapy after 3 months, after an accurate evaluation of the benefit/risk ratio.

Discussions and Conclusions: We did not find evidence of correlation between FTY and skin malignancies. Patients treated with FTY need to undergo regular immunological and dermatological follow ups in order to capture as early as possible atypical naevi. Immunological features of patients should be considered to schedule more appropriate management strategy during FTY therapy. Longer follow-ups and larger cohorts will be necessary to verify these findings.

Table1. Baseline characteristics of the cohort and skin phototypes

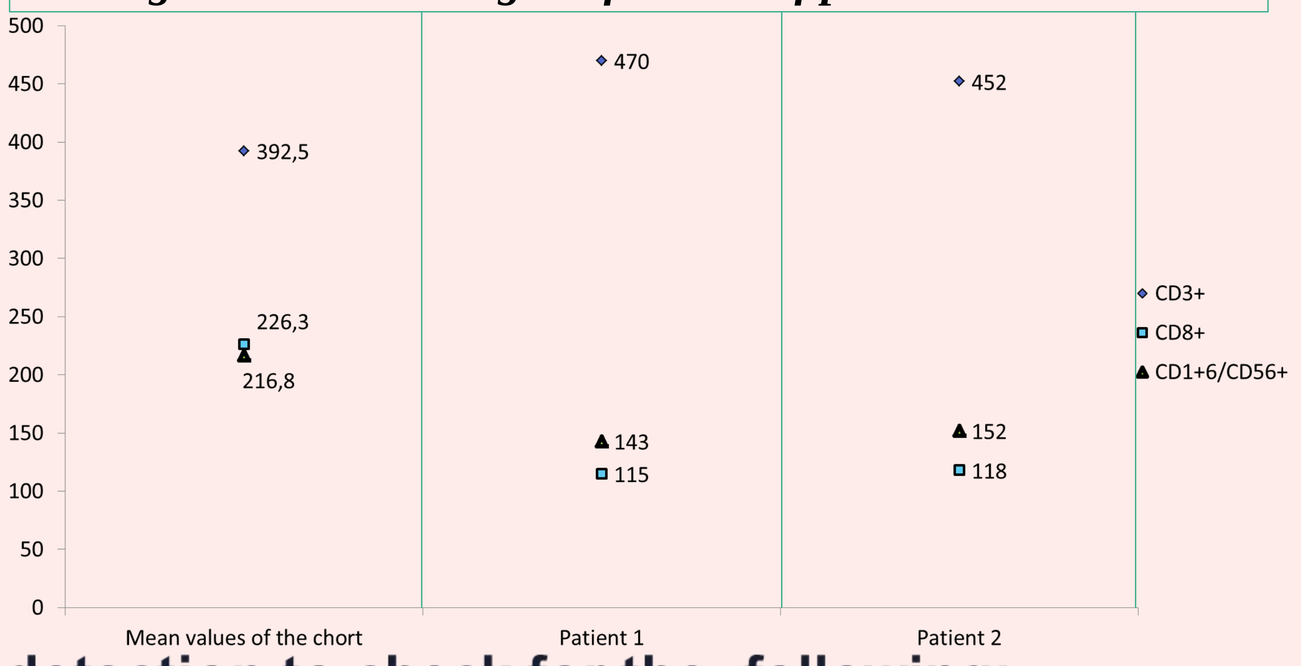
	N = 198
Sex: F	132/98 (67%)
M	66/98 (33%)
Mean age at FTY start (SD)	38 6.54
Previous use of immunosuppressant	40/198 (20.2%)
History of sunburns	32/198 (16.2%)
> 10 naevi	79/198 (39.9%)
History of melanoma	4/198 (2.2%)

1	3
2	170
3	18
4	3
5	5
6	/

Table2. Predictive factors for atypical naevi

	Atypical naevi	
Predictor	**OR (95% CI)**	**P**
Male sex	0.58 (0.82-2.26)	0.52
Previous use of IS	1.32 (0.54-1.62)	0.19
Skin phototype	0.96 (0,42-1,15)	0.21
Higher number of naevi	**1.62 (0.98-1)**	**0.03**
Age at FTY beginning	1.14 (0.85-1.88)	0.39
History of sunburns	1.10 (0.7-1.89)	0.43
History of maelanoma	1.11 (0.96-1.21)	0.50

Figure 1. Immunological features of patients with BCC



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