LYMPHOCYTE COUNT AS BIOMARKER OF MRI ACTIVITY IN A MULTIPLE SCLEROSIS DIMETHYL-FUMARATE-TREATED COHORT

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Objective: In Multiple Sclerosis (MS) clinical trials, Dimethyl-Fumarate (DMF) was associated with reduced absolute lymphocyte counts (LC), to a variable extent. While lymphopenia seems not to be related to drug's mechanism, very few information are provided about the role of the absolute LC as possible marker of treatment response. We aimed to assess the predictive value of LC for Magnetic Resonance Imaging (MRI) activity in a real life setting of DMF treated Relapsing-Remitting (RR)-MS patients.

Matherials and Methods: We collected clinical and demographic data at the DMF beginning (T0). All patients had a baseline MRI within 6 months before DMF beginning. LC was assessed at T0 and after 3 (T3) and 6 (T6) months of therapy by flow cytometry, in the same laboratory. The occurrence of Gadolinium enhancing (Gd+) and new T2 lesions, at MRI scans at T6 and after 12 months (T12), defined MRI activity. To correlate LC with these MRI outcomes, at T6 and T12, non-parametric tests were performed (Spearman test). We evaluated using multivariate logistic regression models, whether LC can be a predictive factor for MRI response to treatment.

Results: Ninety DMF-treated patients (**Table 1**) were followed up for a mean period of 15 ± 7 months. From T0 to T3 we observed a significant reduction of 15.36% in LC (from 1940 ± 667,60/ul to 1642,18 ± 1184,75/ul, Wilcoxon p value = 0.001). We observed a direct correlation between LC at T3 and the occurrence of Gd+ (rs=0.29, p=0.017) and new T2 lesions at T6 (rs=0.25, p=0.046) (**Figure 1**). We also found a direct correlation between LC at T3 and Gd+ (rs=0.3, p=0.033) and new T2 lesions at T12 (rs=0.33 p=0.019)(**Figure 2**). At the multivariate models, adjusted for age and sex, predictive factors for the occurrence of Gd+ lesions at T12 resulted LC at T0 (p=0.05, OR=1.003, CI=1.0-1.006) and at T3 (p=0.037, OR=1.084, CI= 0.997-1); LC at T3 were confirmed as predictive factors also for new T2 lesions at T12(p=0.005, OR=1.010 CI=0.99-1).

Table 1. Baseline characteristics of cohort

	N = 90
Sex: F	52 (57,8%)
M	38 (42,2%)
Mean age at DMF start (years)	38 ± 10.77
Disease duration	12.9 ± 8.03
EDSS at DMF start	2.99 ± 1.46
Last treatment pre-DMF: Naïve	14 (15%)
First line	68 (75.6%)
Second line	8 (8.9%)
WBC at baseline (n°/ul)	6387.8± 2051.9
LC at baseline (n°/ul)	1940 ± 667.60
Patients with new T2 lesion at baseline MRI (%)	54 (60%)
Patients with Gd+ lesion at baseline MRI(%)	25 (27,7%)

WBC = White Blood count; LC = Lymphocyte count ; Gd+= Gadolinium enhancing; DMF= Dimethyl-Fumarate; Values expressed as mean (±SD)

Figure 1. Correlation between LC at T3 and MRI at T6

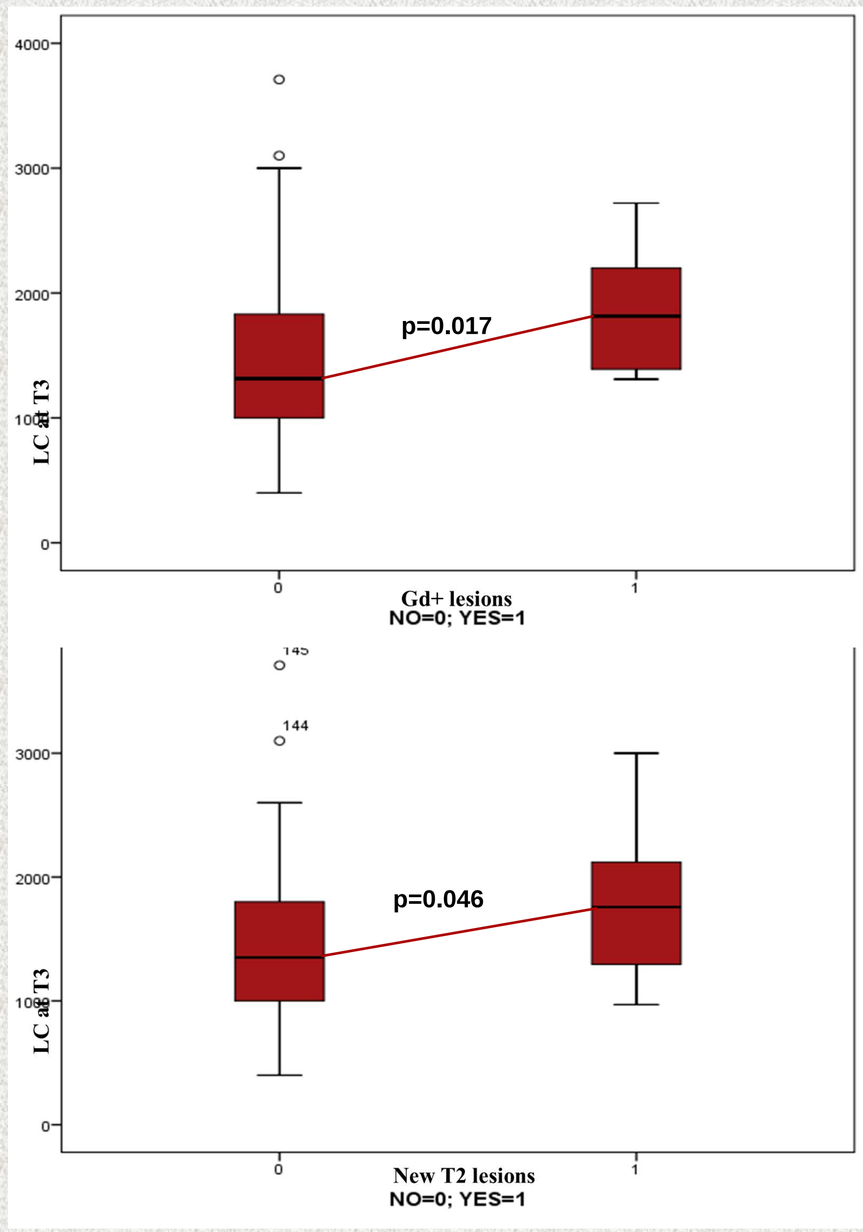

Figure 2. Correlation between LC at T3 and MRI at T12

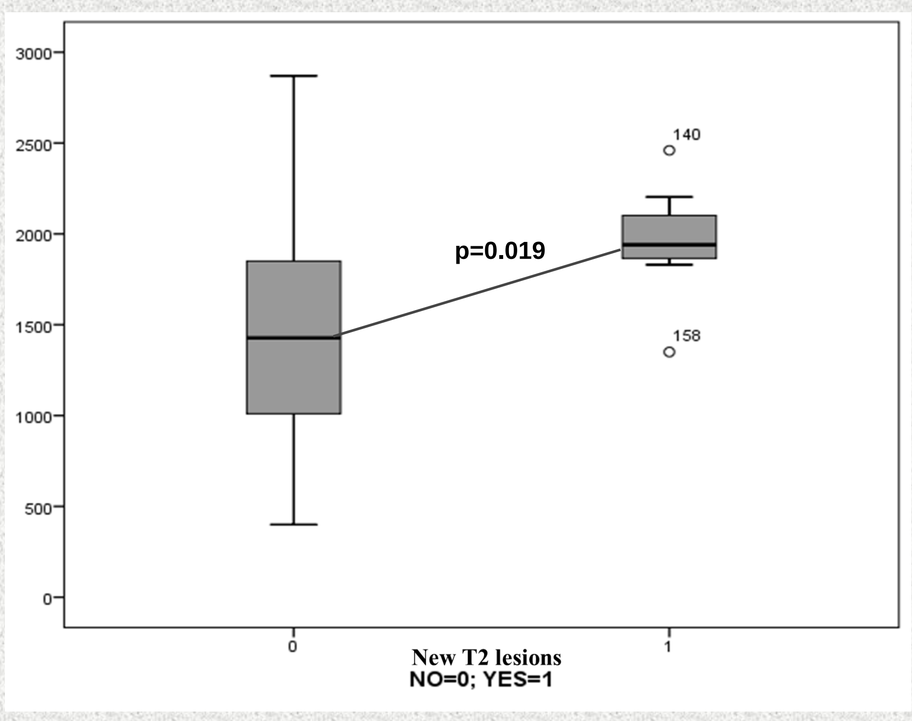

Table2. Predictors of MRI activity at T12

	Gd+ lesions		New T2 lesions	
Predictor	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Male sex	0.98(0.88-1.35)	0.22	0.96(0.73-1.14)	0.22
Age at DMF beginning	1.26 (0.93-1.31)	0.59	1.19(0.31-2.13)	0.34
LC at T0	**1.003 (1.0-1.006)**	**0.05**	1.13(0.795-0.97)	0.32
LC at T3	**1.084 (0.997-1)**	**0.037**	**1.01 (0.99-1)**	**0.005**
WBC at T0	1. (0.96-1.54)	0.14	1.31 (0.81-1.41)	0.61
WBC at T3	1.001 (0.99-1.14)	0.56	1.15 (0.99-1.34)	0.51

Conclusions: Our results suggests that DMF-induced changes in the absolute LC could be considered to evaluate treatment response from the early phases of therapy.

References

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