Lymphocyte subsets changes as biomarker of therapeutic response in Fingolimod treated relapsing MS

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BACKGROUND

The scenario of Multiple Sclerosis (MS) therapies is constantly evolving. Therefore the identification of potential biomarkers for therapeutic response can be useful in clinical practice.

OBJECTIVES

To correlate lymphocyte count (LC) and changes in lymphocyte subsets with treatment response in a cohort of 119 Fingolimod (FTY) treated relapsing MS patients.

METHODS

LC and lymphocyte subsets (**CD3+, CD4+, CD8+, CD56+, CD19+**) were assessed at the start of FTY (**T0**) and after 6 and 12 months of therapy (**T6** and **T12** , respectively) by flow cytometry. Brain and spinal cord MRI and neurological examination were performed at baseline and every 6 months. Occurrence of relapses, new T2- or Gadolinium positive (Gd+) lesions were recorded during the first and the second semester of treatment. Simple and multivariate logistic regression models, adjusted for age and sex, were used for the analyses.

RESULTS

One-hundred and nineteen patients (69% female; mean age: 38.3±9 years) were followed-up for six months, and 89 of them for 12 months. During the first 6 months of therapy, a higher number of ***CD3+*** (OR 1.003 IC 95% 1-1.005, p=0.04) and ***CD8+*** (OR 1.005 IC 95% 1-1.010, p=0.05) and a lower number of ***CD56+*** (OR 0.99 IC 95% 0.98-1, p=0.04) were predictive of a higher ***incidence of relapses***, a lower change ***(Δ) of CD4+*** between T0-T6 was associated with an increased ***risk of new T2-lesions*** (OR -1.002 IC 95% 1-1.004, p=0.04) and a lower ***Δ of total LC*** (OR 1.005 IC 95% 1.001-1.008, p=0.007), ***CD3+*** (OR 1.006 IC 95% 1.002-1.011, p=0.005) and ***CD8+*** (OR 1.007 IC 95% 1.002-1.012, p=0.009) were associated with the ***occurrence of Gd+ lesions***.

In the subgroup of patients followed-up to 12 months, the ***Δ of total LC*** (OR 1.004 IC 95% 1-1.008, p<0.05) and ***CD8+*** (OR 1.009 IC 95% 1.001-1017, p=0.02) between T6-T12 predicted the ***occurrence of Gd+ lesions***.

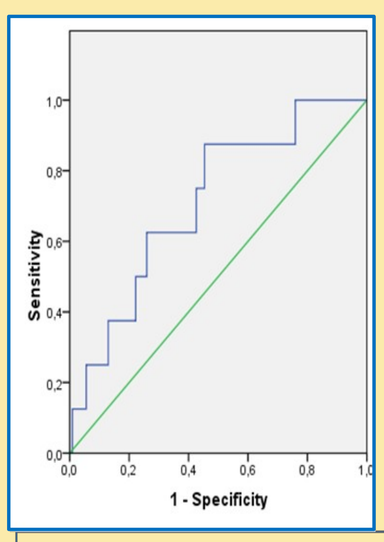
ROC curves (*Figure 2*) enabled to identify ***cut-off values of CD3+ and CD8+*** predicting a higher ***risk of relapses*** during the first 6 months and a ***cut-off value of total LC*** predicting the ***occurrence of Gd+ lesions*** during 12 months of therapy.

Figure 1 *Temporal profile of lymphocytes changes as absolute values and delta(Δ)*

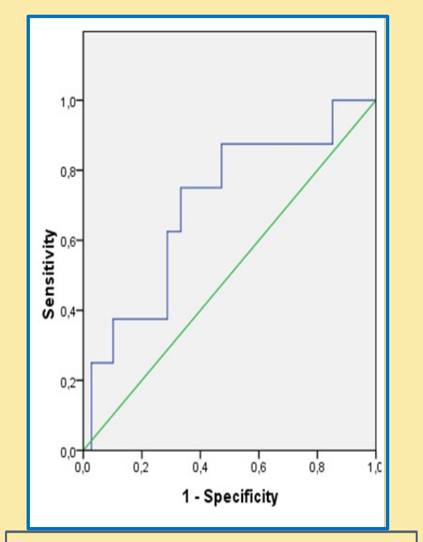
	LC	CD3+	CD4+	CD8+	CD56+	CD19+
T0	2131.31 ±619.58	1561.90 ±518.16	981.62 ±352.34	517.31 ±216.89	227.38 ±130.22	325.76 ±140.02
T6	597.39 ±245.42	343.1 ±220.98	106.78 ±112.15	181.02 ±125.65	207.25 ±103.19	34.47 ±23.7
T12	670.12 ±311.95	392.5 ±270.4	119.65 ±151.93	216.38 ±158.36	226.21 ±123.39	35.87 ±25.35

Δ%	T0-T6	T6-T12
LC	-71%	+70.5%
CD3+	-78%	+36%
CD4+	-89,1%	+15.4%
CD8+	-65%	+19,5%
CD56+	-8.8%	+23.7%
CD19+	-89.4%	-1.4%

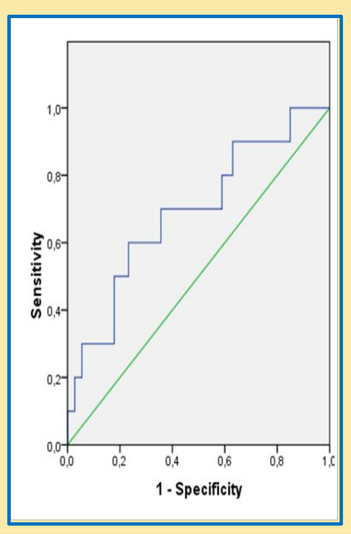
Figure 2 *ROC curves (Area under the curve, AUC>0,70)*



CD8+ at T6 vs Relapses at T6
AUC 0,71
p<0,05
Best cut-off 123.69/ul
(sensitivity 87%, specificity 55%)



CD3+ at T6 vs Relapses at T6
AUC 0,701
p<0,05
Best cut-off 262.02/ul
(sensitivity 87%, specificity 54%)



LC at T12 vs Gd+ lesions at T12
AUC 0,70
p<0,05
Best cut-off 591.50/ul
(sensitivity 70%, specificity 48%)

CONCLUSION

Our study demonstrated the ***potential role of lymphocyte subsets changes as biomarker*** to early identify ***FTY-treatment response***. Further studies will be necessary to verify the accuracy and reproducibility of our results.

References
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Sato DK et al. *J Neuroimmunol 2014*; 268(1-2):95-8