Prognostic parameters of medium-term response to fingolimod treatment in Relapsing Remitting Multiple Sclerosis patients

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Background: Fingolimod (FTY) is highly effective in Relapsing Remitting Multiple Sclerosis, with ~50% patients showing no evidence of disease activity (NEDA) at 2-year follow-up. Nonetheless, the early identification of non-responders (NR) to second-line therapy is urgent, to promptly address these subjects to more aggressive drugs.

Aims: we investigated the persistence of response to FTY after 4 years of treatment, searching for prognostic markers of treatment failure.

Patients and methods: 339 patients treated with FTY for >1 year were classified according to NEDA at 4-years and to time to first relapse (TFR). Logistic and cox regression analyses were applied to identify baseline and on-treatment (1st year) parameters of NR.

Results: At 4 years, 63% of patients were free from clinical relapses and 35% were NEDA. A higher level of baseline disease activity (numbers of relapses and brain MRI active lesions) was associated with a higher risk of EDA and with a shorter TFR ($p < 0.05$). Female gender and a younger age at disease onset were associated with a higher risk of drug failure, together with previous natalizumab therapy ($p < 0.05$). Interestingly, disease reactivation during the first year was highly predictive of long-term treatment failure: having at least one relapse had a positive predictive value (PPV) of 0.75 for NR, while having at least one active MRI lesion had a PPV=0.73 and showing both clinical and MRI activity had a PPV=0.86.

Conclusions: although the proportion of NEDA patients decreased at 4-year compared to 2-year follow-up, most of patients were clinically stable 4 years after FTY start. Our data emphasize the need for a close disease monitoring during the first year of fingolimod treatment, towards an early identification of NR patients that require treatment optimization.