

## **Recurrence of disease activity after fingolimod discontinuation is not rare in older patients previously stable on treatment**

Vasiliki Pantazou<sup>1</sup>, Caroline Pot<sup>1</sup>, Renaud Du Pasquier<sup>1</sup>, Geraldine Le Goff<sup>1</sup>, Marie Théaudin<sup>1</sup>

<sup>1</sup>Division of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

### **Abstract**

**Background :** There is growing evidence from post-marketing studies that recurrence of disease activity (RDA) and even rebound activity after fingolimod (FTY) discontinuation are not rare.

**Aims and Methods:** From the 255 Relapsing Remitting Multiple Sclerosis patients who initiated FTY in the Lausanne MS clinic, 97 discontinued the medication. We retrospectively reviewed patient demographics, reason for discontinuation, type of Disease Modifying Drug (DMD) prescribed after FTY discontinuation, clinical and MRI outcome after discontinuation. RDA was defined as either clinical and/or MRI activity and rebound was considered when disease activity after discontinuation was much higher than before FTY onset.

**Results:** Median FTY treatment duration before discontinuation was 33 months (range 6-183). There were 72 females (74.2%). 42 (43.3 %) patients were on FTY as a first line therapy, 43.3 % had switched from Interferon (IFN), 9.3 % from natalizumab (NTZ) and 5.1 % from other DMDs. Median follow-up after discontinuation was 17 months (range 5-72). Reasons for FTY discontinuation were: (i) estimated high risk of PML (positive JCV status, age > 45 yo and treatment duration >2 years) (n=31, 32.3 %), patients were then mostly switched to teriflunomide (TRF) (n=16, 61.5 %) or dimethyl fumarate, (ii) lack of efficacy (n=29, 30.2 %), patients were then mostly switched to NTZ or anti-CD20 therapy), (iii) pregnancy planning (n=14, 14.6 %), (iv) side effects (n=9, 9.4 %) and (v) patients' convenience (n=10, 10.4 %). RDA occurred in 38 patients (40.4 %). From the 23 patients who experienced clinical relapses within 6 months (median 1, 1-5), 16 (72.7 %) had no clinical activity on FTY. 31 patients (81.6 %) had MRI activity (median 3 new T2 lesions per patient, range 1-38). Twelve patients experienced a rebound activity with a median of 8 new T2 lesions (2-38) and 1 relapse (0-3) per patient. Four of those patients had no DMD at time of rebound, 2 were on TRF and 1 on ocrelizumab. Although severe rebound was noted in 2 patient switched for PML risk, 10 of

these 31 patients (32.3 %) showed RDA despite no evidence of disease activity during FTY treatment. Among those patients, younger age strongly correlated with RDA ( $p=0.017$ ), while initial EDSS ( $p=0.397$ ), clinical ( $p=0.370$ ) or MRI activity ( $p=0.657$ ) did not reach statistical significance.

Conclusion: RDA occurred in almost 40 % of our patients and 10 % had a severe rebound activity. Absence of treatment after FTY discontinuation was the main risk factor for rebound. Surprisingly, 30 % of the older patients, who were expected to have a less active disease given their age and the absence of disease activity for several years on FTY experienced RDA, which was severe in 2 patients.