Clinical activity after Fingolimod cessation: disease reactivation or rebound?

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Background. In the last years several reports about a possible rebound after fingolimod (FTY) discontinuation in patients with Multiple Sclerosis (MS) were reported. On the other side, no rebound was found in the FTY randomized clinical trials, including more than 2000 subjects. It is still debated if the so-called rebound is really related to FTY discontinuation rather than the natural course of highly active MS.
The study *aimed* to survey the prevalence of severe reactivation and rebound after FTY discontinuation in a large cohort of MS Italian patients.

Methods. Patients with RRMS treated with FTY since at least 6 months, who stopped treatment for reasons not related to inefficacy were included in this analysis. A severe reactivation was defined as a relapse with an associated EDSS increase of at least 2 points or 2 or more relapses in the 6 months following FTY discontinuation. A severe reactivation was considered a rebound if these criteria have never been fulfilled in the patient's previous medical history.

Results

A total of 108 patients satisfied the inclusion criteria. Clinical and demographic features are shown in figure 1. We selected 90 patients with no relapses in the last 6 months under FTY. The ARR before, during, and after FTY are reported in figure 2. The clinical evidence after FTY-stop is reported in figure 3. Among the 6 patients with severe reactivation, 1 had a relapse associated with an EDSS increase of 6 points, 2 had a relapse associated with an EDSS increase of 2 points and 1 had 3 relapses over 6 months. Four patients out of 90 (4.4%) were defined as rebound.

Figure 1

Age, mean (SD)	37.3 (10)
Females/Males, n(%)	86 (79.6)/22 (20.4)
EDSS, median (range)	2.5 (0-8.5)
Disease duration (years), median (range)	8.8 (0.2-32.2)
ARR pre-FTY, mean (SD)	0.95 (0.81)
Patients with relapses pre-FTY	76.7%

Figure 2

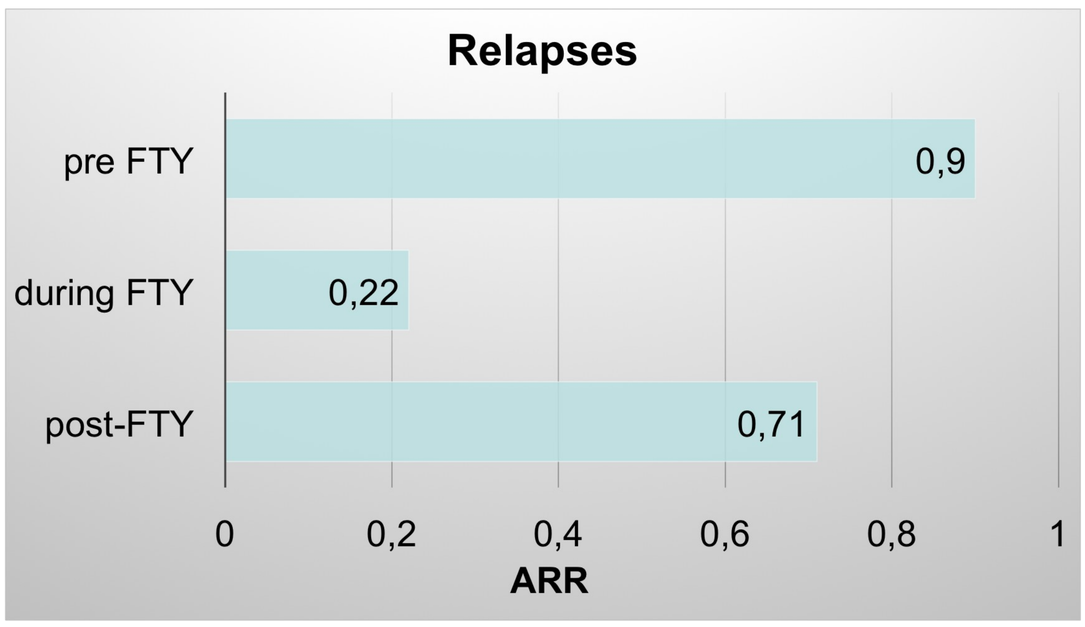
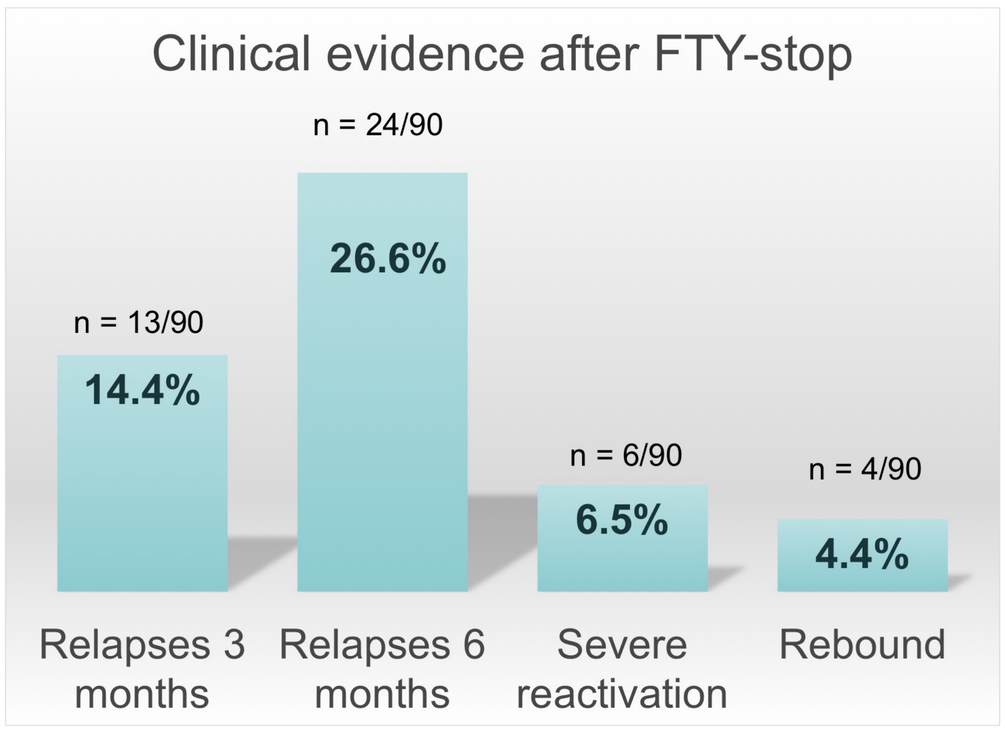


Figure 3



Conclusions

The present study showed that more than 25% of patients risk to have a relapse within 6 months after FTY discontinuation. This is an expected result, being fingolimod approved in Italy as second line therapy in MS. Nevertheless, the risk of severe reactivation and rebound is lower than previously described.

Reference Hatcher SE, et al. Rebound syndrome in patients with multiple sclerosis after cessation of fingolimod treatment.