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**Switching to alemtuzumab from fingolimod or other therapies: impact of wash-out period on disease activity**

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**Objective:** To evaluate the ARR during alemtuzumab administered after fingolimod and after other disease modifying therapies (DMTs).

**Background:** Recently, an unexpected high disease activity during alemtuzumab was described in MS patients switching from fingolimod. The authors suggested that the lack of alemtuzumab efficacy could be due to the prolonged sequestration of lymphocytes induced by fingolimod.

**Methods:** Patients who started alemtuzumab after fingolimod or other DMTs were included in this retrospective multicentric analysis. Previous therapy, wash-out period duration and relapses occurrence (during previous therapy, in the wash-out period and during alemtuzumab) were retrospectively assessed and analysed by a negative binomial model. Time to relapse or to new T2 lesions or time to disability progression (NEDA), whatever occurred first, was analysed using Cox model.

**Results:** 159 patients who started alemtuzumab in 12 MS centers in Italy were included in this study (Age: 37.6 years, SD: 9.3; 73.6% females; median EDSS: 3.5, range: 0-8; mean disease duration: 9.8 years, SD: 6.2; median follow-up 319 days). Seventy-two patients (44.4%) were previously treated with fingolimod (pre-FTY; mean duration time: 2.3 years, SD: 1.3), 78 (48.1%) were previously treated with other therapies (pre-other; 44 natalizumab) and 12 (7.5%) were naïve patients. The mean number of relapses in the year pre-discontinuation of last treatment was 1.18 (SD: 1.03) in pre-FTY and 0.94 (SD: 1.61) in pre-other ( $p=0.086$ ). Eight pre-FTY patients (11.1%; ARR=0.183, SD: 0.47) and eight pre-other patients (10.3%; ARR=0.14, SD: 0.46) showed at least one relapse during alemtuzumab without significant differences between the two groups ( $p=0.41$ ). A longer washout period was associated with a higher ARR on alemtuzumab ( $p=0.044$ ) independent from previous therapy ( $p$  for interaction = 0.43). Previous treatment did not impact on time to first event ( $p=0.85$ ; either relapse, disease progression, or MRI activity), as did not washout time ( $p=0.70$ ), or their interaction ( $p=0.78$ ).

**Conclusions:** In this cohort, the previous DMTs did not influence the ARR during alemtuzumab. Moreover, the longer the washout, the higher the ARR, regardless of prior therapy. According to these results, a previous fingolimod treatment does not impact on alemtuzumab efficacy.

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