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Abstracts

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Lymphocyte recovery after fingolimod discontinuation in patients with MS

Objective To investigate the dynamics of immune cells recovery after treatment discontinuation of fingolimod in real-life clinical practice, we analyzed the course of lymphocyte reconstitution and its potential influencing factors in patients with multiple sclerosis (MS).

Methods We analyzed leukocyte, lymphocyte, and granulocyte counts of 58 patients at 3, 6, and 12 months after fingolimod cessation and the following parameters as potential risk factors for a prolonged lymphopenia up to 12 months: age; sex; Expanded Disability Status Scale and disease duration at the time of fingolimod start; type and number of previous immunomodulatory treatments; fingolimod treatment duration; lymphocyte count at baseline before fingolimod, at fingolimod stop, and at the time of therapy switch; time interval between fingolimod cessation and new treatment initiation; type of the follow-up immunomodulatory treatment; and corticosteroid administration after fingolimod cessation.

Results All patients showed a decline in the lymphocyte count under fingolimod with no relevant leukopenia or neutropenia. One year after discontinuation, still 22% of the patients were lymphopenic and 54% of them did not reach 80% of the baseline lymphocyte value. Low lymphocyte counts before fingolimod start, under fingolimod, and at therapy switch, successive treatment with rituximab, and pretreatment with mitoxantrone were significantly associated with a prolonged immune cell recovery.

Conclusions Prolonged lymphopenia after fingolimod cessation exists in a subgroup of patients with MS and should be considered in clinical practice, particularly when changing treatment regimens.

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Cladribine vs other drugs in MS: Merging randomized trial with real-life data

Objective Cladribine tablets were tested against placebo in randomized controlled trials (RCTs). In this study, the effectiveness of cladribine vs other approved drugs in patients with relapsing-remitting MS (RRMS) was compared by matching RCT with observational data.

Methods Data from the pivotal trial assessing cladribine tablets vs placebo (CLARITY) were propensity score matched to data from the Italian multicenter database i-MuST. This database included 3,150 patients diagnosed between 2010 and 2018 at 24 Italian MS centers who started a disease-modifying drug. The annualized relapse rate (ARR) over 2 years from treatment start and the 24-week confirmed disability progression were compared between patients treated with cladribine and other approved drugs (interferon, glatiramer acetate, fingolimod, natalizumab, and dimethyl fumarate), with comparisons with placebo as a reference. Treatment effects were estimated by the inverse probability weighting negative binomial regression model for ARR and Cox model for disability progression. The treatment effect has also been evaluated according to baseline disease activity.

Results All weighted baseline characteristics were well balanced between groups. All drugs tested had an effect vs placebo close to that detected in the RCT. Patients treated with cladribine had a significantly lower ARR compared with interferon (relapse ratio [RR] = 0.48; $p < 0.001$), glatiramer acetate (RR = 0.49; $p < 0.001$), and dimethyl fumarate (RR = 0.6; $p = 0.001$); a similar ARR to that with fingolimod (RR = 0.74; $p = 0.24$); and a significantly higher ARR than natalizumab (RR = 2.13; $p = 0.014$), confirming the results obtained by indirect treatment comparisons from RCTs (network meta-analyses). The relative effect of cladribine tablets 10 mg (cumulative dose 3.5 mg/kg over 2 years) was higher in patients with high disease activity vs all treatments except fingolimod and natalizumab. Effects on disability progression were largely nonsignificant, probably because of the lack of power for such analysis.

Conclusion In patients with RRMS, cladribine tablets showed lower ARR compared with matched patients who started interferon, glatiramer acetate, or dimethyl fumarate; was similar to fingolimod; and was higher than natalizumab. The beneficial effect of cladribine tablets was generally amplified in the subgroup of patients with high disease activity.

Classification of evidence This study provides Class III evidence that for patients with RRMS, cladribine-treated patients had lower ARR compared with interferon, glatiramer acetate, or dimethyl fumarate; similar ARR compared with fingolimod; and higher ARR compared with natalizumab.

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Neurology 2021;96;57
DOI 10.1212/WNL.0000000000011260