



Real-world experience of cladribine treatment in relapsing-remitting multiple sclerosis: A Danish nationwide study

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ABSTRACT

Background: Cladribine is a nucleoside analogue interfering with synthesis and repair of DNA. Treatment with cladribine leads to a preferential reduction in lymphocytes, resulting in profound depletion of B-cells with a rapid recovery of naïve B-cells, while T-cells show a lesser but long-lasting depletion. It is approved for treatment of relapsing multiple sclerosis (MS). Cladribine tablets 3.5 mg/kg bodyweight are administered in two yearly treatment courses, each including two treatment series lasting 4 or 5 days, one at the start of the first month and the other at the start of the second month.

Objective: To describe treatment patterns of cladribine in a real-world setting.

Methods: Registry based observational cohort study with prospectively enrolled cases from December 2017 through June 2021. The data source is The Danish Multiple Sclerosis Registry, which is a near complete nationwide population-based registry. Outcomes were length of the treatment, preceding and following treatments, treatment response, and safety data.

Results: In total 268 patients had started therapy with cladribine tablets, 89 men and 179 women, with a median age of 40 years (interquartile range (IQR) 32–48). The disease course was relapsing-remitting MS in 97.8% of the patients, and at treatment start the median time from disease onset was 8.1 years (IQR 4.2–14.5) and EDSS 2.5 (IQR 1.5–3.5). Thirty-four patients (12.7%) were treatment naïve while 56 (20.9%) had received one previous disease-modifying therapy (DMT), 67 (25.0%) two, and 111 (41.4%) three or more previous DMTs.

In total, 214 (80.0%) patients had completed the full treatment of two courses of cladribine, while 54 (20.0%) had received only one course of cladribine tablets. The median follow-up time after cladribine initiation was 34.7 months (IQR 23.3–43.7). Compared with an annualized relapse rate (ARR) of 0.67 (95% CI [0.56, 0.79]) in the year prior to start of cladribine, ARR was reduced to 0.11 (95% CI [0.08, 0.15]) in year 0–2 after 3-month re-baseline with cladribine (84.8% reduction).

Adverse events, reported in 44 (16.4%) of the patients, were mild or moderate, and herpes zoster was only reported in 2 patients. In total, 30 (11.2%) patients discontinued cladribine treatment, of whom 7 (2.6%) discontinued because of adverse effects and 12 (4.5%) discontinued because of disease activity.

Conclusion: In this nationwide review of all Danish patients starting therapy with cladribine tablets in a real-world setting, cladribine treatment was safe, and the therapeutic response was as expected from previous clinical trials. A prolonged observation period is necessary to assess the long-term benefit and risk of cladribine.

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