Title: Should cladribine be upgraded to a first line multiple sclerosis disease-modifying therapy?

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Background:

In Canada, there are currently 22 disease modifying therapies (DMTs) approved for treatment in relapse-remitting MS (RRMS). There are no official guidelines recommending how and when to start patients on which therapy beyond the general recommendation of treating aggressively and early. Cladribine (Mavenclad®) was approved for treatment in British Columbia, Canada, in 2017 as a second line DMT for the treatment of highly active RRMS. To qualify for coverage, patients must demonstrate an inadequate response to one or more prior DMT.

Objectives:

We investigate the longitudinal outcomes (change in EDSS, time until next DMT) of cladribine in two cohorts of patients with MS.

Methods:

This is a retrospective observational study using patient charts from the Fraser Health Multiple Sclerosis Clinic in Burnaby, British Columbia, Canada. Data acquisition was performed using several electronic medical record programs and statistical analysis was done using GraphPad PRISM software. Two cohorts were analyzed: patients on cladribine prior to its approval (cohort 1) and patients on cladribine after its approval (cohort 2).

Results:

In cohort 1, we had 9 patients with an average age of 37 years old (22-50 years old). There were 8 females and 1 male who started cladribine in 2005. The average time post cladribine without another DMT was 11 years (0.8-18.7 years). Four patients never started a DMT (one passed away in 2023 at age 59 after requesting medical assistance in dying) and the other five patients started a new DMT an average time of 6.2 years later. Over a median course of 16 years, 6 had worsening in EDSS (mean= +1.8), 2 had stable EDSS and 1 had improved EDSS (mean= -1.0).

In cohort 2, since the approval of cladribine in 2017, there has been an escalation in the number of patients starting cladribine in the last 2 years (62/104). Out of 104 patients, the average age was 42 years old. 77.9% of patients were female and 22.1% were male. Thus far, 59 patients have completed 2 cycles of cladribine with a median time of 35 months since the first cycle (range: 12-69 months). Three patients have started a third cycle of cladribine. None have started any new DMTs. We had pre- and post-cladribine EDSS scores for 57 patients. During a median time of 3 years, 82.5% of patients had stable or improved EDSS whereas only 17.5% of patients had worsened EDSS. The average EDSS worsening in the latter population was 1.3.

Conclusion:

Cladribine is well-tolerated and appears to reduce disease progression in most patients who receive it. Given the well-established literature support of early aggressive treatment in the MS disease course, we argue that cladribine should be covered as a first-line treatment.