

Therapy Transition from Fingolimod to Oral Cladribine: Eliminating the Washout

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BACKGROUND

- When planning care for patients with multiple sclerosis (MS), clinicians often balance the need for a timely transition to a new treatment and the potentially lasting immunologic effects of previous treatments.
- Clinical trials are designed to limit the carryover of previous medications when evaluating current therapy.
- In clinical practice, these washouts are often shortened to prevent relapse, but there is a lack of data to formally guide the optimal timeframe.
- Cladribine labelling recommends waiting to initiate cladribine until the absolute lymphocyte count (ALC) is within normal limits. For patients receiving fingolimod, waiting until the absolute lymphocyte count normalizes may result in a prolonged washout period, which may increase the risk of relapse or rebound disease activity. Following fingolimod discontinuation, peripheral lymphocyte counts typically return to the normal range in 1 to 2 months. Associated rebound occurs at a median of 50 days after treatment cessation but may occur as early as 4 weeks after fingolimod discontinuation.
- Transitioning without significant washout was chosen to leverage the pharmacokinetic and pharmacodynamic properties of the medications involved. Cladribine has a high volume of distribution, which indicates extensive tissue distribution and should reach lymphocytes when retained in lymph tissue. Further, cladribine and its metabolites are substantially accumulated and retained in lymphocytes. Cladribine lymphocyte nadir counts typically occur 2 to 3 months following the initiation of treatment, which may reduce the risk of rebound when the transition period is kept to a minimum.

OBJECTIVES

To evaluate the effect on absolute lymphocyte count and safety of transitioning from fingolimod to cladribine with a transition duration of 0 to 3 days during year 1 of oral cladribine therapy.

Striking a balance between treatment initiation and effects of previous treatment need not result in a lengthy washout

METHODS

Patients from our cohort were included in this retrospective review if the following criteria were met:

Completed full first year course of treatment

Completed baseline laboratory and at least two out of three follow up laboratory checks scheduled for months 2, 6 and 11

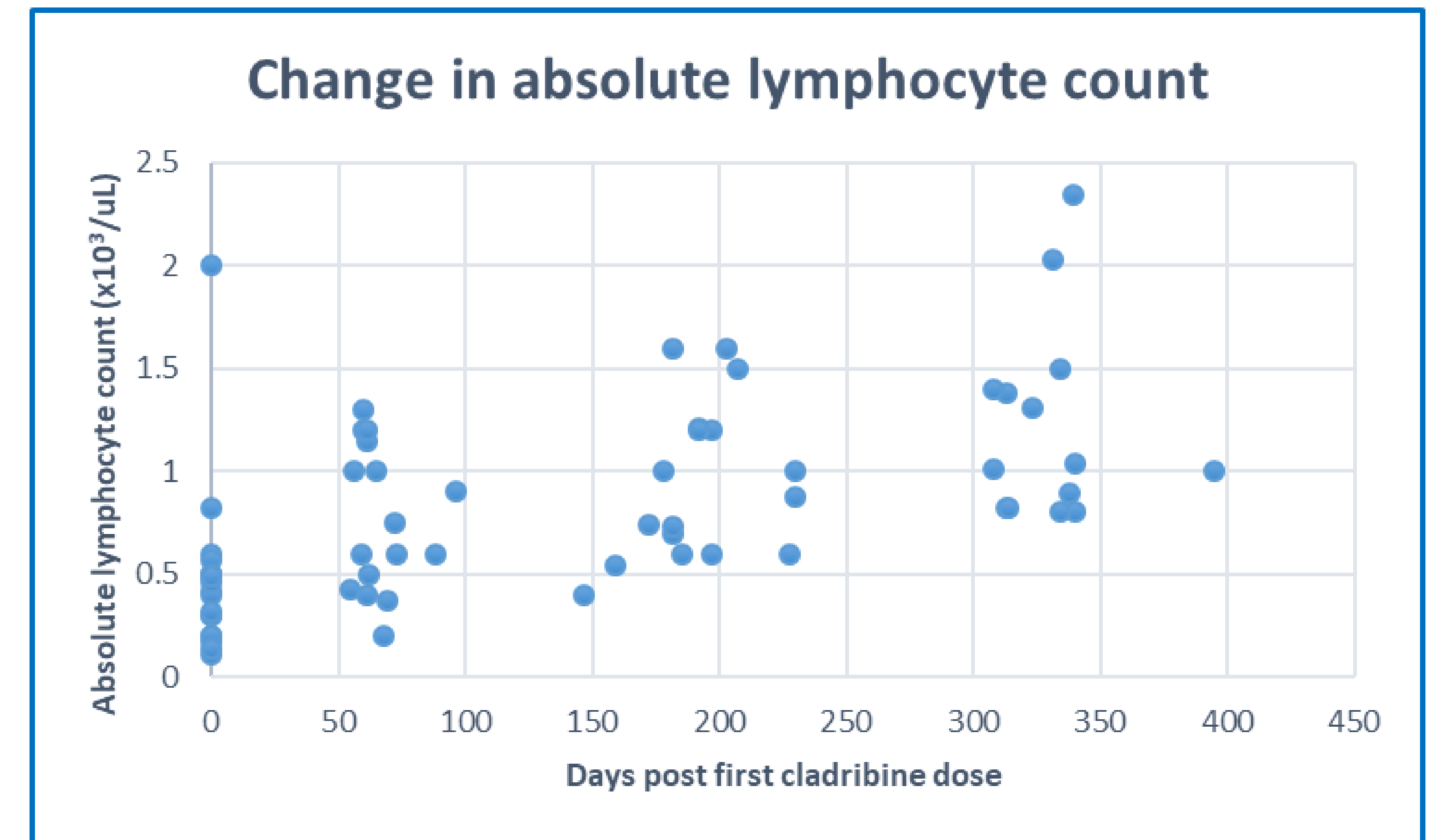
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RESULTS

- Sixteen patients met the criteria and were included in the reported cohort.
- Despite low absolute lymphocyte counts at the time of medication transition, recovery of lymphocyte counts following treatment transition was not negatively impacted.
- Reviewing outcomes through the end of year 2, the rate of infections in our cohort was lower than reported in the product label.



CONCLUSIONS

From a safety perspective, a washout period when switching from fingolimod to cladribine appears to be unnecessary. Despite the lack of washout, this transition did not adversely affect the reconstitution of lymphocytes and did not result in worsening lymphopenia from baseline.

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