



ASSESSING THE INCIDENCE OF LYMPHOPENIA WITH THE USE OF DIMETHYL FUMARATE IN MULTIPLE SCLEROSIS



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INTRODUCTION

Dimethyl fumarate (DMF) is an oral medication approved for the treatment of relapsing forms of Multiple Sclerosis (MS). **In pivotal MS studies involving DMF, there was a mean decrease in absolute lymphocyte count (ALC) by approximately 30%, with approximately 5% of patients in these studies developing grade III lymphopenia (ALC <500).** The true and complete significance of this is yet to be established, but it may correlate with increased infection rates, non-adherence rates, and side-effect profiles.

Furthermore, the mechanism by which DMF-associated lymphopenia occurs is not known. It has been postulated that the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway is involved.

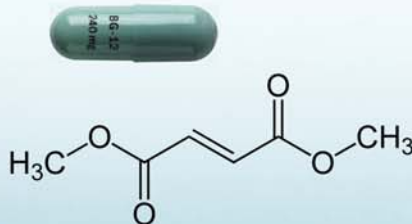
STUDY AIMS

Our aims with this study were to:

1. Assess the incidence of lymphopenia among MS patients taking DMF under routine care
2. Stratify rates according to grades of severity in order to glean insight for clinical application

METHODS

A retrospective chart review was conducted on all patients in our MS clinic who were prescribed DMF between March 2013 and March 2015 under routine care. Those who began treatment and had available pre- and post-dosing complete blood counts (CBC) that included ALC were included in analysis. Patients were excluded if their pre-CBCs occurred more than 6 months prior to starting DMF. Lymphopenia was classified by severity into: **grade I (ALC 800–1000); grade II (ALC 500–799); and grade III (ALC <500).**

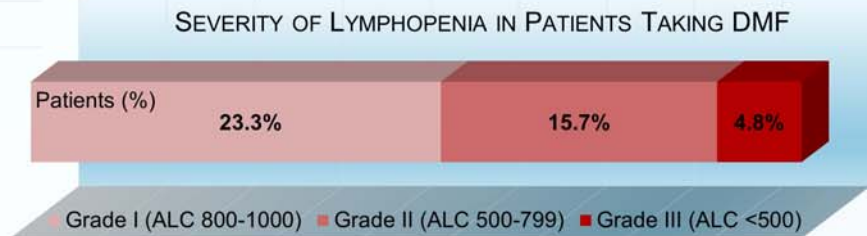


RESULTS

A total of 311 patients were prescribed DMF, and 210 met criteria for inclusion. Female-to-male ratio was ~3:1. Average age was 47 years (range, 18 to 75).



- The incidence of lymphopenia over the course of the study was 33.8% (71 patients).
- The average decrease in ALC from pre-CBC to any post-CBC was 31.5%



CONCLUSIONS

Over the 32-month monitoring period in our study, **more than a third of patients with MS developed lymphopenia following the initiation of DMF. Levels were severe in 14% of these patients.** The importance of close ALC monitoring cannot be overemphasized.

The remaining results from our study are consistent with previously published data. However, studies are scarce, and there remains limited understanding of the role of DMF-mediated lymphopenia in clinical sequelae.

The growing understanding of DMF's action on haematopoietic stem cell (HSC) function may help elucidate this role. **By up-regulating Nrf2, DMF may affect the cyclin D-dependent pathway in cell cycle regulation and disrupt the balance between HSC quiescence and proliferation, potentially impacting ALC.** Further studies are needed to assess this and its clinical implications for patients with MS.

REFERENCES

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