**Lymphocyte Count Reductions in Relapsing-Remitting MS Patients Treated with Delayed-Release Dimethyl Fumarate: An Integrated Analysis of the Placebo-Controlled Studies**

**INTRODUCTION**

Dimethyl fumarate (DMF) is approved in the United States and Europe for the treatment of patients with relapsing-remitting multiple sclerosis (MS) with or without a prior disease-modifying therapy (DMT) or with disease characteristics considered high risk for disability progression. Studies have shown that DMF is associated with long-term reductions in lymphocyte counts.

Among delayed-release DMF-treated patients, there was a clear pattern of an increase in lymphocyte counts, with a decrease in lymphocyte counts not returning to baseline after the last dose (Figure 3).

**OBJECTIVE**

To describe the clinical relevance of lymphocyte count reductions in patients treated with delayed-release DMF and to explore the association between lymphocyte count reductions and infections.

**METHODS**

Study Design

- The Phase 2b study, DEFINE, and CONFIRM were randomized, placebo-controlled, double-blind, parallel group, placebo-controlled trials conducted in patients with relapsing-remitting MS.
- The DEFINE and CONFIRM studies were conducted after the ENDORSE study, which was an open-label Phase 2b study.

**RESULTS**

**RESULTS**

**Patient Characteristics**

- A subset of 1,473 patients were randomized and treated with DMF in the Phase 2b study, DEFINE, and CONFIRM studies.
- The mean age of the study population was 42 years, with a median follow-up of 2 years.
- The mean baseline WBC and lymphocyte counts were similar across the placebo, DMF, and delayed-release DMF groups.

**Table 1: Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>DMF 120 mg QD</th>
<th>DMF 120 mg TID</th>
<th>DMF 240 mg TID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.4</td>
<td>42.4</td>
<td>42.5</td>
<td>42.4</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>55</td>
<td>60</td>
<td>57</td>
<td>59</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168.6</td>
<td>167.2</td>
<td>168.3</td>
<td>168.4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72.5</td>
<td>72.7</td>
<td>73.3</td>
<td>73.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.8</td>
<td>24.8</td>
<td>24.9</td>
<td>24.7</td>
</tr>
</tbody>
</table>

**Table 2: Baseline characteristics**

**Table 3: Incidence of CTC grades for selected key lymphocyte counts**

<table>
<thead>
<tr>
<th>Category</th>
<th>CTC grade 0</th>
<th>CTC grade 1</th>
<th>CTC grade 2</th>
<th>CTC grade 3 or 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/100</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
</tr>
<tr>
<td>2/100</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
</tr>
<tr>
<td>3/100</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
</tr>
</tbody>
</table>

**Table 4: Incidence of infections, serious infections, and opportunistic infections**

**CONCLUSIONS**

- Infections occurred at a similar rate in all treatment groups, with no significant differences observed. No new or unexpected infections were observed.
- This study provides important insights into the clinical relevance of lymphocyte count reductions in patients treated with delayed-release DMF, highlighting the need for continued monitoring and appropriate clinical interventions.

**References**

4.REFERENCES

**Disclosures**

- The authors have no financial disclosures.

- All authors are employees of Biogen Idec.

**For an electronic version of this article, please see our website**