Infections and Grade 3 or 4 Lymphopenia in Patients Taking Cladribine Tablets 3.5 mg/kg: Data from an Integrated Safety Analysis

S. Cook, T. Leist, G. Comi, X. Montalban1,2, E. Sylvester, C. Hicking, F. Dangond

INTRODUCTION

• Results from CLARITY, CLARITY Extension, ORACLE-MEL, and ONWARD show that cladribine tablets given annually for 2 years in short-course durations are efficacious in a spectrum of patients with multiple sclerosis.

• The most common adverse event (AE) was lymphopenia, reflecting the mode of action of cladribine.

• An integrated analysis of safety showed that the incidence of infections overall was not higher in patients treated with cladribine 3.5 mg/kg than in patients receiving placebo, except for a small increased risk of herpes zoster.

OBJECTIVE

• To describe the incidence and types of infections in patients treated with cladribine 3.5 mg/kg during periods of Grade 3 or 4 lymphopenia.

• To compare infections and Grade 3 or 4 lymphopenia in 2 patient populations: (1) Patients Receiving Cladribine Tablets 3.5 mg/kg: Data from an Integrated Safety Analysis

METHODS

• A monotherapy oral cohort was derived from CLARITY, CLARITY Extension, ORACLE-MEL, and the PREMIERE registry, with 923 patients receiving cladribine tablets 3.5 mg/kg and 641 receiving placebo.

• The AE profile for cladribine tablets 3.5 mg/kg during the exact periods of Grade 3 or 4 lymphopenia was analyzed.

• Periods of Grade 3 or 4 lymphopenia were defined as the onset of the Grade 3 or 4 lymphopenia to first Grade 2 or lower plus 2 weeks. Periods of Grade 3 or 4 lymphopenia were defined as the Grade 3 or 4 lymphopenia to first Grade 3 or 4 lymphopenia plus 2 weeks.

• Adjusted AE incidences per 100 patient-years (Adj-AE per 100PY) were calculated.

RESULTS

Incidence of Infections Overall (Monotherapy Oral Cohort)

• In the entire monotherapy oral cohort, the incidence rate for infections overall, severe infections, infections leading to discontinuation, or opportunistic infections was not higher for patients receiving cladribine tablets compared with patients receiving placebo (Table 1).

Table 1. Overview of Infections in Patients Receiving Placebo or Cladribine Tablets 3.5 mg/kg (Monotherapy Oral Cohort)

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>Placebo (n=804)</th>
<th>Cladribine Tablets (n=923)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infections</td>
<td>1,763</td>
<td>2,060</td>
</tr>
<tr>
<td>Adverse events</td>
<td>1,572</td>
<td>1,820</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>158</td>
<td>170</td>
</tr>
<tr>
<td>Severe adverse events</td>
<td>11</td>
<td>13</td>
</tr>
</tbody>
</table>

DISCUSSION

• Severe lymphoma resulted in an increased frequency of infections but did not have any differential effect on the type of infectious AEs in patients treated with cladribine tablets 3.5 mg/kg monotherapy.

• The profile of herpes zoster was uncomplicated, consistent with the findings of previous safety analyses.

• In general, patients with Grade 4 lymphopenia are more susceptible to infections. If lymphocytopenia drops below 200 cells/mm³ during treatment with cladribine tablets 3.5 mg/kg, and herpes prophylaxis according to local standard practice should be considered during the time of Grade 4 lymphopenia.

CONCLUSIONS

REFERENCES

ACKNOWLEDGMENTS

DISCLOSURES

Presented at European Charcot Foundation (EFC) 2017; 30 November – 2 December; Baveno, Italy