Reduction of lymphopenia by cladribine tablets under re-treatment guidelines: a long-term follow-up analysis of patients in the ORACLE-MS study

T Leist, G Comi, M S Freedman, BAC Cree, PK Coyle, H-P Hartung, P Vermeersch, E Sylvester, D Damian, D Bangdok
Division of Clinical Neuroimmunology, Thomas Jefferson University, Jefferson Medical College, Philadelphia, PA, USA; Department of Neurology and Institute of Experimental Neurology, University Vita-Salute San Raffaele, Ospedale San Raffaele, Milan, Italy; Department of Medicine, University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; University of California, San Francisco, CA, USA; Stony Brook University, Department of Neurology, Stony Brook, NY, USA; Department of Neurology, Heinrich Heine University, Düsseldorf, Germany; Pôle de Neurologie, Université de Lille Nord de France, Lille, France; Merck KGaA, Darmstadt, Germany; EMD Serono, Inc., Billerica, MA, USA

OBJECTIVE

To assess severity and recovery from lymphopenia in the ORACLE-MS long-term follow-up (LTFU) among patients treated with cladribine tablets during the ORACLE-MS initial treatment period (ITP).

RESULTS

During the ITP (up to 2 consecutive years), CTCAE Grade 3 lymphopenia occurred in 46 (22.3%) and 74 (36.3%) patients receiving cladribine tablets 3.5 mg/kg and 5.25 mg/kg, respectively, and 1 (0.5%) patient receiving placebo. – Grade 4 lymphopenia was limited to 3 patients: 1 (0.5%) treated with cladribine tablets 3.5 mg/kg and 2 (1.0%) treated with cladribine tablets 5.25 mg/kg.

Following the ITP, 84 patients entered the LTFU and did not receive further treatment (Table 1).

The patients were reflective of the baseline population of the ORACLE-MS study. In the LTFU, 47 patients completed the 2 years of the ITP and 14 of these entered the LTFU and received no further treatment.

In the cladribine tablets 3.5 mg/kg group, 78 patients completed the 2 years of ITP, and 36 of these entered the LTFU and received no further treatment. In the cladribine tablets 5.25 mg/kg group, 65 patients completed the 2 years of ITP and 34 of these entered the LTFU and received no further treatment.

CONCLUSIONS

In the ORACLE-MS, the occurrence of CTCAE Grade 3 lymphopenia was dose-related. Grade 4 lymphopenia was observed in < 1% of patients.

The re-treatment guidelines introduced in ORACLE-MS appeared to limit the occurrence of Grade 3 lymphopenia.

Among the patients entering the LTFU who were originally treated with cladribine tablets 3.5 mg/kg during ITP, patients who had Grade 4 lymphopenia at the LTFU baseline (end of the ITP).

Patients entered into cladribine tablets under re-treatment guidelines after the 2-year double-blind ITP.

DISCLOSURES

This study was sponsored by EMD Serono, Inc.* (in the USA) and Merck Serono SA – Geneva, an affiliate of Merck KGaA, Darmstadt, Germany (DE). The authors would like to thank their patients and their families, investigators, co-investigators, and the staff in each of the participating centers and, at Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by Jackie Campbell of Vivid Communications, Springer Healthcare, Cheshunt, UK, and was funded by Merck KGaA, Darmstadt, Germany.

REFERENCES


ACKNOWLEDGMENTS

TABLE 1. Patients not treated at entry to LTFU

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<th>Cladribine tablets 5.25 mg/kg</th>
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<tr>
<td>Plasmapheresis (n=4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Mc Donald’s conversiona</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
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<tr>
<td>Received cladribine tablets or subcutaneous interferon beta-1a (n=24) after conversion to CDMS or McDonald MS in LTFU</td>
<td>0 (0.0)</td>
<td>1 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Discarded LTFU (n=2)</td>
<td>14 (100.0)</td>
<td>38 (100.0)</td>
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