Infusion-Related Reactions in the Phase III Double-Blind, Placebo-Controlled ORATORIO Study of Ocrelizumab in Primary Progressive Multiple Sclerosis

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**Therapeutics, Five Prime Therapeutics, Genzyme, GSK, GW Pharma, Merck, Merck Serono, Novartis, Protein Discovery...**

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**METHODS**

**Study Design**

- Patients were randomized (2:1) to receive OCR 600 mg, given as two 300-mg intravenous (IV) infusions 14 days apart, or placebo (PBO) given as two 300-mg intravenous infusions of sodium chloride 0.9% (0.9%).
- Patients were randomized (2:1) to receive OCR 900 mg, given as two 450-mg intravenous infusions 14 days apart, or placebo (PBO) given as two 450-mg intravenous infusions of sodium chloride 0.9% (0.9%).

**Endpoints**

- Infusion-related reactions (IRRs) have been observed with the administration of drugs, including monoclonal antibodies such as ocrelizumab.
- IRRs typically occur during or a few hours post-infusion, although symptoms may be delayed for up to 24 hours and may vary in severity.
- The incidence of IRRs in patients with PBO treated in ORATORIO was assessed in a safety analysis.

**RESULTS**

- **Infusion-Related Reactions in the Phase III Double-Blind, Placebo-Controlled ORATORIO Study of Ocrelizumab in Primary Progressive Multiple Sclerosis.**

**Table 2. Percentage of patients with 11 IRR by time of onset and by dose and severity in ORATORIO.**

<table>
<thead>
<tr>
<th>Event</th>
<th>Time of Onset</th>
<th>Placebo</th>
<th>OCR 600 mg</th>
<th>OCR 900 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Within 24 hours post-infusion (while patients were not in the clinic)</td>
<td>0.1</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Rash</td>
<td>Within 24 hours post-infusion (while patients were not in the clinic)</td>
<td>0.0</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>One hour post-infusion (while patients were in the clinic)</td>
<td>0.0</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>One hour post-infusion (while patients were in the clinic)</td>
<td>0.0</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Asthenia</td>
<td>One hour post-infusion (while patients were in the clinic)</td>
<td>0.0</td>
<td>0.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- **Infusion-related reactions were generally mild to moderate in severity and were generally manageable.**
- **Patients who withdrew from treatment due to an IRR were managed with infusion adjustments and symptomatic treatment.**
- **The addition of antihistaminics with methylprednisolone as premedication appeared to decrease the incidence of IRRs.**
- **Table 2. Percentage of patients with 11 IRR by time of onset and by dose and severity in ORATORIO.**

**REFERENCES**


**ACKNOWLEDGMENTS**

- Presented at the 2016 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC); National Harbor, MD, USA; June 1–4, 2016.