A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Phase III Trial to Evaluate Efficacy and Safety of Ocrelizumab in Primary Progressive Multiple Sclerosis

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BACKGROUND

- Patients with primary progressive multiple sclerosis (PPMS) experience disability progression from disease onset.
- Observational studies and open-label extensions of phase II trials in PPMS have suggested that Ocrelizumab may slow disease progression.
- A better understanding of the pathophysiology of PPMS disease progression is required, and an approved treatment is currently not available.

RESULTS

Baseline demographics and disease characteristics

- The treatment arms were well balanced.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Ocrelizumab</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Time to onset of disability progression confirmed after 212 weeks (A)</td>
<td>18.4 weeks</td>
<td>17.9 weeks</td>
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<tr>
<td>Change in whole brain volume from baseline to Week 120</td>
<td>20% reduction in placebo</td>
<td>13.9% reduction in placebo</td>
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<tr>
<td>Disability progression</td>
<td>24% reduction in placebo (p&lt;0.001)</td>
<td>25% reduction in placebo (p&lt;0.001)</td>
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Study endpoints

- **Primary endpoint:** Disability progression
  - Time to onset of disability progression
  - Change in whole brain volume
  - Total volume of brain T2 hyperintense lesions

Study completion

- The median treatment duration was approximately 3 years.
- Of patients withdrawn from the study treatment at the clinical cut-off date, 11% (in the OCR arm) and 20% (in the placebo arm) were due to AEs.

Safety

- The proportion of patients reporting adverse events (AEs) was similar in the OCRE and placebo groups.
  - 85.9% of OCRE-treated patients and 85.8% of placebo patients experienced ≥1 AE.

Conclusions

- Ocrelizumab was generally well tolerated.
- It significantly slowed disability progression and slowed whole brain volume loss compared to placebo.
- Overall, the results of ORATORIO provide strong evidence that Ocrelizumab has the potential to change the natural history of PPMS.

REFERENCES


DISCLOSURES

- A number of the principal investigators and key leaders/researchers involved in the current study have been consultants, advisory board members, or have received research support from Biogen, Biogen Idec, Eisai, Genentech, Hoffmann-La Roche, Merck, Merck Serono, Novartis, Teva, or United Therapeutics. In addition, EMD Serono received financial support from Biogen, Genentech, Merck, and Teva.

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