Open-Label Phase III Extension Studies to Evaluate the Long-Term Safety and Efficacy of Ocrelizumab in Relapsing MS and Primary Progressive MS

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Background

• Ocrelizumab (OCR) is a humanized monoclonal antibody that selectively targets CD20 cells while preserving the B-cell pool and preserving the in vivo B-cell repertoire.
• In trial results of Phase III, double-blind, double-dummy trials (OPERA I and OPERA II) enrolling multiple sclerosis (MS) trials, OCR showed superior efficacy compared with interferon (IFN) β-1a (Figure 1).
• Further, OCR met the primary efficacy outcome in the Phase III, randomized, double-blind, placebo-controlled study of ocrelizumab in relapsing multiple sclerosis (MS) (OPERA IV: Figure 2).

Methods

• ORATORIO: 517 of 549 patients (94%) who completed the double-blind treatment phase entered the OLE phase: 410 patients randomized to OCR in OPERA I, 340 patients randomized to OCR in OPERA II, 326 patients randomized to OCR in ORATORIO (96%, 95%, and 94% for OPERA I, OPERA II, and ORATORIO studies, respectively).
• The great majority of patients who completed double-blind treatment phases entered the OLE phases: 418 patients randomized to IFN β-1a in OPERA I, 362 patients randomized to OCR in OPERA II, and 352 patients randomized to OCR (96% of 366 patients who completed the 96-week double-blind treatment phase).

Results

• In OPERA I (94% of 362 patients) who completed the double-blind treatment phase, the final analysis was performed at 96 weeks (Week 192 dose). The primary outcome was the percentage of patients who relapsed in the OLE phase compared to the double-blind phase. The percentage of patients who relapsed during the OLE phase was 3.2%, which is significantly lower than the 6.7% observed in the double-blind phase (p < 0.001).
• In OPERA II (95% of 340 patients) who completed the double-blind treatment phase, the final analysis was performed at 96 weeks (Week 192 dose). The primary outcome was the percentage of patients who relapsed in the OLE phase compared to the double-blind phase. The percentage of patients who relapsed during the OLE phase was 2.9%, which is significantly lower than the 6.7% observed in the double-blind phase (p < 0.001).
• In ORATORIO (94% of 326 patients) who completed the double-blind treatment phase, the final analysis was performed at 96 weeks (Week 192 dose). The primary outcome was the percentage of patients who relapsed in the OLE phase compared to the double-blind phase. The percentage of patients who relapsed during the OLE phase was 3.2%, which is significantly lower than the 6.7% observed in the double-blind phase (p < 0.001).

Conclusions

• Long-term safety, tolerability, and efficacy of ocrelizumab in RRMS and PPMS will continue to be assessed in the OPERA I, OPERA II, and ORATORIO studies.
• The great majority of patients who completed double-blind treatment phases entered the OLE phases.
• The final analysis of the OLE phases will provide long-term data regarding ocrelizumab in patients with RRMS and PPMS.

References

4. AAN 2016; Oral S49.001.
5. ACTRIMS 2016; Poster P024.