Reduction in 48-Week Confirmed Disability Progression After 5.5 Years of Ocrelizumab Treatment in Patients With Primary Progressive Multiple Sclerosis
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Objective:
Previous studies demonstrated the efficacy of ocrelizumab on 12-week and 24-week confirmed disability progression (CDP). We examine the efficacy of ocrelizumab versus placebo on 48-week CDP in the extended controlled treatment (ECT) period, and long-term outcomes in patients switching to or maintaining ocrelizumab therapy in the open-label extension (OLE) of the ORATORIO Phase III trial (NCT01194570) in primary progressive multiple sclerosis (PPMS).

Background:
In the double-blind period (DBP) of ORATORIO, the risk of 24-week CDP was reduced by 25% for ocrelizumab versus placebo (p=0.037). After 5.5 years’ (264 weeks) follow-up, 12-week/24-week disability progression outcomes favored those on earlier and continuous treatment with ocrelizumab, compared with delayed initiation.

Design/Methods:
At the end of the DBP, patients remained on randomized blinded treatment until the trial outcome was evaluated (ECT period). At the start of the OLE period, patients continued ocrelizumab or switched from placebo to ocrelizumab. Time to onset of 48-week CDP (CDP48) was analyzed for the ECT and OLE periods through Week 264.

Results:
In the ECT period, ocrelizumab reduced the risk of CDP48 by 34% (p=0.001) versus placebo. Overall, 72% patients entered the OLE – the last after 240 weeks on randomized treatment. The proportion of patients with CDP48 was lower in the continuous ocrelizumab versus placebo-ocrelizumab group at Week 168 (30.5% vs 44.4%; Δ=13.9%; p<0.001), Week 192 (34.8% vs 48.5%; Δ=13.7; p<0.001) and Week 264 (43.7% vs 53.1%; Δ=9.4; p=0.03). Analysis of 48-week Timed 25-Foot Walk, 9-Hole Peg Test and composite CDP will be presented.

Conclusions:
These analyses indicate the effect of ocrelizumab on CDP48 was greater than on 12-week and 24-week CDP, potentially due to higher specificity for permanent disability accumulation. In accordance with previous analyses, CDP48 data demonstrate consistent and sustained benefit with ocrelizumab treatment, and advantages for accrued disability for patients starting earlier on continuous ocrelizumab.