Ocrelizumab treatment reduced levels of neurofilament light chain and numbers of B cells in the cerebrospinal fluid of patients with relapsing multiple sclerosis in the OBOE study

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Objective:
To provide interim analysis (IA) results from the relapsing multiple sclerosis (RMS) cohort of OBOE (Ocrelizumab Biomarker Outcome Evaluation; NCT02688985), a cerebrospinal fluid (CSF) and blood biomarker study.
Background:
Serum and CSF levels of neurofilament light chain (NfL) and CSF lymphocyte numbers are emerging biomarkers of axonal damage and inflammation, respectively. Responses of these biomarkers to ocrelizumab (OCR) may improve the understanding of MS pathophysiology and therapeutic mechanism of action.
Design/Methods:
Patients with RMS received OCR 600-mg infusions every 24 weeks. CSF samples were obtained by lumbar puncture (LP) before OCR and at 12, 24 or 52 weeks after initial OCR treatment. Patients in a nonrandomized RMS reference arm underwent two LPs 12 weeks apart prior to initiation of OCR. The primary endpoint is change in CSF NfL levels and lymphocyte numbers between pre- and posttreatment time points. All enrolled patients (n=100) are included in this IA.
Results:
Pretreatment CSF and serum NfL levels correlated strongly ($r=0.78$; $p<0.001$). Both serum and CSF NfL levels correlated with numbers of T1 gadolinium-enhancing lesions and new/enlarging T2 lesions on brain MRI. OCR significantly reduced serum NfL (−13.1%, −18.6% and −30.8%), CSF NfL (−24.5%, −40.0% and −54.7%) and CSF B cells (−85.5%, −84.8% and −94.0%) at Weeks 12, 24 and 52, respectively. CSF T cells were reduced by ≈60% across the same time points, but reductions were significant only at Week 12. Reference-arm samples showed no significant changes in CSF/serum NfL or CSF lymphocyte numbers over 12 weeks.
Conclusions:
In RMS patients, ocrelizumab significantly decreased CSF/serum NfL and CSF B cells, suggesting that treatment reduces ongoing axonal injury and compartmentalized CNS inflammation. CSF B cells were almost completely depleted in most patients at Weeks 12, 24 and 52, whereas CSF T cells were moderately reduced in many but not all patients.