Design of two phase III open-label trials evaluating ocrelizumab in patients with relapsing-remitting multiple sclerosis and suboptimal response to disease-modifying treatment

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Background: Suboptimal treatment response is not uncommon in relapsing-remitting multiple sclerosis (RRMS), despite an increase in available disease-modifying treatments (DMTs). Disease activity early during DMT is associated with rapid progression of disability and poorer long-term outcomes. Breakthrough disease and treatment side effects are reasons to consider medication switch. Ocrelizumab (OCR), a recombinant humanised monoclonal antibody that selectively targets CD20+ B cells, has demonstrated superior efficacy compared with interferon beta-1a in 2 identical, randomized, double-blind, Phase III trials (OPERA I; OPERA II) in patients with relapsing MS.

Objective: To report the study design and status of CHORDS (US and Canada; NCT02637856) and MA30005 (Europe), 2 prospective, multicentre, open-label efficacy and safety studies in patients with RRMS who have had suboptimal response to an adequate course of a DMT.

Methods: Patients will receive OCR as an initial dose of two 300mg intravenous (IV) infusions (600mg total) separated by 14 days, followed by one 600mg IV infusion every 24 weeks for at least 4 doses (up to a max of 96 weeks). Entry criteria include: diagnosis of RRMS (McDonald, 2010), disease duration ≤10 years, treated with ≤2 prior DMT regimens ≥6 months with discontinuation of the last due to suboptimal disease control, defined as 1 of the following despite being on a stable dose of the same DMT for ≥6 months: ≥1 clinically reported relapse; or ≥1 T1 gadolinium-enhanced (Gd+) lesion; or ≥2 new/enlarging T2 lesions on MRI. For those on stable doses of the same DMT for >1 year, events must have occurred within the prior 12 months of treatment with this DMT. The primary outcome measure in both studies is the proportion of patients free of any protocol-defined events during a 96-wk period, i.e. no protocol-defined relapses, no 24-week confirmed disability progression (based on Expanded Disability Status Scale score), no T1 Gd+ lesions, and no new/enlarging T2 lesions (defined as no evidence of disease activity [NEDA] in MA30005).

Results: Enrolment began in 2016 with a planned total of 600 patients in each study. Studies are ongoing; updated status will be reported.

Conclusions: These studies will provide information on the efficacy and safety of OCR in patients who have had a suboptimal response to a DMT.

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