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Subcutaneous Ocrelizumab in Patients With Multiple Sclerosis: Results of the Phase Ib Dose-Finding OCARINA I Study

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Introduction:

Ocrelizumab (OCR) is approved for the treatment of relapsing and primary progressive multiple sclerosis (RMS/PPMS) as an intravenous (IV) 600 mg formulation administered every 6 months. A novel OCR subcutaneous (SC) formulation utilising recombinant human hyaluronidase is being developed.

Objectives/Aims:

OCARINA I (NCT03972306) is a Phase Ib, dose-escalation, open-label study designed to select the appropriate OCR SC dose for the subsequent Phase III trial. The dose selection was based on safety, tolerability and pharmacokinetic data in patients with RMS or PPMS.

Methods:

Patients with RMS or PPMS (18–65 years; Expanded Disability Status Scale score 0.0–6.5) were enrolled into two groups: Previously treated with OCR IV (group A) or naive to OCR (group B). Patients received single ascending doses of OCR SC (40, 200, 600, 1,200 mg). Following dose escalation, new patients in group A were randomised (1:1) to receive either a single 600 mg OCR IV or the candidate SC dose, which was predicted to result in similar exposure as the 600 mg IV dose, while being safe and well tolerated. The area under the concentration-time curve for both formulations was used to select the OCR SC dose. Patients in all cohorts could enter a dose continuation phase receiving the candidate dose, then later the final selected dose, for up to 3 years.

Results:

In cohort A (n=53 OCR SC; n=35 OCR IV) and cohort B OCR SC (n=46), the majority of patients were female (72.7%/63.0%); mean age (standard deviation) at baseline was 45.7 (10.2) and 39.7 (9.2) years, respectively. During the dose escalation phase, OCR SC was well tolerated across all doses tested. Initially 1,200 mg was selected as the candidate SC dose, but subsequently 920 mg was chosen as the final SC dose based on all data available. Median treatment duration with OCR SC 1,200 mg or 920 mg was 96 weeks, with 94.7% receiving ≥3 doses. Injection site reactions were the most common adverse events, with erythema, pain and swelling being the most common symptoms, all of which were mild/moderate. Additional safety and tolerability data, results on immunogenicity and patient satisfaction will be reported.

Conclusion:

The selected ocrelizumab SC 920 mg dose was well tolerated and is expected to provide a similar exposure to the approved 600 mg ocrelizumab IV dose in a larger cohort, which is being assessed in the Phase III OCARINA

II (NCT05232825) study.

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