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Ensemble-plus Study Design: An Investigation of Shortened Ocrelizumab Infusion Time on Infusion-related Reactions in Patients with Relapsing Multiple Sclerosis from the Phase Iiib Ensemble-plus Study

B. Yamout¹, B. Brochet², C. Nos³, M. S. Freedman⁴, J. Killstein⁵, J. Overell⁶, R. Buffels⁷, K. Fitovski⁷, L. Mehta⁸, Q. Wang⁷, H. Hartung⁹

¹Multiple Sclerosis Center Clinical Research, American University of Beirut Medical Center , Beirut, Lebanon

²University of Bordeaux, Bordeaux, France

³Multiple Sclerosis Center of Catalonia, Hospital Vall D'hebron, Barcelona, Spain ⁴University of Ottawa and The Ottawa Hospital Research Institute, Ottawa, Canada ⁵Department of Neurology, Vu University Medical Center, AMsterdam, Netherlands ⁶Institute of Neurological Sciences, Glasgow, United Kingdom

⁷F. Hoffmann-la Roche Ltd, Basel, Switzerland

⁸Genentech, Inc., South San Francisco, United States of America

⁹Department of Neurology, Ukd, Center of Neurology and Neuropsychiatry and Lvr-klinikum, Heinrich-heine University Düsseldorf, Düsseldorf, Germany

Background: Ocrelizumab is an intravenously administered, humanised anti-CD20+ monoclonal antibody approved for the treatment of relapsing forms of multiple sclerosis (MS) and primary progressive MS. Infusion related reactions (IRRS) are the most common adverse event related to ocrelizumab. The currently approved infusion time for ocrelizumab is approximately 5.5-6h which includes premedication and infusion set-up (1h), ocrelizumab infusion (3.5-4h) and post-infusion observation (1h). A reduction in infusion time may reduce the burden of administration on the patient, nursing staff and hospital facilities. Ensemble-plus, a substudy of an ongoing phase III, open-label, single-arm investigation of the effectiveness and safety of ocrelizumab in patients with early-stage relapsing-remitting MS (ensemble [nct03085810]), will assess the impact of reducing infusion time on ocrelizumab-related IRRS. The objective is to describe the design of the ensemble-plus substudy.

Methods: In the single-arm ensemble study, patients (age 18–55 years; disease duration ≤3 years; EDSS score 0–3.5; relapse or T1 gadolinium-enhancing lesions in prior 12 months; treatment-naïve) receive ocrelizumab 600mg infusions every 24 weeks for 192 weeks; premedication per label will be provided. In the ensemble-plus substudy, a subgroup of eligible patients from the main ensemble study will be randomised with equal allocation into a conventional infusion group (3.5hr infusion duration) and a shorter infusion group (2hr infusion duration) at the next scheduled infusion under a double-blind setting. In addition, 300 newly enrolled patients, first recruited into ensemble, will be randomised for evaluation of IRRS starting at the week 24 infusion. Patients with prior serious ocrelizumab-related IRRS will be excluded. Irr frequency and severity will be assessed during the period following the first randomised infusion in ensemble-plus.

Results: The first patient enrolled into ensemble-plus is expected to occur in september 2018.

Conclusions: Ensemble-plus will help to establish the safety profile of ocrelizumab when administered with a shorter infusion period.