Title

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

Short title

ENSEMBLE-PLUS study design (required for meeting app; <45 characters)

Authors

B Brochet (main author),[1] C Nos,[2] MS Freedman,[3] J Killestein,[4] J Overell,[5] R Buffels,[6] K Fitovski,[6] L Mehta,[7] Q Wang,[6] H-P Hartung[8]

Affiliations

[1]University of Bordeaux, Bordeaux, France; [2]Multiple Sclerosis Center of Catalonia, Hospital Vall d'Hebron, Barcelona, Spain; [3]University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; [4]Department of Neurology, VU University Medical Center, Amsterdam, The Netherlands; [5]Institute of Neurological Sciences, Glasgow, United Kingdom; [6]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [7]Genentech, Inc., South San Francisco, CA, USA; [8]Department 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.

Objective

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-naive) 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.

Current word count: 300 words (maximum 300 words in abstract body)

Disclosures

Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

B Brochet or his institution has received honoraria for consulting, speaking at scientific symposia and serving in advisory board or research support from Actelion, Biogen Idec, Merck Serono, Sanofi Genzyme, Bayer, MedDay, by F. Hoffmann-La Roche Ltd, Teva, Novartis and institutional support from ANR, ARSEP and LFSEP (all with approval by the general director of CHU de Bordeaux).

C Nos has received speaking honoraria from Novartis, and travel funding from Biogen Idec, Merck, F. Hoffmann-La Roche and TEVA.

MS Freedman has received research or educational grants by Genzyme Canada and honoraria or consultation fees from Actelion/Johnson & Johnson, BayerHealthcare, BiogenIdec, Chugai, Celgene Canada, Clene Nanomedicine, EMD Canada, Genzyme, Merck Serono, Novartis, Hoffman La-Roche, Sanofi-Aventis, Teva Canada Innovation. He has served as a member of company advisory board, board of directors or other similar groups for Actelion/Johnson & Johnson, BayerHealthcare, BiogenIdec, Clene Nanomedicine, Genzyme, Hoffman La-Roche, Merck Serono, MedDay, Novartis, Sanofi-Aventis and has participated in a company sponsored speaker's bureau for Sanofi-Genzyme.

J Killestein has accepted speaker and consulting fees from Merck, Biogen, Teva, Genzyme, Roche and Novartis.

J Overell has received honoraria for speaking engagements and attendance at advisory boards, and conference travel support, from Teva, Novartis, Merck Serono, Genzyme, Roche, Allergan, WebMD Global and Biogen. His department has received educational funds, research support and funds to provide nursing and administrative staff from Novartis, Genzyme, Roche, and Biogen.

R Buffels is an employee of F. Hoffmann-La Roche Ltd.

K Fitovski is an employee of F. Hoffmann-La Roche Ltd.

L Mehta is an employee of Genentech, Inc./F. Hoffmann-La Roche Ltd.

Q Wang is an employee of F. Hoffmann-La Roche Ltd.

H-P Hartung has received honoraria for consulting, serving on steering committees and speaking at scientific symposia with approval by the Rector of Heinrich-Heine University Düsseldorf from Bayer, Biogen, F. Hoffmann-La Roche Ltd, GeNeuro SA, Genzyme, MedImmune, Merck Serono, Novartis, Octapharma, Opexa, Teva and Sanofi.