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

Peer-reviewed author version

Bermel, R.; Comi, G.; Eralinna, J. -P.; Leist, T. P.; Nicholas, R.; Oreja-Guevara, C.; Siva, A.; VAN WIJMEERSCH, Bart; Wiendl, H.; Bernasconi, C.; Buffels, R.; Csoboth, C.; Han, J.; Musch, B. & Vermersch, P. (2016) Design of two phase III open-label trials evaluating ocrelizumab in patients with relapsing-remitting multiple sclerosis and suboptimal response to disease-modifying treatment. In: MULTIPLE SCLEROSIS JOURNAL, 22, p. 615-616 (Art N° P1180).

Handle: http://hdl.handle.net/1942/24073

Reference (Published version):
Bermel, R.; Comi, G.; Eralinna, J. -P.; Leist, T. P.; Nicholas, R.; Oreja-Guevara, C.; Siva, A.; Van Wijmeersch, Bart; Wiendl, H.; Bernasconi, C.; Buffels, R.; Csoboth, C.; Han, J.; Musch, B. & Vermersch, P.(2016) Design of two phase III open-label trials evaluating ocrelizumab in patients with relapsing-remitting multiple sclerosis and suboptimal response to disease-modifying treatment. In: MULTIPLE SCLEROSIS JOURNAL, 22, p. 615-616 (Art N° P1180)

DOI: 10.1021/jacs.7b04981
Handle: http://hdl.handle.net/1942/24073

Abstract: P1180

Type: Poster

Abstract Category: Therapy - disease modifying - Immunomodulation/Immunosuppression

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 min 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.

Sponsored by F. Hoffmann-La Roche Ltd.

Disclosure: Robert Bermel has received consulting fees from Biogen, Novartis, Genentech-Roche, and Genzyme.

Giancarlo Comi, in the past year, has received compensation for consulting services from Roche, Novartis, Teva, Sanofi, Genzyme, Merck, Excemed, Almirall, Chugai, Receptos, Forward Pharma and

received compensation for speaking activities from Roche, Novartis, Teva, Sanofi, Genzyme, Merck, Excemed, Almirall, Receptos.

Juha-Pekka Erälinna has received travel grants from Roche, Biogen, Novartis, Sanofi Genzyme, Teva, and consultancy honoraria from Roche, Biogen, Novartis, Sanofi Genzyme, Teva.

Thomas Leist has received compensation for: consulting from Genentech, Biogen, EMD Serono, Teva Neuroscience, Sanofi Genzyme, Bayer, Novartis; as a speaker from Biogen; Novartis, Genentech, Teva Neuoscience, Sanofi Genzyme; and for research from Alkerems, Sun Pharma, Novartis.

Richard Nicholas has received honorarium for speaking and advisory boards from Bayer, Biogen, Genzyme, Merck Serono, Roche; for organizing staff from Biogen, Genzyme, Novartis; and as a principal investigator from Biogen, Novartis.

Celia Oreja-Guevara has received honorarium for speaking and advisory boards from Genzyme, Biogen-Idec, Merck, Teva, Roche and Novartis.

Aksel Siva has received honoraria or consultation fees and/or travel and registration coverage for attending

several national or international congresses or symposia, from Merck Serono, Biogen Idec/Gen Pharma of Turkey, Novartis, Genzyme, Teva and Roche; honoraria for educational presentations at programmes & symposia prepared by Excemed internationally and at national meetings and symposia sponsored by Merck-Serono, Novartis, Teva and Biogen Idec/Gen Pharma of Turkey.

Bart Van Wijmeersch has received financial support/study grants, speaker fees, advisory board membership from Bayer, Biogen, Genzyme/Sanofi, Merck Serono, Novartis, Roche, Teva.

Heinz Wiendl has received grant/research support from Bayer HealthCare, Biogen Idec, Deutsche Forschungsgesellschaft, Else Kröner Fresenius Foundation, Fresenius Foundation, German Ministry for Education and Research, Hertie Foundation, Interdisciplinary Center for Clinical Studies in Münster, Germany, Merck Serono, Novartis, NRW Ministry of Education and Research, sanofi-aventis/Genzyme, and Teva Pharmaceutical Industries. He has received Consulting fees from Bayer HealthCare, Biogen Idec, Fresenius Medical Care, GlaxoSmithKline, GW Pharmaceuticals, Merck Serono, Novartis, Sanofi-Genzyme BioVentures, and Teva Pharmaceutical Industries.

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Regine Buffels is an employee and shareholder of F. Hoffmann-La Roche Ltd.

Csilla Csoboth is an employee and shareholder of Genentech, Inc.

Jian Han is an employee and shareholder of Genentech, Inc.

Bruno Musch is an employee and shareholder of Genentech, Inc.

Patrick Vermersch has received financial grant/research support from Biogen Idec, Genzyme, Bayer, Merck and Serono; and has received consulting fees Biogen Idec, Genzyme, Bayer, Novartis, Merck Serono, GSK and Almirall.