

Five years of ocrelizumab in relapsing multiple sclerosis

OPERA studies open-label extension

Stephen L. Hauser, MD, Ludwig Kappos, MD, Douglas L. Arnold, MD, et al.

Cite as: *Neurology*® 2020;95:e1854-e1867. doi:10.1212/WNL.0000000000010376

Correspondence
Dr. Koendgen
harold.koendgen@roche.com

Study question

Is ocrelizumab (OCR) a safe, tolerable and effective treatment for relapsing multiple sclerosis (RMS) over a long-term (up to 5 years) follow-up of the open-label extension (OLE) of the OPERA trials?

What is known and what this paper adds

Two pivotal phase 3 trials demonstrated superior efficacy of OCR treatment for RMS over 2 years vs interferon β -1a (IFN β -1a) with a favorable benefit-risk profile. This extension phase provides evidence for OCR's sustained efficacy, tolerability and safety after up to 5 years of treatment, and benefits for patients switching from IFN β -1a.

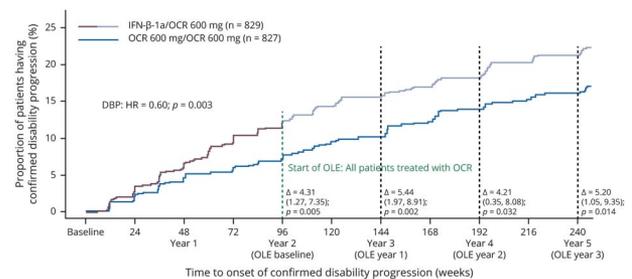
Methods

This OLE phase of the double-blind, randomized, placebo-controlled OPERA I and II trials included 1,325 adults with RMS who either continued receiving 600-mg OCR infusions every 24 weeks (i.e., continuers) or switched to OCR infusions after having received thrice-weekly 44- μ g IFN β -1a s.c. (i.e., switchers). The 96-week OPERA trials occurred between 2011 and 2015 at a diverse set of international centers, and these analyses extend the initial observations into the first 3 years of OLE. The main outcomes were the likelihoods of 24-week confirmed disability progression (CDP) at the end of year 5, annualized relapse rate (ARR), brain MRI activity between years 3 and 5, whole-brain volume (WBV) changes from baseline at the end of year 5, and overall safety.

Results and study limitations

One thousand one hundred seventy-four of 1,325 patients (89%) entering the OLE completed year 5. The cumulative percentage of patients with 24-week CDP was lower among continuers than switchers (16.1% vs 21.3%; $p = 0.014$). Patients who switched from IFN β -1a showed a rapid reduction in ARR, and continuers maintained a low ARR throughout the OLE phase; no differences in ARR at years 3, 4 and 5 between continuers and switchers were seen. All continuers and switchers had near-complete and sustained

Figure Time to onset of 24-week CDP during the DBP and OLE phase in continuers (dark blue) and switchers (purple-light blue)



Abbreviations: CDP = confirmed disability progression; DBP = double-blind phase; HR = hazard ratio; OCR = ocrelizumab; OLE = open-label extension.

suppression of new brain MRI lesions from years 3–5, and continuers had smaller from-baseline WBV loss than switchers (–1.87% vs –2.15%; $p < 0.01$). Adverse events in the OLE were similar to those previously reported. These findings serve as Class III evidence that earlier and continuous OCR treatment provides benefit on clinical and MRI outcomes. Limitations include lack of a control arm and blinding, but the use of data from international centers favors generalizability.

Registration, study funding, and competing interests

These trials were funded by Hoffmann-La Roche and were registered at ClinicalTrials.gov (NCT01247324/NCT01412333). Some authors report receiving personal fees, committee appointments, and research support from healthcare companies, including F. Hoffmann-La Roche Ltd; serving as trial investigators for healthcare companies, including F. Hoffmann-La Roche Ltd; receiving funding from foundations and the EU; and being employees and shareholders of healthcare companies, including F. Hoffmann-La Roche Ltd. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

Neurology[®]

Five years of ocrelizumab in relapsing multiple sclerosis: OPERA studies open-label extension

Stephen L. Hauser, Ludwig Kappos, Douglas L. Arnold, et al.
Neurology 2020;95:e1854-e1867 Published Online before print July 20, 2020
DOI 10.1212/WNL.0000000000010376

This information is current as of July 20, 2020

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/95/13/e1854.full
References	This article cites 14 articles, 2 of which you can access for free at: http://n.neurology.org/content/95/13/e1854.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): All Clinical Neurology http://n.neurology.org/cgi/collection/all_clinical_neurology All Clinical trials http://n.neurology.org/cgi/collection/all_clinical_trials Multiple sclerosis http://n.neurology.org/cgi/collection/multiple_sclerosis
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

