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Five years of ocrelizumab in relapsing multiple sclerosis

OPERA studies open-label extension

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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.

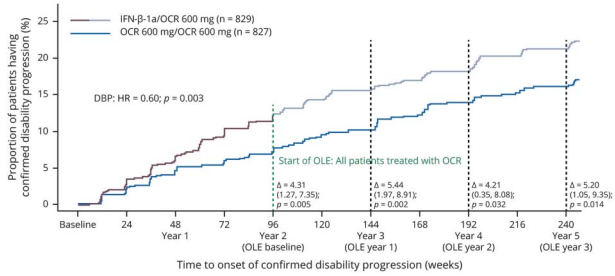
Methods

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-μg 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 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.

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.

Registration, study funding, and competing interests

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