FULL-LENGTH ARTICLE NPub.org/e7gybt

Safety of Ocrelizumab in Patients With Relapsing and Primary Progressive Multiple Sclerosis

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Study Question

What is the long-term safety of ocrelizumab (OCR) in patients with relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS)?

What Is Known and What This Paper Adds

Ongoing safety surveillance is important to understand OCR's long-term benefit-risk profile. In the pivotal clinical trials that demonstrated the safety and efficacy of OCR for the treatment of patients with RMS and PPMS, infections were among the most frequently reported adverse events (AEs) in patients treated with OCR, although the rates of serious infections (SIs) were numerically lower in OCR-treated patients compared with controls. An imbalance of malignancies in patients treated with OCR was also observed during the controlled treatment period, mostly driven by a higher rate of breast cancer, although these events were uncommon. This analysis provides Class III evidence that long-term, continuous treatment with OCR has a consistent and favorable safety profile in patients with RMS and PPMS.

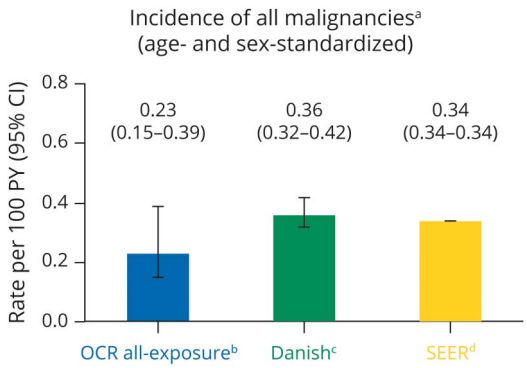
Methods

These long-term safety analyses are based on prospectively planned, standardized evaluations of clinical and laboratory data from all patients who received OCR in 11 clinical trials, and from postmarketing data for selected AEs. Standard criteria for determining seriousness and severity of AEs were used. To account for different exposure lengths, rates of AEs per 100 patient years (PY) were presented. Incidence rates of SIs and malignancies were contextualized using epidemiologic sources.

Results and Study Limitations

As of January 2020, 5,680 patients with multiple sclerosis had received OCR across multiple clinical trials, resulting in 18,218 PY of exposure, with >50% receiving ≥5 doses of OCR and 28% receiving ≥10 doses of OCR. The overall rate of AEs per 100 PY was 248 (95% CI, 246–251). The rates of serious AEs, infusion-related reactions, and infections per 100 PY were 7.3 (95% CI, 7.0–7.7), 25.9 (95% CI, 25.1–26.6), and 76.2 (95% CI, 74.9–77.4), respectively. These rates were similar to those observed during the controlled treatment periods of the phase 3 trials and did not increase over time. The rates per 100 PY for SIs (2.01; 95% CI, 1.81–2.23) and malignancies (0.46; 95% CI, 0.37–0.57) did not show year-on-year variation and were consistent with ranges reported in epidemiologic data. Study limitations include the absence of control groups during open-label extension periods, possible response biases due to under-reporting, and attrition over follow-up.

Figure Comparison of Cumulative Standardized Incidence Rates of Malignancies



Standardized incidence rates per 100 PY (95% CI) derived using a direct standardization method that applies age–sex specific rates to the US population (2010 census), with restriction to the age range of the MS clinical trials (15–59 years).

Registration, Study Funding, and Competing Interests

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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.

