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Infusion-Related Reactions with Ocrelizumab in Relapsing Multiple Sclerosis: Over 9 Years of Data from OPERA OLE

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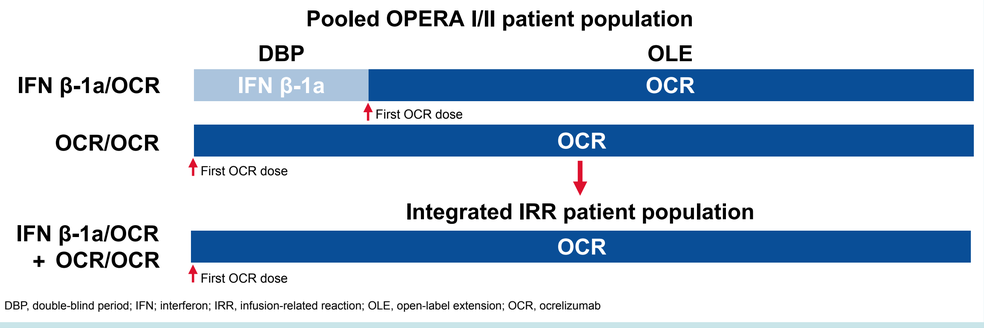
BACKGROUND

- Infusion-related reactions (IRRs), the most common adverse events in the ocrelizumab (OCR) OPERA I/II studies (NCT01247324/ NCT01412333), were typically mild to moderate, were most frequent with the first infusion, and decreased with subsequent doses[1,2]
- Long-term data on the IRR profile of OCR are useful for clinical practice
- By looking at 9 years of data from the OPERA open-label extension (OLE) (data cut: November 2021), the long-term IRR safety profile of OCR was characterised in patients with relapsing multiple sclerosis (PwRMS)

METHODS

- In the 96-week double-blind period (DBP) patients were randomised to OCR or IFN β-1a
- Patients continued OCR or switched from IFN β-1a to OCR in the OLE (clinical cut-off date: November 2021)
- IRR analyses are based on integrated data for all patients who received OCR
- The frequency, severity and types of IRR were analysed during and 24 hours post-infusion

Pooled OPERA I/II Patient Population



DBP, double-blind period; IFN; interferon; IRR, infusion-related reaction; OLE, open-label extension; OCR, ocrelizumab

RESULTS

Patient Disposition

- Over 9 years, a total of 1,448 PwRMS underwent randomisation (OCR all-exposure population) in the OPERA I and OPERA II studies
- As of November 2021, after up to 9 years of continuous therapy, the majority of patients (65.7%; 951/1,448) remained on OCR

IRR Incidence and Severity

1,448 patients with RMS
23,116 OCR infusions

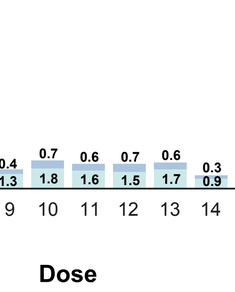
35.2% (510/1,448) of patients had **one or more** IRRs

33.1% (480/1,448) of patients had **mild-to-moderate** IRRs

2.0% (29/1,448) patients had **severe** IRRs

<0.1% (1/1,448) of patients had a **life-threatening** IRR (bronchospasm at first infusion)[a]

Follow-up period 9 **Years**



[a]There were no Grade 5 (fatal) IRRs.
IRR, infusion-related reaction; OCR, ocrelizumab; RMS, relapsing multiple sclerosis.

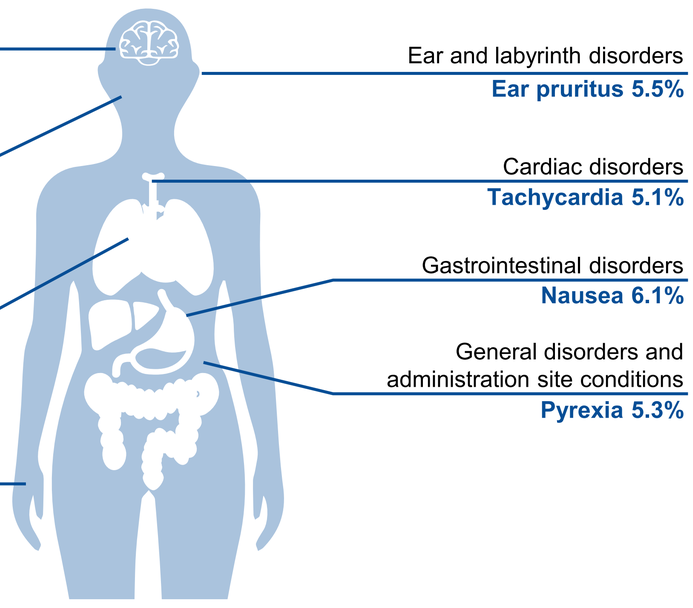
IRRs by Dose and Severity

After infusion 1, IRRs decreased in frequency and severity with subsequent dosing (up to infusion 23); no serious IRRs occurred

[a]Bronchospasm at first infusion.
IRR, infusion-related reaction.

Most Frequent (≥10%) and Other Frequent (≥5–<10%) IRR Symptoms

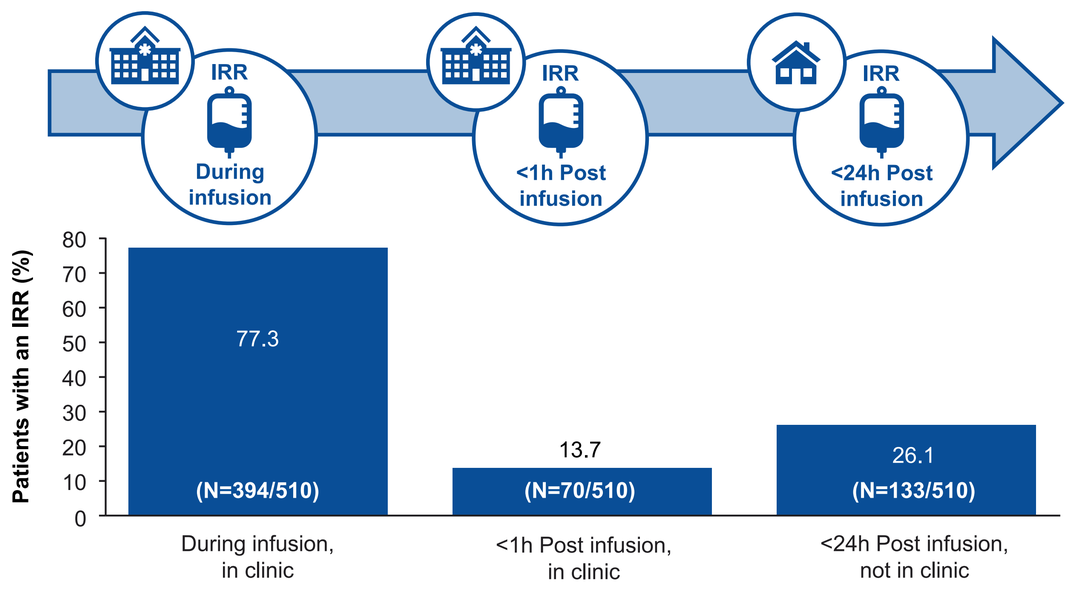
The IRR symptom pattern remained consistent over time



Patients with symptom, expressed as percent of patients with an IRR (n=510).

Timing of IRR Symptoms (During Infusion, <1 Hour and <24 Hours Post Infusion)

The majority of IRRs were reported during the infusion (77.3%) and decreased in incidence 1 hour post infusion (while patients were in the clinic) and 24 hours post infusion (while patients were not in the clinic)



h, hour; IRR, infusion-related reaction.

Discontinuations Due to IRRs

34 (2.3%) infusions led to discontinuation of OCR infusion. Most discontinuations (n=22) happened at Infusion 1 and decreased with subsequent infusions

Follow-up period 9 **Years**

1,448 patients with RMS received **23,116** OCR infusions

25.8% (373/1,448) of patients had an infusion **intervention**

2.3% (34/1,448) of infusions led to **discontinuation** of OCR infusion

Most discontinuations were at **first infusion**[a]

[a]Frequency of infusion discontinuations decreased after the first infusion: Dose 1, Day 1: 1.5%; dose 10: 0.1%; dose 21: 0.0%.
OCR, ocrelizumab; RMS, relapsing multiple sclerosis.

Symptomatic Treatment of IRRs

Where medication was used for symptomatic treatment of an IRR, the most commonly used were antihistamines, anti-inflammatories and analgesics

The most frequently used treatment classes were:
Antihistamines (15.5%)
Corticosteroids (6.0%)
Analgesics (3.3%)
Nonsteroidal anti-inflammatories (2.5%)

Out of these, the most commonly used treatments were:
Diphenhydramine (2.6%)
Methylprednisolone (2.3%)
Paracetamol (3.2%)
Ibuprofen (1.7%)

IRR Outcomes

1,448 patients with RMS received **23,116** OCR infusions

35.2% (510/1,448) of patients had **one or more** IRRs

99.7% (1,175/1,178) of IRRs **recovered** or **resolved**[a]

[a]There were no IRRs that recovered or resolved with sequelae.
IRR, infusion-related reaction; OCR, ocrelizumab; RMS, relapsing multiple sclerosis.

Infusion Compliance

Over 9 years of continuous OCR treatment, treatment compliance was very high, with most patients (>99%) completing dose administration[a]

[a]Defined as receiving more than 80% of the planned OCR dose at each infusion.

CONCLUSIONS

- Over more than 9 years of continuous ocrelizumab treatment, IRRs after the first dose remained low, were manageable and did not impact long-term treatment
- The very high compliance observed with ocrelizumab infusions over 9 years, supports the use of ocrelizumab as a safe and convenient intravenous anti-CD20 therapy for long-term use in patients with multiple sclerosis

REFERENCES

1. Mayer L, *et al. Mult Scler Relat Disord.* 2019;30:236–43;
2. Hauser SL, *et al. Neurology* 2021;97:e1546–e1559.

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