The Patient Impact of 10 Years of Ocrelizumab Treatment in Multiple Sclerosis: Long-Term Data from the Phase III OPERA and **ORATORIO** Studies

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STUDY AIMS

To assess the long-term (10-year) impact of OCR on disability accumulation in patients with relapsing and primary progressive MS

CONCLUSIONS

After long-term (10 years) continuous ocrelizumab treatment:

Almost 8 out of 10 PwRMS and a third of PwPPMS were progression-free on EDSS >90% of PwRMS did **not need a walking aid** and >80% of PwPPMS did **not need** a wheelchair

BACKGROUND



Preserving patient function, by optimally **slowing** disease progression, is the key treatment goal across the MS continuum^{1–3}

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Early treatment with ocrelizumab extends the progression-free event window by almost 10 years in PwRMS, compared with a lower-efficacy DMT

The notable impact of a decade of ocrelizumab treatment in reducing disability accumulation reinforces the role of early treatment in preserving patient function across the MS spectrum



OCR, the only anti-CD20 monoclonal antibody approved for the treatment of both RMS and PPMS,^{4,5} has a decade of safety and efficacy experience in clinical trials, and over **300,000 patients have been treated** in trial and post-marketing settings^{6–9}

METHODS



Disability Measures^a

aCDW was previously termed confirmed disability progression; bCDW requires at least one of the following: (1) an increase in EDSS score of ≥1.0 points from a BL score of ≤5.5 points, or a ≥0.5-point increase from a BL score of >5.5 points; (2) a 20% increase from BL in time to complete the 9HPT; (3) a 20% increase from BL in the T25FW.

9HPT, Nine-Hole Peg Test; BL, baseline; cCDW, composite confirmed disability worsening; CDW, confirmed disability worsening; EDSS, Expanded Disability Status Scale; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; T25FW, Timed 25-Foot Walk.

Patient Populations, Baseline Demographics and Disease Characteristics^a

OPERA I/II PATIENT POPULATION	ORATORIO PATIENT POPULATION			OPERA I/II RMS (OCR; N=827)	OPERA I/II RMS (IFN; N=829)	ORATORIO PPMS (OCR; N=488)	ORATORIO PPMS (PBO; N=244)
RMS diagnosis (McDonald 2010) ¹⁰	PPMS diagnosis (McDonald 2005) ¹¹	$\overline{\diamondsuit}$	Age years, mean±SD	37.1±9.2	37.2±9.2	44.7±7.9	44.4±8.3
Age 18–55 years, inclusive	Age 18–55 years, inclusive	¶ ¶	Female n (%)	541 (65.4)	552 (66.6)	237 (48.6)	124 (50.8)
MRI activity consistent with MS	MS disease duration <10 years if EDSS ≤5.0 <15 years if EDSS >5.0		Time since symptom onset years, mean±SD	6.7±6.2	6.5±6.1	6.7±4.0	6.1±3.6
EDSS 0.0–5.5, inclusive	EDSS 3.0–6.5, inclusive	EDSS	EDSS score	2.8±1.3	2.8±1.3	4.7±1.2	4.7±1.2
≥2 relapses in the previous 2 years or one relapse in prior 12 months	Documented history or presence of elevated IgG or ≥1 IgG OCB	T25FW	T25FW seconds, mean±SD	7.9±9.9	7.2±9.2	14.8±21.2	12.9±15.5
Treatment naïve or previously treated	Treatment naïve or previously treated	9НРТ	9HPT seconds, mean±SD	24.5±13.1	24.0±8.3	31.9±23.3	30.6±13.4

Baseline demographics and disease characteristics were representative of relapsing and primary progressive MS disease, and were similar between treatment and comparator arms

^aData shown for DBP; clinical cut-off date for the analyses was 25 November 2022; for OPERA I/II (NCT01247324/NCT01412333) and ORATORIO (NCT01194570), data from patients up to Week 528 were used for the 10-year analyses. Patient disposition is available in the Supplementary Materials.

9HPT, Nine-Hole Peg Test; DBP, double-blind period; EDSS, Expanded Disability Status Scale; IFN, interferon β-1a; IgG, immunoglobulin G; MS, multiple sclerosis; OCB, oligoclonal band; OCR, ocrelizumab; PBO, placebo; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; SD, standard deviation; T25FW, Timed 25-Foot Walk.

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RESULTS



Effect of a Delay in OCR Initiation on 48W-CDW on EDSS^a

After 10 years, most PwRMS did not experience disability accumulation with continuous OCR treatment. In RMS and PPMS, patients who initiated OCR early maintained the benefit ତୁରୁ ଦୁରୁ

Time to Walking Aid (RMS) and Time to Wheelchair (PPMS)



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compared with patients who switched after just 2 years (RMS) or 3 years (PPMS)

^aFor results on the effect of a delay in OCR initiation on 48W-cCDW on EDSS, please see the Supplementary Materials.

48W-cCDW. 48-week composite confirmed disability worsening; 48W-CDW, 48-week confirmed disability worsening; CDW, confirmed disability worsening; CI, confidence interval; DBP, double-blind period; ECP, extended controlled period; EDSS, Expanded Disability Status Scale;

HR, hazard ratio; IFN, interferon β-1a; OCR, ocrelizumab; OLE, open-label extension; PBO, placebo; PPMS, primary progressive multiple sclerosis; PwPPMS, patients with primary progressive multiple sclerosis; PwRMS, patients with relapsing multiple sclerosis; RMS, relapsing multiple sclerosis.

Over 10 years, in PwRMS and PwPPMS there was a 42% and 30% reduction in the risk of requiring a walking aid or a wheelchair in those who initiated OCR earlier vs delayed treatment

CDW, confirmed disability worsening; HR, hazard ratio; IFN, interferon β-1a; OCR, ocrelizumab; PPMS, primary progressive multiple sclerosis; PwPPMS, patients with primary progressive multiple sclerosis; PwRMS, patients with relapsing multiple sclerosis; RMS, relapsing multiple sclerosis.

Disability Event Rate Expressed as Annualised Repeated 48W-CDW-EDSS



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Over 10 years, the annualised, repeated 48W-CDW-EDSS event rate infers patients would be expected to be progression-free for the next 34.5 and 8.3 years after the last event, in PwRMS and PwPPMS

^aSee Supplementary Materials for annualised repeated event rate plots.

48W-CDW, 48-week confirmed disability worsening; EDSS, Expanded Disability Status Scale; IFN, interferon β-1a; OCR, ocrelizumab; PBO, placebo; PwPPMS, patients with primary progressive multiple sclerosis; PwRMS, patients with relapsing multiple sclerosis

DISCLOSURES

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