The Patient Impact of 11 Years of Ocrelizumab Treatment in Multiple Sclerosis: Long-Term Data from the Phase III OPERA and ORATORIO Studies

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OBJECTIVE

To assess the long-term (11-year) impact of ocrelizumab on disability accumulation in patients with relapsing and primary progressive MS

KEY TAKEAWAYS

After 11 years, continuous ocrelizumab treatment was effective in controlling long-term disease activity and preventing disability accumulation:

- Three-quarters of patients with RMS were progression-free and >90% did not need a walking aid
- A third of patients with PPMS were progression-free and 80% did not need a wheelchair

The impact of over a decade of ocrelizumab treatment in reducing disability accumulation reinforces the role of early treatment in preserving patient function across the MS spectrum[1–3]

INTRODUCTION

- OCR, the first and only anti-CD20 monoclonal antibody approved for the treatment of both RMS and PPMS,[4,5] has a robust long-term safety and efficacy experience across the spectrum of disease[6]
- Over 11 years, more than 350,000 patients have been treated with OCR in trial and post-marketing settings, corresponding to >1 million patient years[6,7]
- Understanding the long-term impact of OCR on patient function is therefore important

NB: Limitations inherent in all long-term, observational, open-label extension studies of DMTs remain pertinent to this study (e.g., possible attrition bias due to temporal decrease in patient numbers)

METHODS

OPERA I/II and ORATORIO: Efficacy Outcomes

Measures of disability progression[a]

CDP–EDSS: Defined as ≥1.0 increase in EDSS from baseline score (or 0.5 increase in EDSS score if baseline EDSS >5.5) confirmed at 48 weeks

REPEATED CDP–EDSS: Defined by expanding the first-event definition such that the subsequent event was rebaselined to the EDSS score at the onset of the previous event

ANNUALISED REPEATED CDP–EDSS EVENT RATE: i.e. the average number of events per year, used to establish the time between two disability progression events

TIME TO KEY DISABILITY MILESTONES: **RMS**: Requiring a **walking aid** **EDSS ≥6** from baseline ≤5.5 — **EDSS ≥6 CDP**; **PPMS**: Requiring a **wheelchair** **EDSS ≥7** from baseline ≤6.5 — **EDSS ≥7 CDP**

See enhanced content QR code for composite CDP outcome[b]

Disease activity

Annualised relapse rate

MRI N/E T2 lesions

See enhanced content QR code for disease activity outcomes (ARR and MRI); in summary: Over 11 years, early and continuous OCR treatment led to an almost complete suppression of disease activity (relapse and MRI measures)

Studies

OPERA I/II: OCR vs IFN β-1a in RMS NCT01247324/NCT01412333
FPI: 31 August 2011/20 September 2011

ORATORIO: OCR vs PBO in PPMS; NCT01194570
FPI: 3 March 2011

See enhanced content QR code for Patient Populations, Baseline Demographics and Disease Characteristics

[a]CDP is also termed confirmed disability worsening; [b]Composite CDP 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.

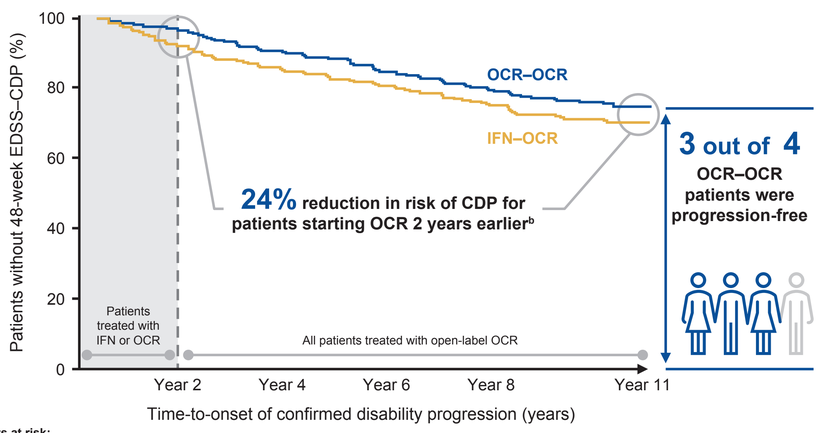
RESULTS

OPERA I/II

ORATORIO

48-Week Confirmed Disability Progression (CDP) on EDSS

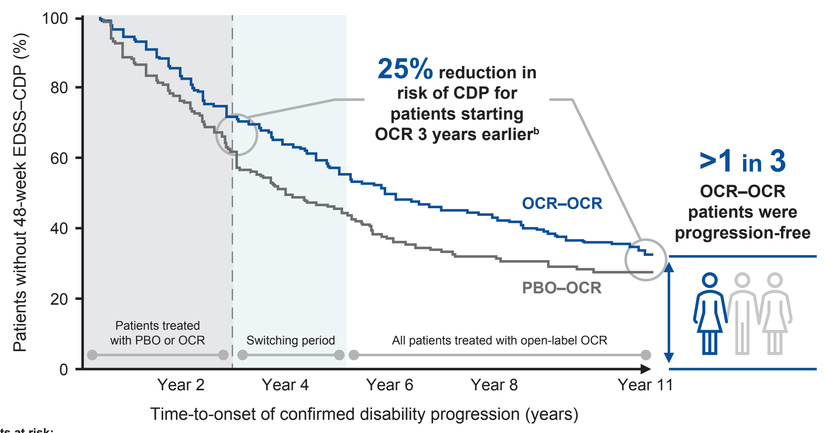
Over an 11-year period[a] of continuous treatment with OCR, **3 out of 4 patients were progression-free**



No. patients at risk:

IFN β-1a/OCR 600 mg (N=829)	829	690	606	512	474	445	416	393	365	331	231	44
OCR 600 mg/OCR 600 mg (N=827)	827	751	699	600	574	539	499	465	433	376	241	46

Over an 11-year period[a] of continuous treatment with OCR, **>1 in 3 patients were progression-free**



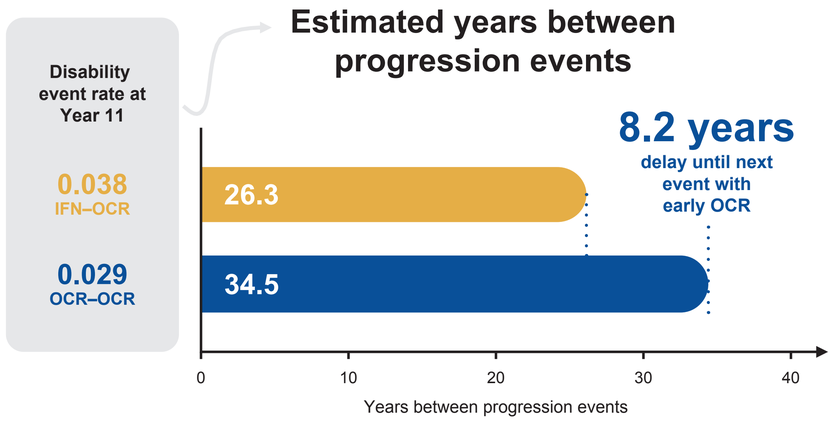
No. patients at risk:

PBO/OCR 600 mg (N=244)	244	197	161	114	95	82	65	57	50	42	39	12
OCR 600 mg/OCR 600 mg (N=488)	487	432	366	300	253	212	180	161	152	129	96	31

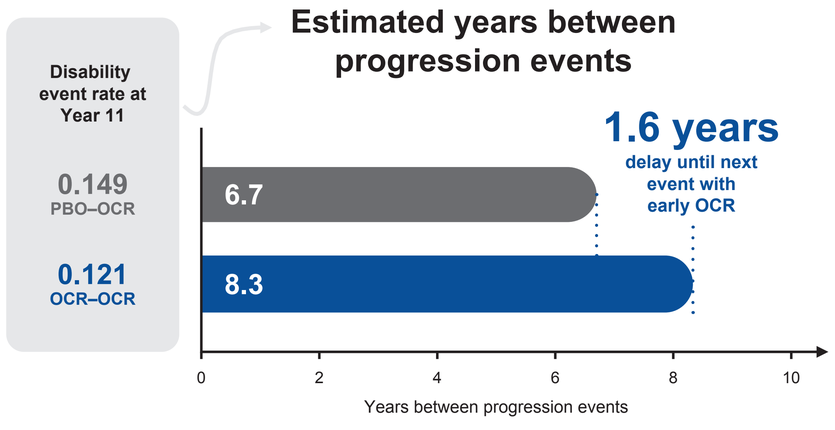
[a]The median follow-up time for patients continuously treated with OCR in the pooled OPERA I/II population was 10.5 years (range 0.0–12.2) and in ORATORIO was 9.9 years (range 0.0–12.6); [b]Average HR over 11-year period: OPERA I/II HR (95% CI): 0.76 (0.61–0.95); p=0.0139. Risk reduction: 24%; ORATORIO HR (95% CI): 0.75 (0.61–0.92); p=0.0047. Risk reduction: 25%.

Disability Event Rate Expressed as Annualised Repeated 48W-CDP–EDSS

Patients initiating OCR 2 years earlier were **estimated to have a 24% (8.2 years) longer interval between disability events**

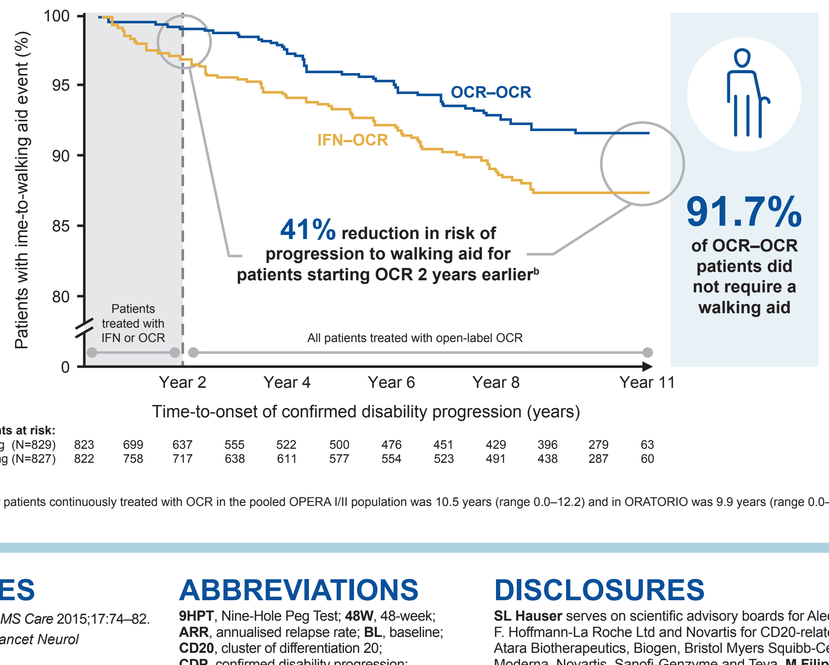


Patients initiating OCR 2 years earlier were **estimated to have a 19% (1.6 years) longer interval between disability events**



Time to Walking Aid

Over an 11-year period[a] of continuous treatment with OCR, **92% of patients did not require a walking aid**

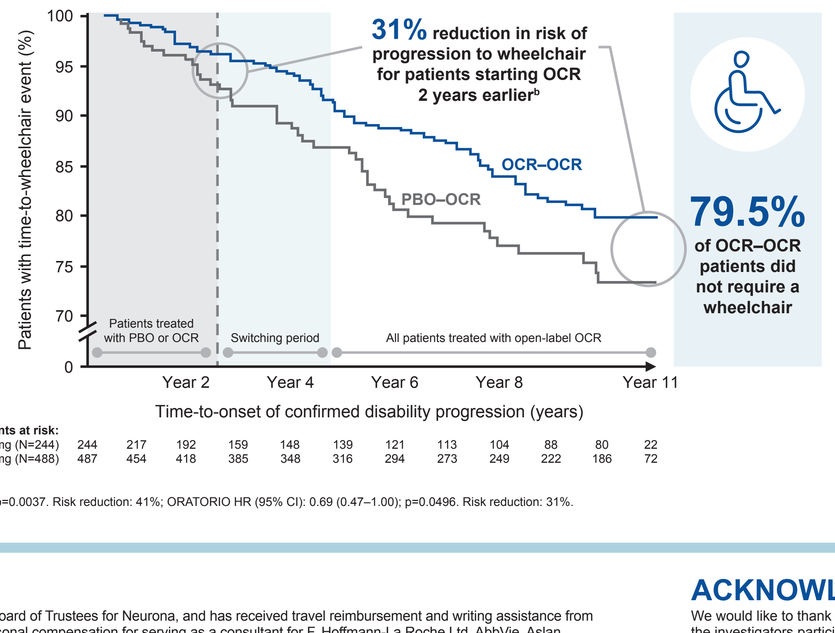


No. patients at risk:

IFN β-1a/OCR 600 mg (N=829)	823	699	637	555	522	500	476	451	429	396	279	63
OCR 600 mg/OCR 600 mg (N=827)	822	758	717	638	611	577	554	523	491	438	287	60

Time to Wheelchair

Over an 11-year period[a] of continuous treatment with OCR, **80% of patients did not require a wheelchair**



No. patients at risk:

PBO/OCR 600 mg (N=244)	244	217	192	159	148	139	121	113	104	88	80	22
OCR 600 mg/OCR 600 mg (N=488)	487	454	418	385	348	316	294	273	249	222	186	72

[a]The median follow-up time for patients continuously treated with OCR in the pooled OPERA I/II population was 10.5 years (range 0.0–12.2) and in ORATORIO was 9.9 years (range 0.0–12.6); [b]Average HR over 11-year period: HR (95% CI): 0.59 (0.41–0.85); p=0.0037. Risk reduction: 41%; ORATORIO HR (95% CI): 0.69 (0.47–1.00); p=0.0496. Risk reduction: 31%.

REFERENCES

1. Wilson LS, *et al. Int J MS Care* 2015;17:74–82.
2. Ontaneda D, *et al. Lancet Neurol* 2019;18:973–980.
3. Cree BAC, *et al. Curr Opin Neurol* 2022;35:262–270.
4. OCREVUS [ocrelizumab] Full Prescribing Information. Genentech, Inc., 2020.
5. OCREVUS [ocrelizumab] Summary of Product Characteristics. Roche Pharma AG, 2020.
6. Hauser SL, *et al. AAN* 2024; Presentation S31.005.
7. Roche data on file.

ABBREVIATIONS

9HPT, Nine-Hole Peg Test; **48W**, 48-week; **ARR**, annualised relapse rate; **BL**, baseline; **CD20**, cluster of differentiation 20; **CDP**, confirmed disability progression; **DMTs**, disease-modifying therapies **EDSS**, Expanded Disability Status Scale; **FPI**, first patient in; **HR**, hazard ratio; **IFN**, interferon; **MS**, multiple sclerosis; **N/E**, new/enlarging; **OCR**, ocrelizumab; **PBO**, placebo; **PPMS**, primary progressive multiple sclerosis; **RMS**, relapsing multiple sclerosis; **T25FW**, Timed 25-Foot Walk.

DISCLOSURES

SL Hauser serves on scientific advisory boards for Alector, Annexon, Accure and Hinge; has previously served on the Board of Trustees for Neurona, and has received travel reimbursement and writing assistance from F. Hoffmann-La Roche Ltd and Novartis for CD20-related meetings and presentations. **G Giovannoni** has received personal compensation for serving as a consultant for F. Hoffmann-La Roche Ltd, AbbVie, Aslan, Atara Biotherapeutics, Biogen, Bristol Myers Squibb-Celgene, GlaxoSmithKline, GW Pharma, Janssen/Johnson and Johnson, Japanese Tobacco, Jazz Pharmaceuticals, LifNano, Merck and Company, Merck KGaA/EMD Serono, Moderna, Novartis, Sanofi-Genzyme and Teva. **M Filippi** is Editor-in-Chief of the *Journal of Neurology* and Associate Editor of *Human Brain Mapping, Neurological Sciences* and *Radiology*; received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche and Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda and Teva; participation in advisory boards for Alexion, Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme and Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol Myers Squibb, Eli Lilly, Novartis and Sanofi-Genzyme; and he receives research support from Biogen Idec., Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM (Fondazione Italiana Sclerosi Multipla). **MS Weber** receives research support from the Deutsche Forschungsgemeinschaft (DFG; WE 3547/5-1), Novartis, Teva, Biogen Idec., Roche, Merck and the ProFutura Program of the Universitätsmedizin Göttingen; is serving as an editor for PLoS One; received travel funding and/or speaker honoraria from Biogen Idec., Merck-Serono, Novartis, Roche, Teva, Bayer and Genzyme. **X Montalban** has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with AbbVie, Actelion, Alexion, Biogen, Bristol Myers Squibb/Celgene, EMD Serono, F. Hoffmann-La Roche Ltd, Immunic, Janssen, MedDay, Merck, Mylan, NervGen, Novartis, Sandoz, Sanofi-Genzyme, Teva, TG Therapeutics, Exemed, MSIF and NMSS. **JA Nicholas** has received consultancy fees from Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Novartis and TG Therapeutics; has received research support from Biogen, Novartis, Genentech, University of Buffalo and PCORI; has served on speakers' bureau for Alexion, Bristol Myers Squibb, EMD Serono, Horizon, Viela Bio and TG Therapeutics. **HM Schneble** is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. **Q Wang** is an employee of F. Hoffmann-La Roche Ltd. **L Kappos** has received no personal compensation. His institutions (University Hospital Basel/Foundation Clinical Neuroimmunology and Neuroscience Basel) have received and used exclusively for research support: Payments for steering committee and advisory board participation, consultancy services and participation in educational activities from: Actelion, Bayer, Bristol Myers Squibb, df-mp Molnia & Pohlmann, Celgene, Eli Lilly, EMD Serono, Genentech, GlaxoSmithKline, Janssen, Japan Tobacco, Merck, MH Consulting, Minoryx, Novartis, F. Hoffmann-La Roche Ltd, Senda Biosciences Inc., Sanofi, Santhera, Shionogi BV, TG Therapeutics and Wellmera; and license fees for Neurostatus-UHB products; grants from Novartis, Innosuisse and Roche.

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