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10 Years of Ocrelizumab Treatment in Multiple Sclerosis: Long-Term Efficacy and Safety Clinical Trial Data

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OPERA I and II (NCT01247324/NCT01412333); ORATORIO (NCT01194570)

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Disclosures

SL Hauser currently serves on the scientific advisory board of Accure, Alector, Annexon, and Hinge. He has previously consulted for BD, Moderna, NGM Bio, and Pheno Therapeutics and served on the Board of Directors of Neurona. Dr. Hauser also has received travel reimbursement and writing support from F. Hoffmann-La Roche and Novartis AG for anti-CD20 therapy–related meetings and presentations.

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JA Nicholas has received consultancy fees from Bristol Myers Squibb, EMD Serono, Genentech, MyMSTeam, Novartis, Octave Bio and TG Therapeutics; has received research support from Novartis, Genentech, Alexion, Octave Bio, Sanofi Genzyme, University of Buffalo and PCORI; serves on speakers' bureau for EMD Serono and TG Therapeutics.

C Chognot and **HM Schneble** are an employees of and shareholders in F. Hoffmann-La Roche Ltd.

Q Wang is an employee of F. Hoffmann-La Roche Ltd.

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, Japan Tobacco, Jazz Pharmaceuticals, LifNano, Merck and Company, Merck KGaA/EMD Serono, Moderna, Novartis, Sanofi-Genzyme and Teva.

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.

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Objective and Methods
OPERA I/II and ORATORIO: Efficacy Outcomes and Safety Assessments

Objective:

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

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

ORATORIO: OCR vs placebo in PPMS
FPI: 3 March 2011

Safety assessments

- AE and SAE rates and AEs leading to withdrawal
- Infusion-related reaction
- Malignancies, including female breast cancer
- Infections and serious infections
- Serious infections in relation to IgG levels
  - In patients with IgG < the lower limit of normal
  - In patients with IgG ≥ the lower limit of normal

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

REPEATED CDP–EDSS: Defined by expanding the first-event definition such that the EDSS was rebaselined at the onset of a 48-week confirmed event

Annualized 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

Disease Activity

Annualized relapse rate

MRI T1 Gd+ lesions

9HPT, Nine-Hole Peg Test; AE, adverse event; BL, baseline; CDP, confirmed disability progression; EDSS, Expanded Disability Status Scale; FPI, first patient in; Gd+, gadolinium-enhancing; OCR, ocrelizumab; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; SAE, serious adverse event; T25FW, Timed 25-Foot Walk.

Results
Patient Populations, Baseline Demographics and Disease Characteristics[a]

OPERA I/II
PATIENT POPULATION

RMS diagnosis (McDonald 2010)[1]

Age 18–55 years, inclusive

MRI activity consistent with MS

EDSS 0.0–5.5, inclusive

≥2 relapses in the previous 2 years or one relapse in prior 12 months

Treatment naïve or previously treated

ORATORIO
PATIENT POPULATION

PPMS diagnosis (McDonald 2005)[2]

Age 18–55 years, inclusive

MS disease duration
<10 years if EDSS ≤5.0
<15 years if EDSS >5.0

EDSS 3.0–6.5, inclusive

Documented history or presence of elevated IgG or ≥1 IgG OCB

Treatment naïve or previously treated

	OPERA I/II RMS (OCR; N=827)	OPERA I/II RMS (IFN; N=829)	ORATORIO PPMS (OCR; N=488)	ORATORIO PPMS (PBO; N=244)
Age years, mean ± SD	37.1 ± 9.2	37.2 ± 9.2	44.7 ± 7.9	44.4 ± 8.3
Female n (%)	541 (65.4)	552 (66.6)	237 (48.6)	124 (50.8)
Time since symptom onset years, mean ± SD	6.7 ± 6.2	6.5 ± 6.1	6.7 ± 4.0	6.1 ± 3.6
EDSS score	2.8 ± 1.3	2.8 ± 1.3	4.7 ± 1.2	4.7 ± 1.2
T25FW seconds, mean ± SD	7.9 ± 9.9	7.2 ± 9.2	14.8 ± 21.2	12.9 ± 15.5
9HPT seconds, mean ± SD	24.5 ± 13.1	24.0 ± 8.3	31.9 ± 23.3	30.6 ± 13.4

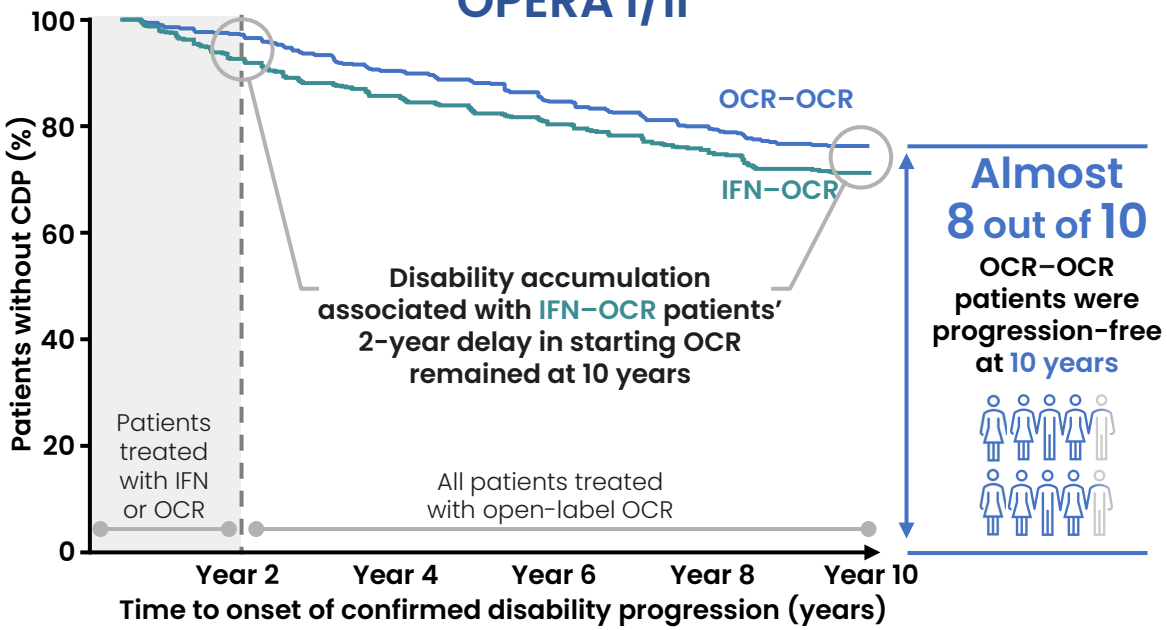
Baseline demographics and disease characteristics were representative of relapsing and primary progressive MS disease, and were similar between treatment and comparator arms

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.
[a]Data shown for DBP; clinical cut-off date for the analyses was 25 November 2022; for OPERA I/II and ORATORIO, data from patients up to Week 528 were used for the 10-year analyses. Patient disposition is available in the Supplementary Materials.
1. Polman CH, *et al. Ann Neurol* 2011;69:292–302; 2. Polman CH, *et al. Ann Neurol* 2005;58:840–846.

Results
Effect of a Delay in OCR Initiation on 48W-CDP on EDSS

At 10 years, almost 8 out of 10 of PwRMS and >1/3 of PwPPMS treated with continuous OCR were progression-free

OPERA I/II



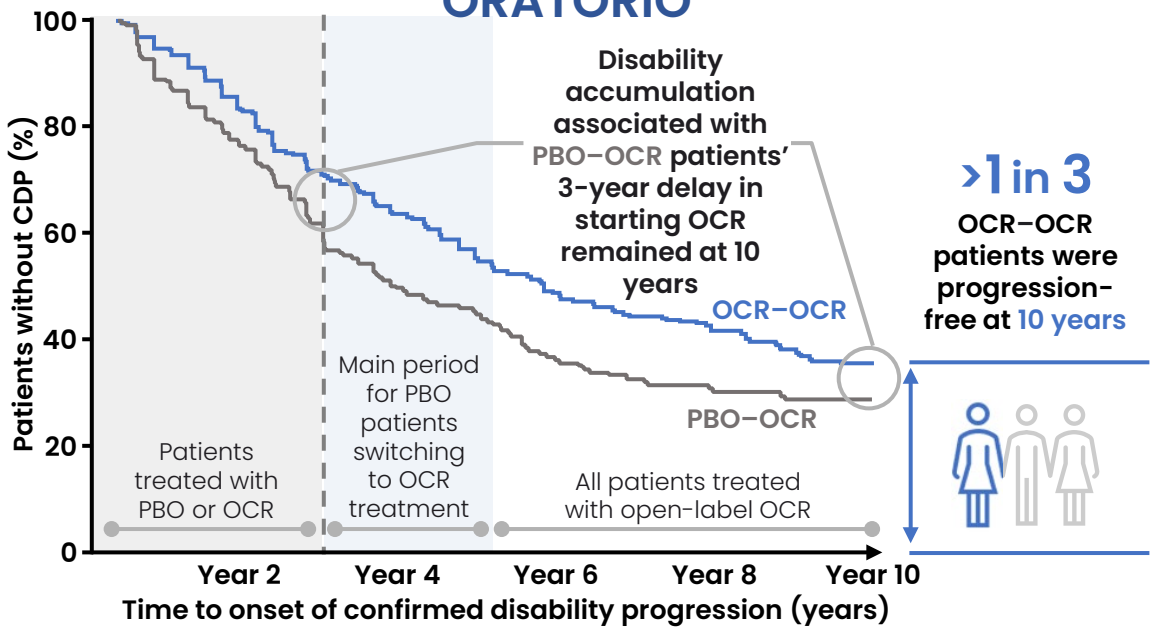
Average DBP+OLE HR (95% CI): 0.76 (0.61, 0.95) p=0.0152. Risk reduction: 24%

No. patients at risk:

IFN beta-1a/OCR 600mg (N=829) 829 789 753 715 690 657 639 618 606 552 540 527 525 512 507 491 490 474 471 461 459 445 445 437 435 417 416 407 403 395 393 381 378 368 365 359 357 343 342 330 329 297 278 142

OCR 600mg/OCR 600mg (N=827) 827 798 778 762 751 735 724 712 699 665 650 633 629 600 599 586 585 574 571 558 557 545 539 524 519 500 499 488 485 471 465 452 448 435 433 420 414 397 390 375 372 335 304 155

ORATORIO



Average DBP+ECP+OLE HR (95% CI): 0.75 (0.61, 0.92) p=0.0047. Risk reduction: 25%

No. patients at risk:

Placebo/OCR 600mg 244 235 216 205 197 187 180 170 161 152 143 134 125 114 109 107 101 95 93 90 89 87 82 78 71 67 65 63 60 59 57 55 51 51 50 49 48 47 44 42 40 40 37 32 26

OCR 600mg/OCR 600mg 487 467 457 443 432 412 401 382 366 346 329 320 309 300 296 280 266 253 247 239 230 223 212 201 196 189 179 172 171 165 160 156 155 153 152 146 140 139 131 129 120 111 109 87 75

After 10 years,[a] most PwRMS did not experience disability accumulation with continuous OCR treatment. In RMS and PPMS, patients who initiated OCR early maintained the benefit compared with patients who switched after just 2 years (RMS) or 3 years (PPMS)

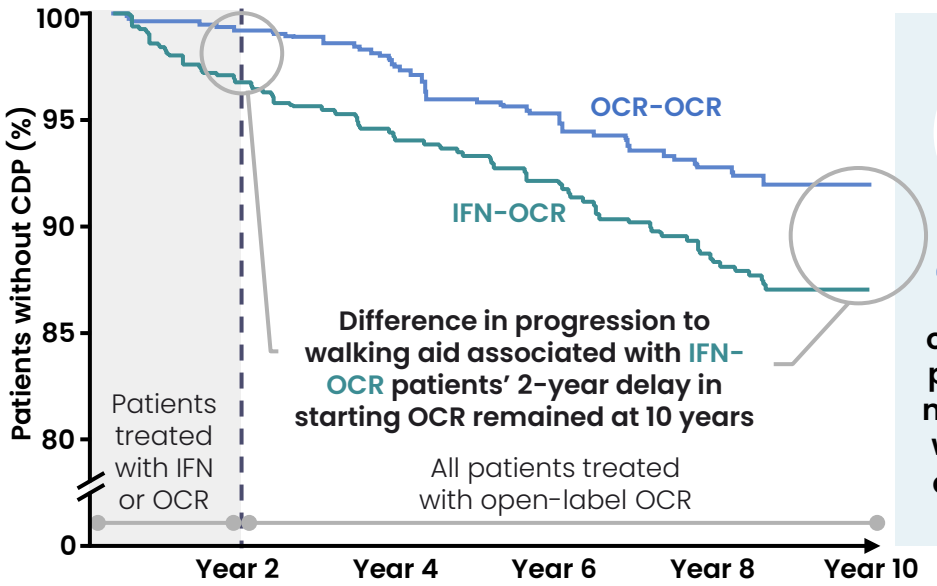
48W-cCDP, 48-week composite confirmed disability progression; 48W-CDP, 48-week confirmed disability progression; CDP, confirmed disability progression; CI, confidence interval; DBP, double-blind period; ECP, extended controlled period; EDSS, Expanded Disability Status Scale; HR, hazard ratio; IFN, interferon 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.

[a]The median follow-up time in OPERA was 10 years.

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

At 10 years, >90% PwRMS and >80% PwPPMS treated with continuous OCR did not require a walking aid or wheelchair, respectively

OPERA I/II



92.1%
of OCR-OCR patients did not require a walking aid at 10 years

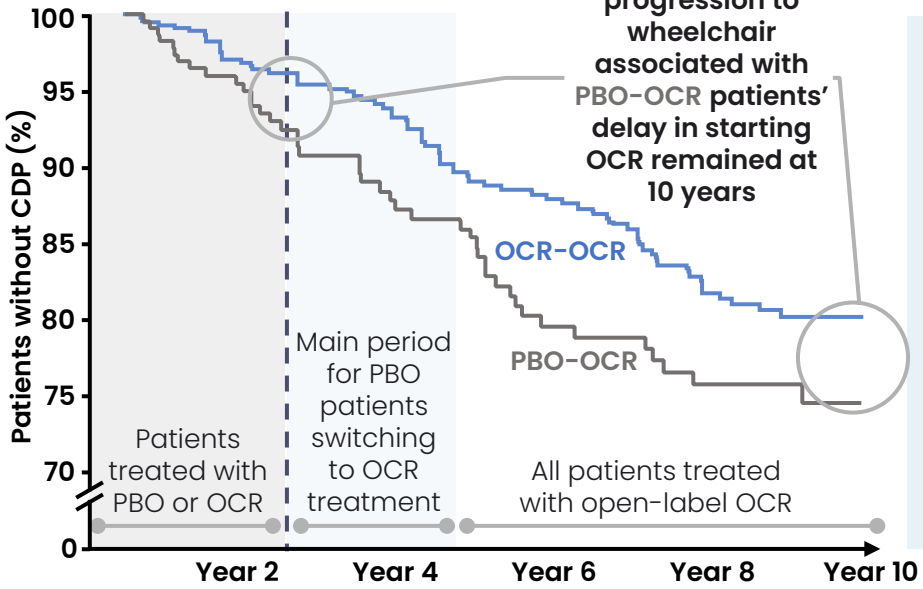
HR (95% CI) = 0.57 (0.40, 0.82) p=0.0022. Risk reduction: 43%

No. patients at risk:

IFN beta-1a/OCR 600mg 823 789 757 719 699 672 660 644 637 586 579 569 566 556 553 539 537 523 520 512 509 501 501 494 492 478 477 467 464 455 452 445 442 432 429 423 418 413 409 394 392 355 337 182 138

OCR 600mg/OCR 600mg 822 793 778 766 758 746 737 726 717 689 680 664 660 638 638 627 625 611 609 593 593 583 577 571 566 555 554 542 541 529 523 512 507 493 491 478 474 460 455 438 435 392 355 187 154

ORATORIO



80.4%
of OCR-OCR patients did not require a wheelchair at 10 years

HR (95% CI) = 0.70 (0.48, 1.03) p=0.0703. Risk reduction: 30%

No. patients at risk:

Placebo/OCR 600mg 244 238 232 225 217 211 204 199 192 185 176 170 163 159 156 155 151 148 145 142 142 142 139 135 128 125 121 117 116 114 113 112 109 108 104 101 99 96 91 88 88 87 82 70 54

OCR 600mg/OCR 600mg 487 471 465 459 454 442 432 426 418 411 404 398 389 385 380 368 359 348 343 337 330 324 316 309 302 298 294 287 285 278 273 265 262 253 249 242 238 234 227 221 214 207 202 171 142

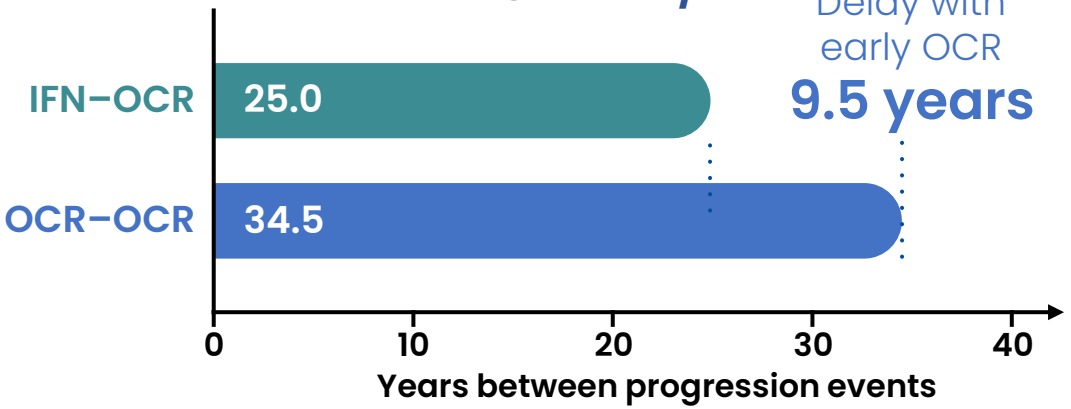
Over 10 years, in PwRMS and PwPPMS there was a 43% and 30% reduction in the risk of requiring a walking aid or a wheelchair in those who initiated OCR earlier vs delayed treatment

CDP, confirmed disability progression; CI, confidence interval; 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.

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

Over 10 years, the annualized, repeated 48W-CDP–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

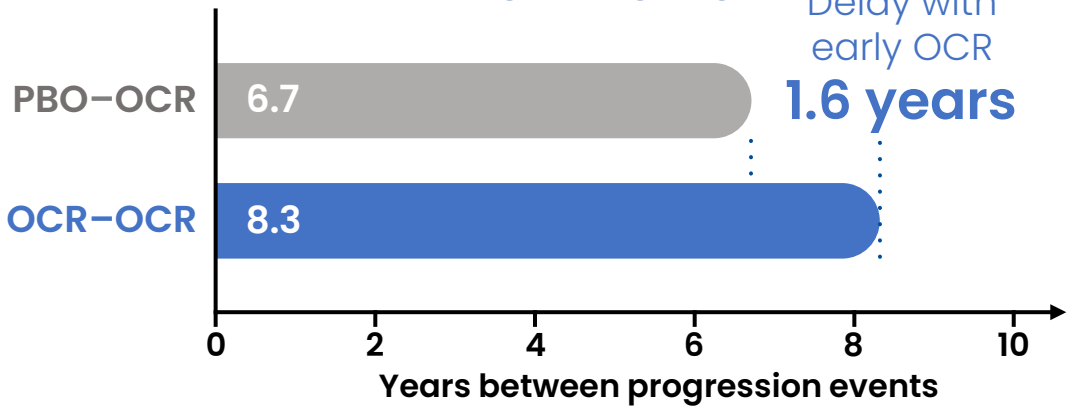
OPERA I/II



10-year annualized event rate

IFN–OCR	OCR–OCR
0.040	0.029

ORATORIO



10-year annualized event rate

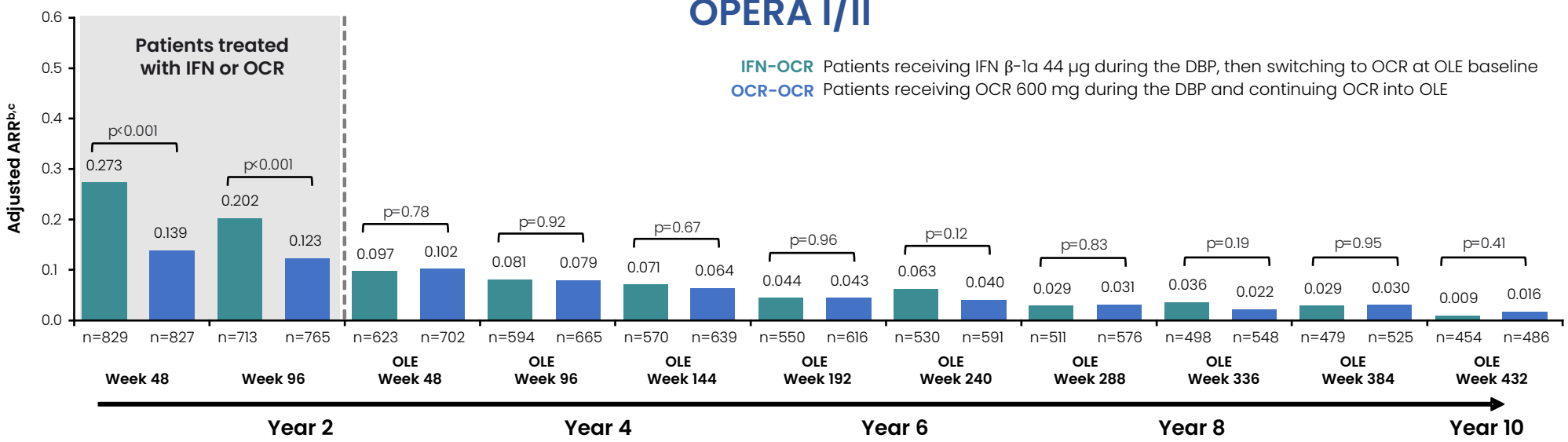
PBO–OCR	OCR–OCR
0.149	0.121

Starting OCR 2 years earlier saves almost 10 years of disease progression in PwRMS and adds almost 2 years of progression event-free lifetime after 10 years[a] in PwPPMS

48W-CDP, 48-week confirmed disability progression; 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.
[a]The median follow-up time in OPERA was 10 years.

Results
OPERA I/II Annualized Protocol Defined Relapse Rate by Year

After 10 years[a] in PwRMS continuously treated with OCR, the ARR (0.016) was equivalent to a relapse every 62.5 years



ARR decreased year-on-year from the pre-switch year to Year 10 in IFN–OCR switchers, and was maintained at low levels in all patients treated with OCR

ARR, annualized relapse rate; DBP, double-blind period; EDSS, Expanded Disability Status Scale; GEE, generalised estimating equation; IFN, interferon; ITT, intention-to-treat; OCR, ocrelizumab; OLE, open-label extension; PwRMS, patients with RMS; ROW, rest of world; RMS, relapsing multiple sclerosis.
[a]The median follow-up time in OPERA was 10 years. [b]The total number of relapses for all patients in the treatment group divided by the total patient-years of exposure to that treatment. [c]DBP year 1 and DBP year 2 data include the intention-to-treat population (number of patients available); for years 4-10 (OLE years 1-8), data include the OLE ITT population (number of patients available). Clinical cutoff date: November 25, 2022. GEE Poisson Model ITT population. Adjusted ARRs from Week 48 to OLE Week 432 (Year 10). Adjusted by randomised treatment, study, baseline EDSS (<4.0 vs ≥4.0), geographical region (US vs ROW), year and treatment-by-year interaction.

Results

Over 10 Years of Continuous OCR Treatment, the Overall Safety Profile Remained Consistent

Adverse event Rate per 100 PY (95% CI)	OPERA (RMS)			ORATORIO (PPMS)		
	CTP[a] (Jul 2015)		CTP + OLE[b] (Dec 2022)	CTP[a] (Jul 2015)		CTP + OLE[b] (Dec 2022)
	IFN β-1a	OCR	OCR	Placebo	OCR	OCR
Total no. of patients	826	825	1,448	239	486	644
Total PY	1,399	1,448	10,814	729	1,606	4,702
Any AEs	296 (287–305)	290 (281–299)	194 (191–196)	259 (247–271)	252 (244–260)	222 (218–227)
AEs leading to withdrawal	3.9 (3.0–5.1)	2.4 (1.6–3.3)	1.3 (1.1–1.5)	1.1 (0.5–2.2)	1.2 (0.8–1.9)	1.0 (0.8–1.4)
Serious AEs	6.3 (5.1–7.8)	5.4 (4.3–6.7)	6.3 (5.8–6.8)	12.1 (9.7–14.9)	10.2 (8.7–11.8)	12.6 (11.6–13.7)
Infections and infestations	67.8 (63.5–72.2)	84.5 (79.9–89.4)	66.0 (64.5–67.6)	72.5 (66.5–79.0)	70.8 (66.8–75.0)	70.0 (67.6–72.4)
Serious infections[c]	1.8 (1.2–2.6)	0.8 (0.4–1.5)	1.8 (1.5–2.0)	3.0 (1.9–4.6)	2.7 (2.0–3.7)	4.4 (3.8–5.0)
IRRs	7.9 (6.5–9.5)	34.9 (31.9–38.1)	11.2 (10.5–11.8)	20.3 (17.2–23.8)	31.0 (28.3–33.9)	16.5 (15.4–17.7)
Malignancies[d,e]	0.1 (0.0–0.5)	0.3 (0.1–0.7)	0.4 (0.3–0.6)	0.3 (0.0–1.0)	0.9 (0.5–1.5)	1.0 (0.7–1.3)
Deaths	0.1 (0.0–0.5)	0.1 (0.0–0.4)	0.1 (0.0–0.2)	0.4 (0.1–1.2)	0.3 (0.1–0.6)	0.5 (0.3–0.7)

In the pooled OPERA I/II and ORATORIO population, the cumulative standardised incidence rates of all malignancies and female breast cancer remained within the range reported in real-world registries.[1,2]

Rate per 100 PY (95% CI)	OCR	SEER	SIR
Malignancies[f]	0.24[h] (0.17–0.37)	0.37 (0.37–0.37)	0.82 (0.61–1.07)
Female breast cancer[g]	0.14 (0.08–0.31)	0.15 (0.15–0.15)	1.05 (0.63–1.63)

Rate per 100 PY (95% CI)	OCR	Danish	SIR
Malignancies[f]	0.24[h] (0.17–0.37)	0.36 (0.32–0.42)	0.83 (0.62–1.09)
Female breast cancer[g]	0.14 (0.08–0.31)	0.19 (0.15–0.23)	0.83 (0.50–1.29)

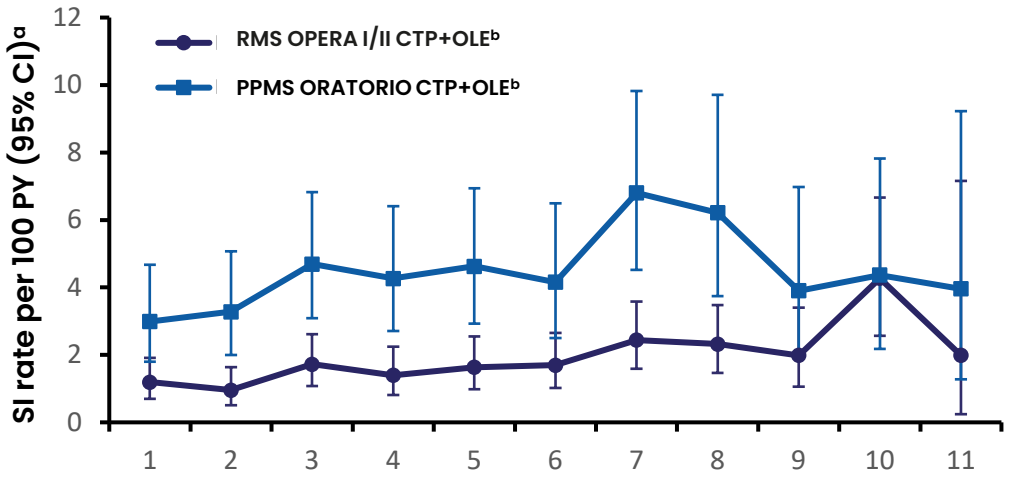
Cumulative AE and SAE incidence rates remained consistent with the rates observed during the CTP
Withdrawal due to AEs was infrequent and did not increase over time

AE, adverse event; CI, confidence interval; CTP, controlled treatment period; IFN, interferon; ECP, extended controlled period; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; NMSC, nonmelanoma skin cancer; OCR, ocrelizumab; OLE, open-label extension; PPMS, primary progressive multiple sclerosis; PY, patient years; RMS, relapsing multiple sclerosis; SEER, Surveillance, Epidemiology and End Results; SIR, standardised incidence ratio; SOC, System Organ Class. COVID-19 related AEs were excluded from this analysis, but patients continued to contribute to the incidence of all other AEs (see Supplementary Material for COVID-19 analysis). AEs were classified according to MedDRA versions 18.0, 18.1, 22.1 and 24.1. Multiple occurrences of the same AE in one patient are counted multiple times, except for malignancies. [a]Data as of April–July 2015; [b]Includes patients who received any dose of OCR during the CTP and associated ECP and/or OLE periods of the Phase III studies, including patients originally randomised to comparator (IFN β-1a or placebo) who switched to open-label OCR treatment (data as of March 2023) [c]Serious infections are defined using AEs falling into the MedDRA SOC 'Infections and Infestations', and using 'Is the event nonserious or serious?' from the AE case report form; [d]Malignancies are identified using AEs falling into the standard MedDRA query 'Malignant tumours (narrow)'; [e]For malignancies, incidence rates are reported and exposure in PY was calculated from first treatment to onset of first malignancy. [f]The standardised incidence rates were reported to allow comparison with the SEER database and the Danish MS Registry, using the direct standardisation method. Standardised incidence rates were derived by applying age–sex specific rates to the 2,000 USA standard population, with restriction to the age range of the MS clinical trials (15–59 years); [g]The SIR, calculated as observed/expected number of events, was determined for all malignancies (excluding NMSC) and female breast cancer, using the SEER database and the Danish MS Registry as reference populations; [h]It excludes NMSC for comparison with SEER rates, as NMSC is not reported in SEER.

1. National Institutes of Health (NIH). Surveillance, Epidemiology and End Results Program. Available from: https://seer.cancer.gov. Accessed 4 April 2024; 2. Nørgaard M, et al. *Mult Scler Relat Disord* 2019;28:81–85.

Results
Serious Infections

SI Rates[a] Remained Stable with Non-Significant Year-on-Year Variation and Within the Range Reported in Real-World Registries[1,2]



Exposure (PY)	1,422 635	1,359 610	1,277 575	1.216 539	1,162 497	1,120 457	1,065 412	991 306	655 282	445 252	101 127
Event rate (per 100 PY)	1.2 3.0	1.0 3.3	1.7 4.7	1.4 4.3	1.6 4.6	1.7 4.2	2.4 6.8	2.3 6.2	2.0 3.9	4.3 4.4	2.0 4.0
Number of SIs	17 19	13 20	22 27	17 23	19 23	19 19	26 28	23 19	13 11	19 11	2 5
N	1,448 644	1,396 626	1,317 594	1,242 558	1,190 518	1,142 477	1,100 434	1,036 366	843 295	522 268	263 224

In the OPERA RMS and ORATORIO PPMS populations, UTI and pneumonia were the most commonly reported SIs; this is consistent with incidence rates and patterns observed in real-world studies[2–4]

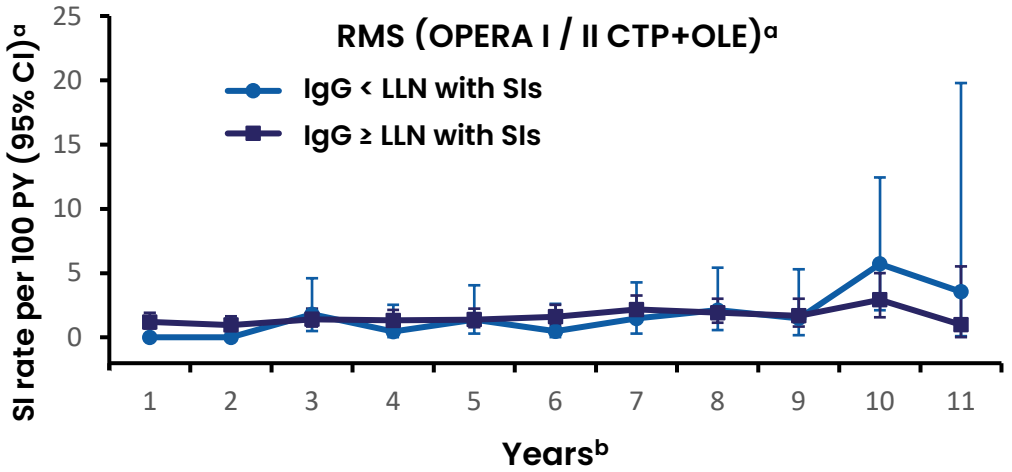
CI, confidence interval; CTP, controlled-treatment period; OCR, ocrelizumab; OLE, open-label extension; PMS, progressive multiple sclerosis; PY, patient years; RMS, relapsing multiple sclerosis; SI, serious infection; UTI, urinary tract infection.
[a]COVID-19 related AEs were excluded from this analysis, but patients continued to contribute to the incidence of all other AEs. [b]Includes patients who received any dose of OCR during the CTP and associated OLE periods of the Phase III OPERA I/II and ORATORIO studies [c]The exposure in PY during Years 8–11 is limited for meaningful interpretation.

1. Wijnands JMA, *et al. J Neurol Neurosurg Psychiatry* 2018;89:1050–1056; 2. Knapp R, *et al. Mult Scler Relat Disord* 2022;68:104245; 3. Wijnands JMA, *et al. Mult Scler* 2017;23:1506–1516; 4. Persson *et al. Mult Scler Relat Disord* 2020;41(1):101982.

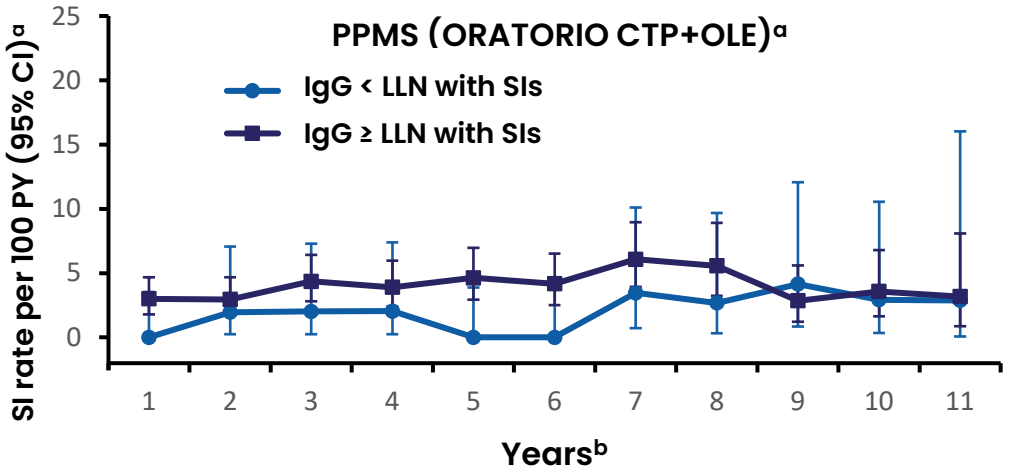
Results
Serious Infections and IgG Levels

During the 10-year OCR treatment period, IgG levels remained above the lower limit of normal for >80% of patients: RMS (1223/1448, 84.5%) PPMS (539/644, 83.7%)

In Both RMS and PPMS Populations, Longer Exposure to OCR Did Not Lead to an Increased Risk of SIs Regardless of IgG Status (Normal Levels or Levels Below the LLN)[a]



Exposure (PY) IgG<LLN	225	224	223	220	216	212	204	188	137	105	28
Exposure (PY) IgG≥LLN	1,420	1,357	1,275	1,214	1,160	1,118	1,063	990	655	445	101
IgG<LLN number of SIs	0	0	4	1	3	1	3	4	2	6	1
IgG≥LLN number of SIs	17	13	18	16	16	18	23	19	11	13	1



Exposure (PY) IgG<LLN	104	102	99	98	95	93	87	75	73	68	35
Exposure (PY) IgG≥LLN	634	609	574	538	496	456	412	306	282	252	127
IgG<LLN number of SIs	0	2	2	2	0	0	3	2	3	2	1
IgG≥LLN number of SIs	19	18	25	21	23	19	25	17	8	9	4

The type, severity, latency and duration of SIs observed during episodes of IgG<LLN were consistent with the overall SIs observed in patients treated with OCR

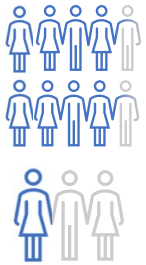
CI, confidence interval; CTP, controlled-treatment period; IgG, immunoglobulin G; LLN, lower limit of normal; OCR, ocrelizumab; OLE, open-label extension; PPMS, primary progressive multiple sclerosis; PY, patient years; RMS, relapsing multiple sclerosis; SI, serious infection.

[a]COVID-19 related AEs were excluded from this analysis, but patients continued to contribute to the incidence of all other AEs. [b]The exposure in PY during Years 8–11 is limited for meaningful interpretation.

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**

Earlier treatment with ocrelizumab (2 years) **extended the progression-free event window by almost 10 years** in PwRMS, compared with a lower efficacy DMT

The low **annualized relapse rate** was maintained

Over a **10-year** follow-up period in clinical trials, **ocrelizumab** continues to exhibit a **stable** and **favourable safety profile**

No new or **unexpected safety findings** were identified, and treatment with ocrelizumab was **well tolerated**

Rates of SIs remained **low** and **stable** over time in both RMS and PMS populations **irrespective of IgG levels**

AEs leading to treatment **withdrawal** remained **infrequent** and were not driven by serious infections

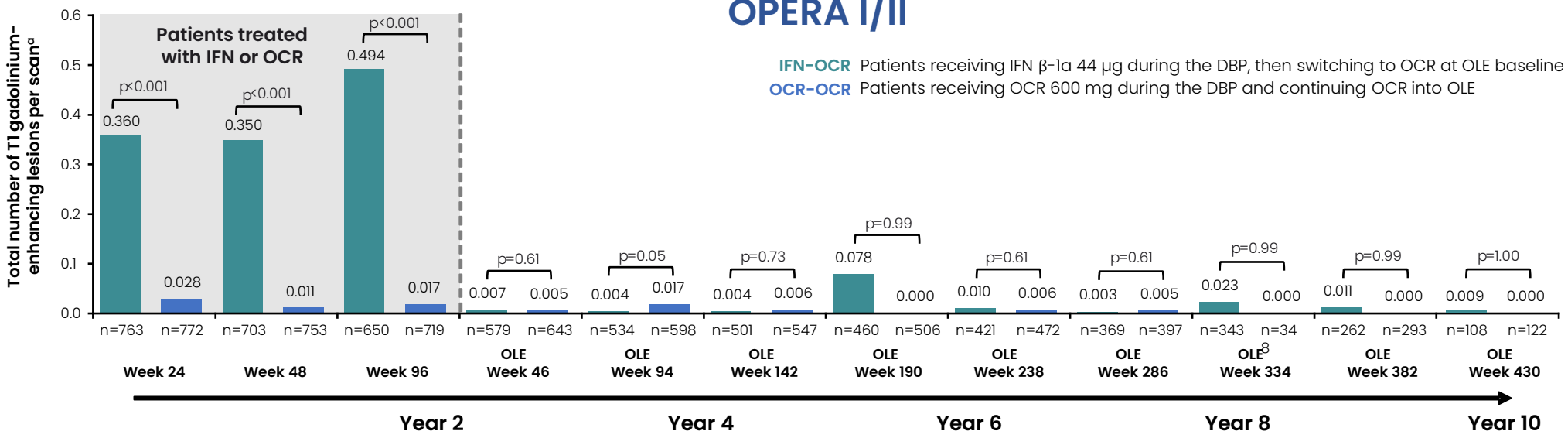
The notable impact of a decade of ocrelizumab treatment in reducing disability accumulation reinforces the role of early treatment in preserving patient function across the MS spectrum

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; PwPPMS, patients with primary progressive multiple sclerosis; PwRMS, patients with relapsing multiple sclerosis.

Supplementary Materials

Results
OPERA I/II MRI – Mean T1 Gd+ lesions

In PwRMS treated early and continuously with OCR, consistent and persistent effects were evident on MRI measures of inflammatory disease activity i.e., the near complete suppression of subclinical disease activity, as measured by MRI

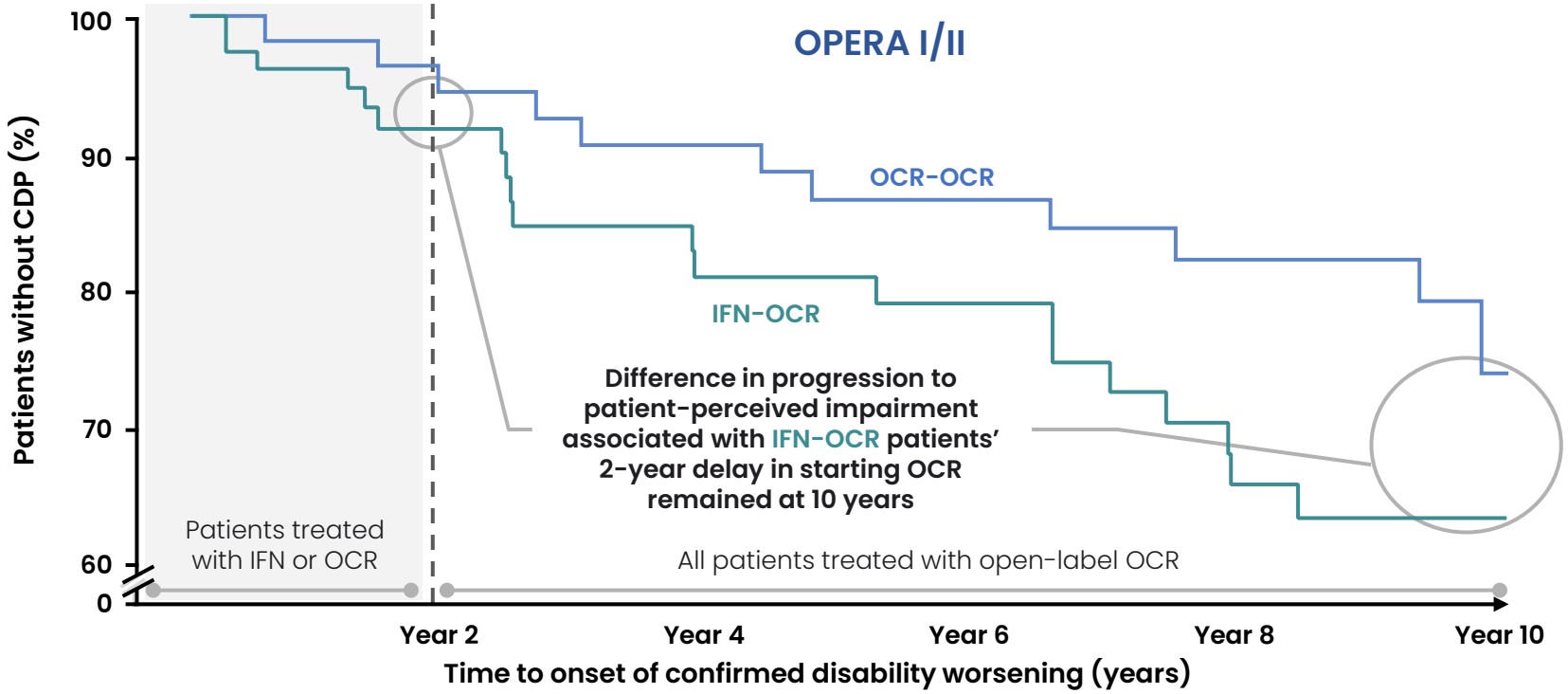


Over 10 years, early and continuous OCR treatment led to an almost complete suppression of MRI activity in PwRMS; these benefits were also seen in patients once they switched from IFN-β-1a to OCR

DBP, double blind period; Gd+, gadolinium-enhancing; OCR, ocrelizumab; OLE, open-label extension; PwRMS, patients with RMS; RMS, relapsing multiple sclerosis.[a]The number of new T1 Gd-enhancing lesions and the number of new or enlarging T2 lesions were analyzed using a negative binomial model; in previously reported analysis[1] of lesion outcomes during the DBP, results were adjusted for study, T1 Gd-enhancing lesion status (present or not) or baseline T2 lesion volume, baseline EDSS score (≤4.0 vs >4.0), and geographic region (United States vs rest of the world). However, as patients had no new T1 Gd-enhancing lesions/new or enlarging T2 lesions at several time points, it was impossible to fit a statistical model, and unadjusted rates were adopted for the OLE instead. Baseline number of T1 Gd-enhancing lesions, mean (unadjusted) T1 Gd+ lesion rate: IFN-OCR, 1.908; OCR-OCR, 1.753.

1. Hauser SL, *et al. N Engl J Med* 2017;376:221–234.

Results
Time-to-onset of confirmed EDSS ≥2



HR (95% CI) = 0.52 (0.24, 1.10) p=0.08. Risk reduction: 48%

No. patients at risk:

IFN beta-1a/OCR 600mg	82	78	76	71	69	66	63	63	63	53	52	48	48	47	46	46	46	44	44	44	44	44	44	41	41	40	40	38	38	34	34	32	32	31	31	29	28	26	26	26	26	22	20	12
OCR 600mg/OCR 600mg	61	58	57	55	55	53	53	51	51	49	49	49	48	47	47	47	47	46	46	45	45	44	44	44	44	43	43	43	43	38	38	37	37	35	35	34	34	31	31	29	29	25	18	13

82.0%

of OCR-OCR patients[a] had no patient-perceived impairment at 10 years

(EDSS ≥2 from baseline ≤1)

Over 10 years, there was a 48% reduction in the risk of having patient-perceived impairment (from a baseline EDSS ≤1) in those who initiated OCR earlier vs delayed treatment

CDP, confirmed disability progression; CI, confidence interval; DBP, double-blind period; EDSS, Expanded Disability Status Scale; HR, hazard ratio; IFN, interferon β-1a; NNT, number needed to treat; OCR, ocrelizumab; OLE, open-label extension; ROW, rest of world.

[a]Impairment perceived by the patient from baseline EDSS score ≤1. HRs were estimated by Cox regression stratified by study, geographic region (US vs ROW) and baseline EDSS (<3.0 vs ≥3.0). Comparison of the survival distributions used the log-rank test.