Preliminary Results of the OPERA I and OPERA II Open-Label Extension Study

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Mark Cascione has received research support from Novartis, Genentech, Biogen, and Genzyme. He has also participated in speakers bureaus for Acorda, Sanofi-Genzyme, Genentech, EMD Serono, Novartis, and Biogen.

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Stephen L Hauser serves on the board of trustees for Neurona, and on scientific advisory boards for Annexon, Symbiotix, and Bionure. He has also received travel reimbursement and writing assistance from F. Hoffmann-La Roche Ltd for CD20-related meetings and presentations.

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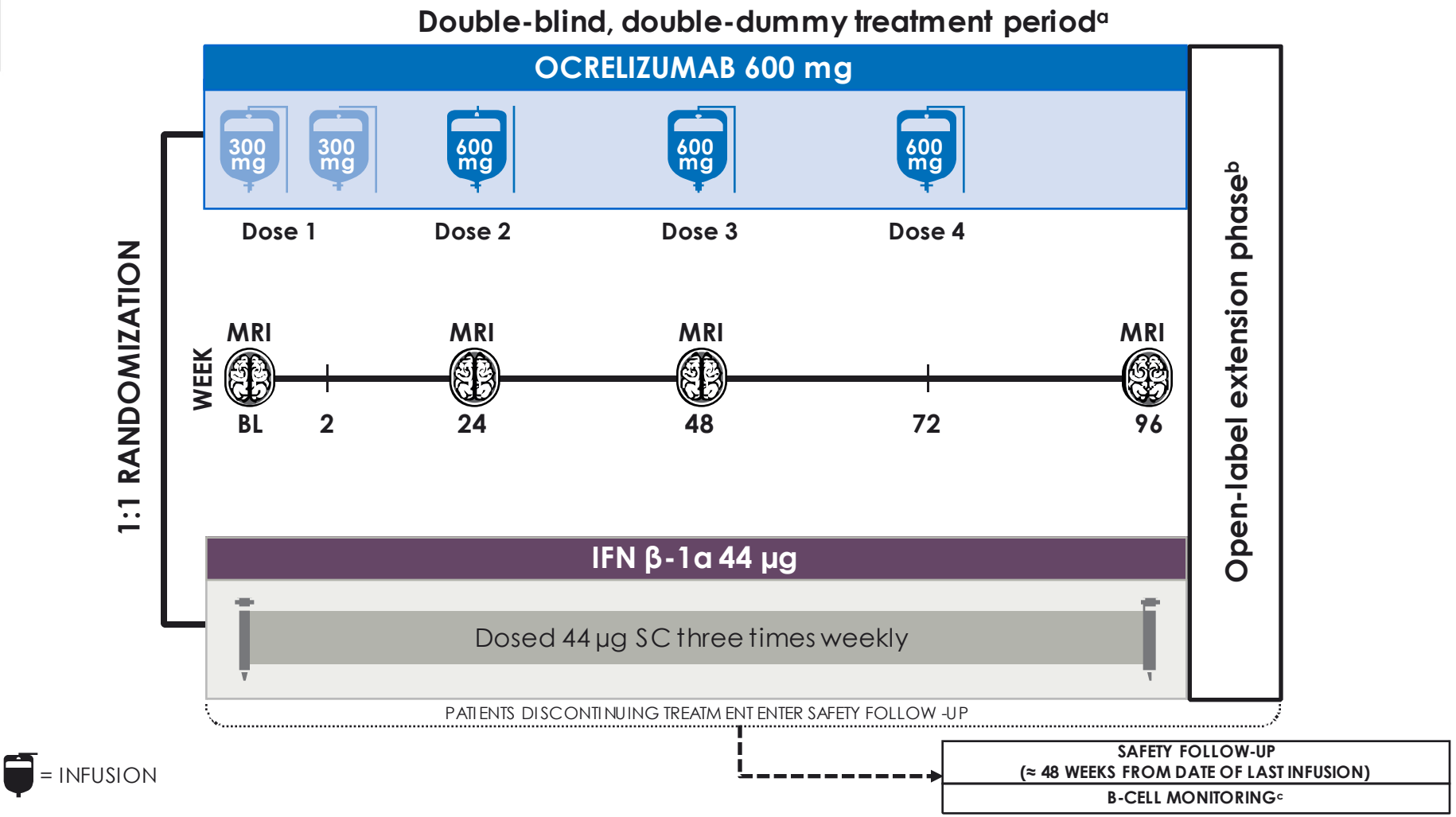
Objective

- To provide a preliminary update on the clinical and MRI metrics of disease activity, including ARR, T1 Gd-enhancing lesions, and new/enlarging T2 lesions from the first year of the open-label extension (OLE) phase of the OPERA studies

ARR, annualized relapse rate; Gd, gadolinium.

OPERA I and OPERA II trials
Study design[1]



[a]Patients in the ocrelizumab group received placebo injections three times weekly, while patients in the IFNβ -1a group received placebo infusions at Days 1 and 15 and Weeks 24, 48 and 72; [b]OLE to provide ongoing safety, tolerability and efficacy data; OLE phase was not mandatory; [c]Continued monitoring occurs if B cells are not repleted.

BL, baseline; EDSS, Expanded Disability Status Scale; IFN, interferon; IV, intravenous; OLE, open-label extension; RMS, relapsing multiple sclerosis; SC, subcutaneous.

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

Pooled OPERA I and OPERA II
Baseline demographics and disease characteristics

	Double-blind treatment period	
	IFN β-1a 44 µg (n=829)	OCR 600 mg (n=827)
Age, yrs, mean (SD)	37.2 (9.2)	37.1 (9.2)
Female, n (%)	552 (66.6)	541 (65.4)
Time since MS symptom onset, yrs, mean (SD)	6.5 (6.1)	6.7 (6.2)
Time since MS diagnosis, yrs, mean (SD)	3.9 (4.9)	4.0 (4.9)
Relapses in previous 12 months, mean (SD)	1.3 (0.7)	1.3 (0.7)
Previously untreated, n (%)[a]	605 (73.0)	604 (73.0)
EDSS, mean (SD)	2.8 (1.3)	2.8 (1.3)
Number of T1 Gd-enhancing lesions, mean (SD)	1.9 (5.0)	1.8 (4.6)
Number of T2 lesions, mean (SD)	51.0 (37.8)	50.1 (38.8)

ITT

[a]Untreated with disease-modifying therapy in 2 years prior to study entry.

EDSS, Expanded Disability Status Scale; Gd, gadolinium; IFN, interferon; ITT, intention to treat; MS, multiple sclerosis; N/E, new or enlarging; OCR, ocrelizumab.

Ocrelizumab was more effective than interferon β-1a in the Phase III OPERA I and OPERA II trials in relapsing MS

Pooled OPERA studies: results from the 96-week double-blind treatment period[a]

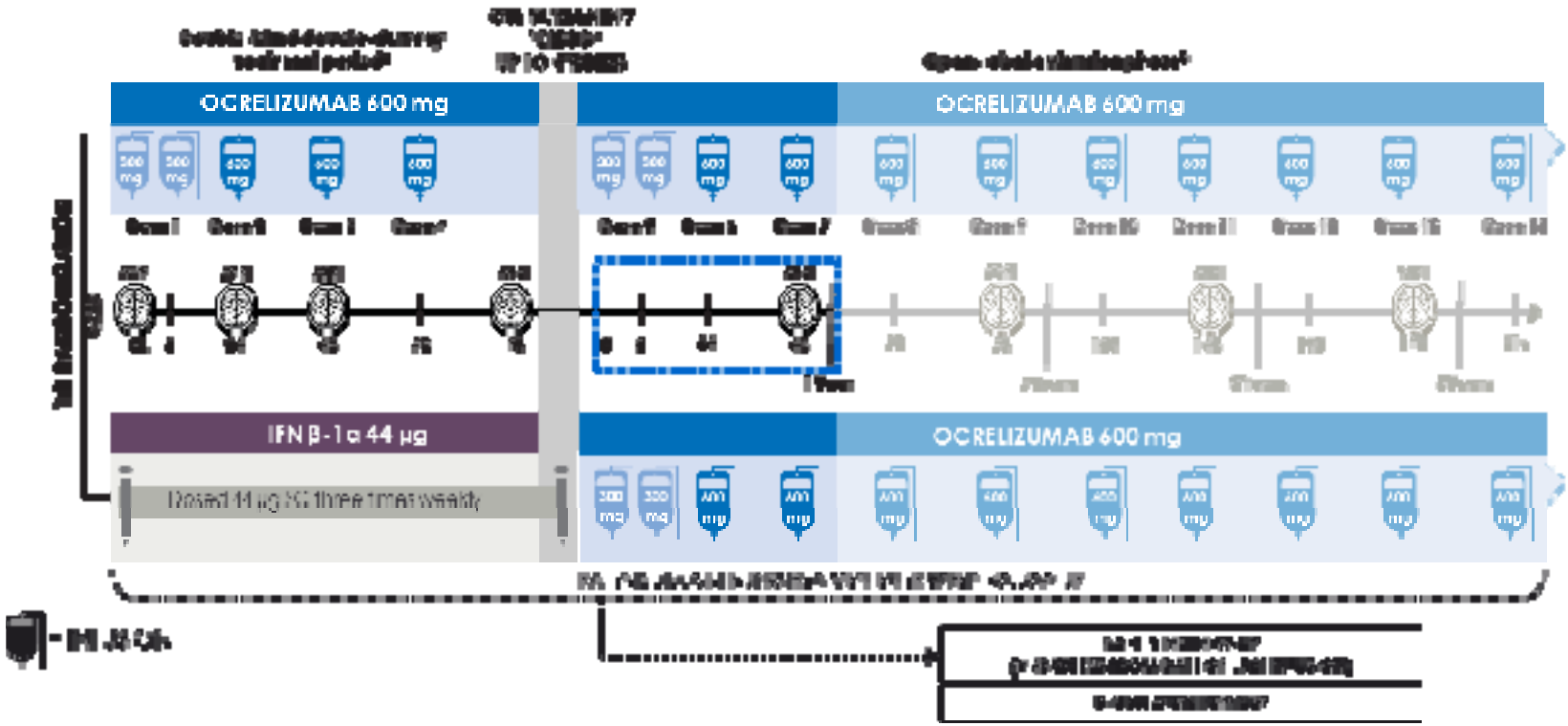
	IFN β-1a 44 µg (n=829)	OCR 600 mg (n=827)
ARR at Week 96 (95% CI)	0.29 (0.25–0.34)	0.16 (0.13–0.19)
Relative reduction (p-value)		**47% (<0.001)**
Mean no. of T1 Gd-enhancing lesions per MRI scan by Week 96 (95% CI)	0.36 (0.28–0.45)	0.02 (0.01–0.03)
Relative reduction (p-value)		**94% (<0.001)**
Mean no. of new/enlarging T2 hyperintense lesions per MRI scan by Week 96 (95% CI)	1.68 (1.44–1.97)	0.33 (0.28–0.39)
Relative reduction (p-value)		**80% (<0.001)**

In the pooled OPERA I and OPERA II studies, ocrelizumab was more effective than IFN β-1a on clinical and imaging metrics of disease activity in patients with relapsing MS[1]

[a]The pooled OPERA outcomes shown here pertain to the analyses in this presentation and are not ordered per the hierarchical statistical analysis plan.
ARR, annualized relapse rate; Gd, gadolinium; IFN, interferon; MS, multiple sclerosis.

1. Hauser SL, *et al. AAN* 2016;Platform presentation S49.003.

OPERA I and OPERA II open-label extension phase
Study design



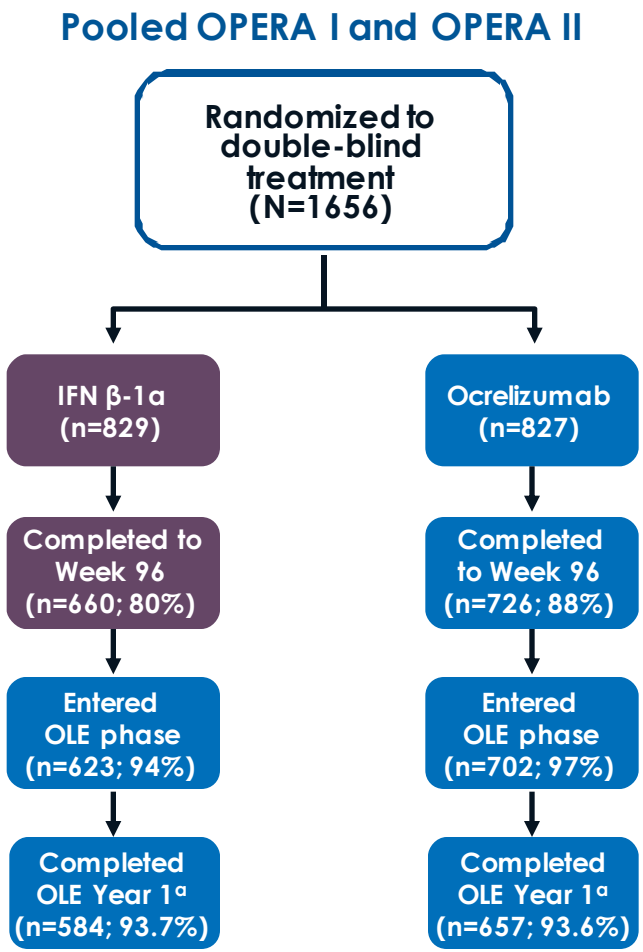
- In the open-label extension phase, the first 600-mg dose of ocrelizumab was administered as two 300-mg infusions given two weeks apart
  - Patients received methylprednisolone prior to each infusion
  - Optional prophylactic treatment with an analgesic/antipyretic and IV or oral antihistaminic 30 to 60 minutes before an infusion was offered to all patients

[a]Patients in the ocrelizumab group received placebo injections three times weekly, while patients in the IFN β-1a group received placebo infusions at Days 1 and 15 and Weeks 24, 48 and 72; [b]OLE was not mandatory. Patients who declined to participate in the OLE entered safety follow-up; [c]Continued monitoring occurs if B cells are not repleted.

IFN, interferon; IV, intravenous; OLE, open-label extension; SC, subcutaneous.

Adapted from Kuhelj R, *et al. EAN* 2016;Poster P11192.

OPERA I and OPERA II open-label extension phase
Patient disposition



[a]Clinical cut off date, January 20, 2016.
IFN, interferon; OLE, open-label extension.

Pooled OPERA I and OPERA II open-label extension phase
Patient demographics and disease characteristics

Pooled OPERA studies: results from the 96-week double-blind treatment period[a]

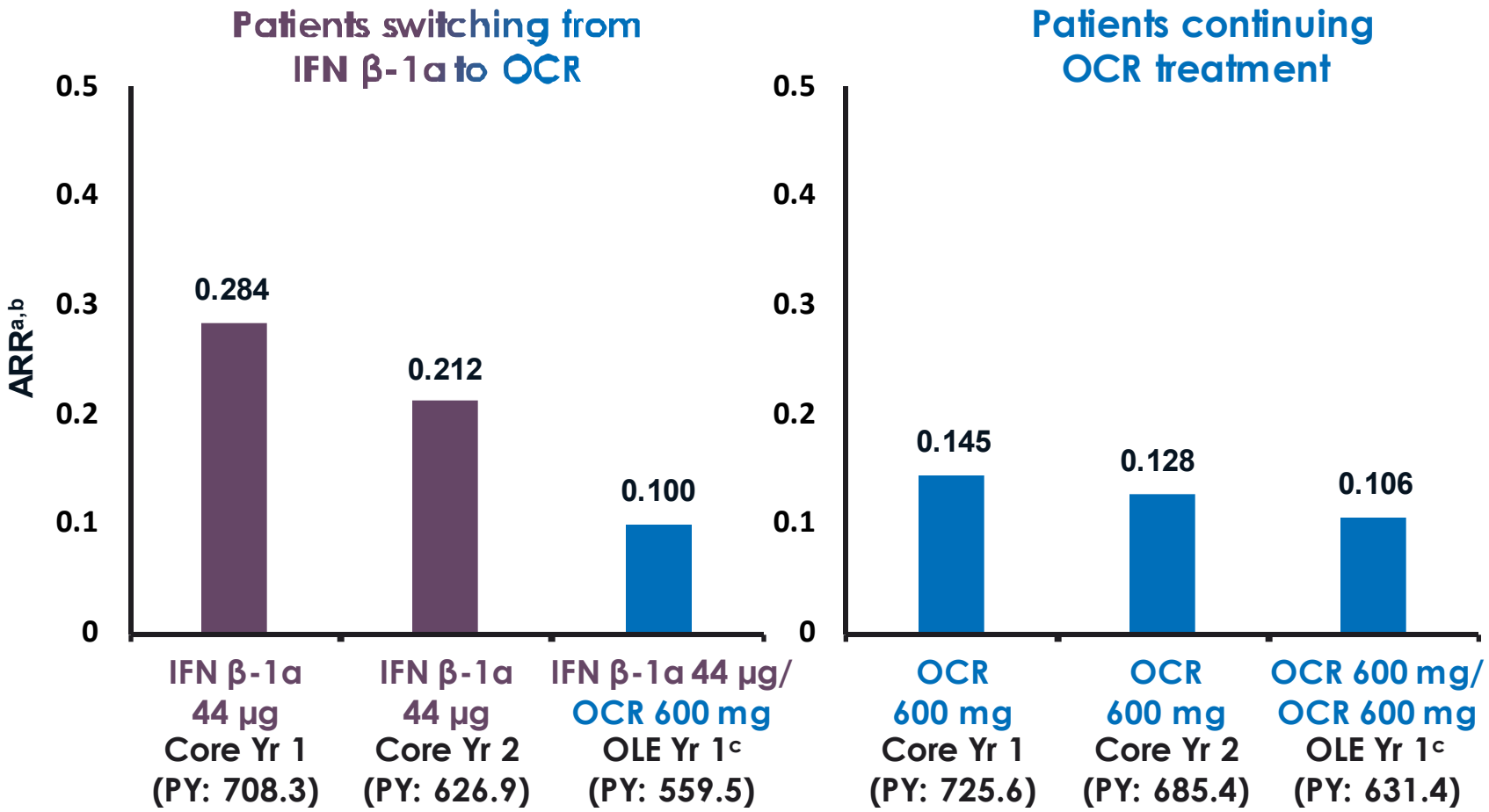
	IFN β-1a 44 µg/ OCR 600 mg (n=623)	OCR 600 mg/ OCR 600 mg (n=702)
Age, yrs, mean (SD)	39.3 (9.2)	39.2 (9.1)
Female, n (%)	408 (65.5)	454 (64.7)
Time since MS symptom onset, yrs, mean (SD)	8.3 (6.1)	8.5 (6.1)
Time since MS diagnosis, yrs, mean (SD)	5.7 (4.8)	5.8 (4.9)
EDSS, mean (SD)	2.7 (1.5)	2.6 (1.3)

The demographics and disease characteristics of the patients who entered the open-label extension phase of the OPERA studies were well balanced

[a]Demographics and disease characteristics at Week 96 of the double-blind treatment period are considered baseline for the OLE phase.
EDSS, Expanded Disability Status Scale; IFN, interferon; MS, multiple sclerosis; OCR, ocrelizumab; OLE, open-label extension.

Pooled OPERA I and OPERA II

Preliminary data: ARR in core study Years 1 and 2 and OLE Year 1

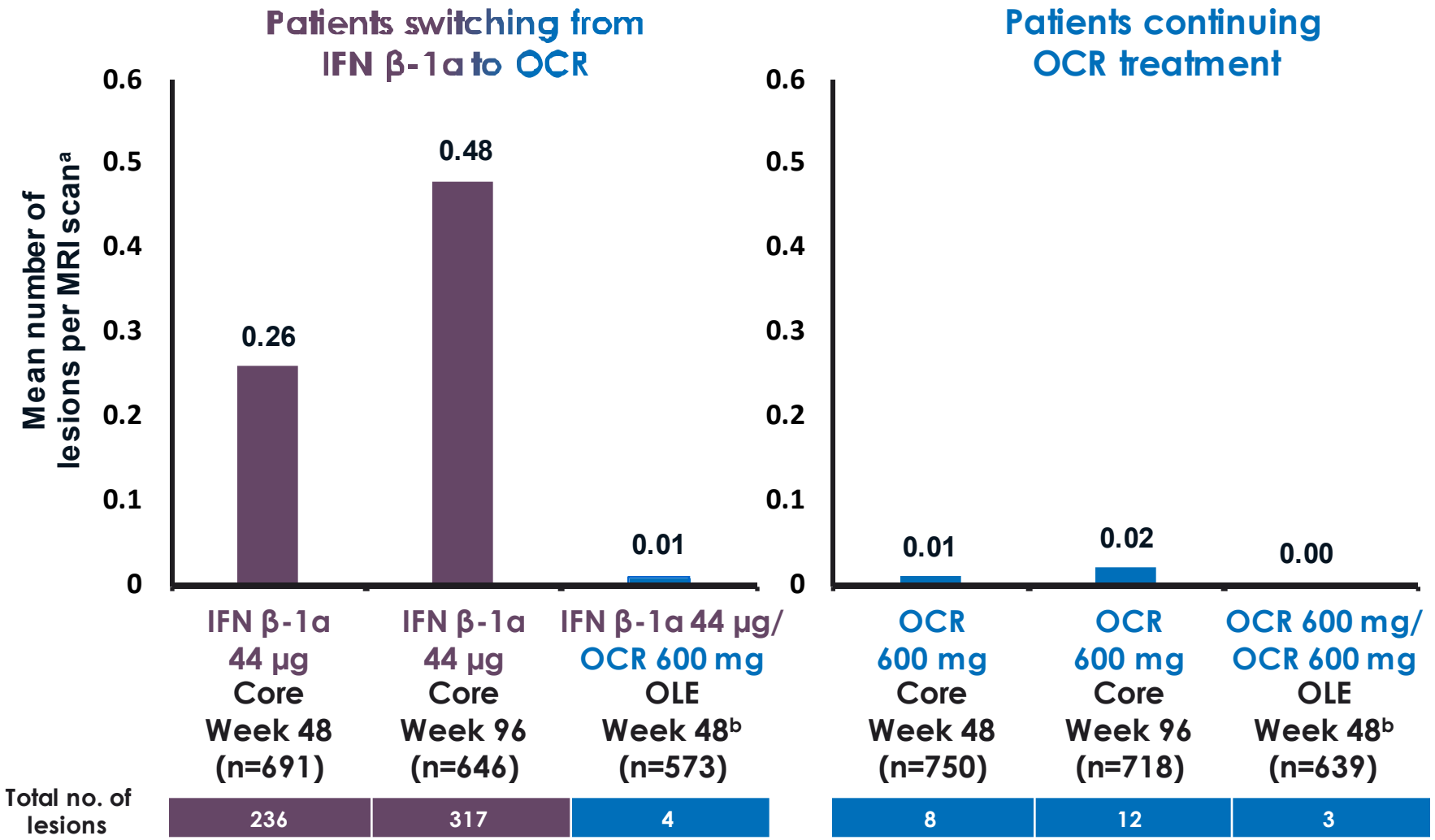


[a]The total number of relapses for all patients in the treatment group divided by the total patient-years of exposure to that treatment; [b]Core Yr 1 and Core Yr 2 data include the ITT population and show the adjusted ARR calculated by negative binomial regression and adjusted for baseline EDSS score (<4.0 vs ≥4.0), and geographic region (US vs ROW). OLE Yr 1 data include the OLE ITT population and show the unadjusted ARR; [c]Clinical cutoff date, January 20, 2016.

ARR, annualized relapse rate; EDSS, Expanded Disability Status Scale; IFN, interferon; ITT, intention to treat; OCR, ocrelizumab; OLE, open-label extension; PY: patient years; ROW, rest of the world.

Pooled OPERA I and OPERA II

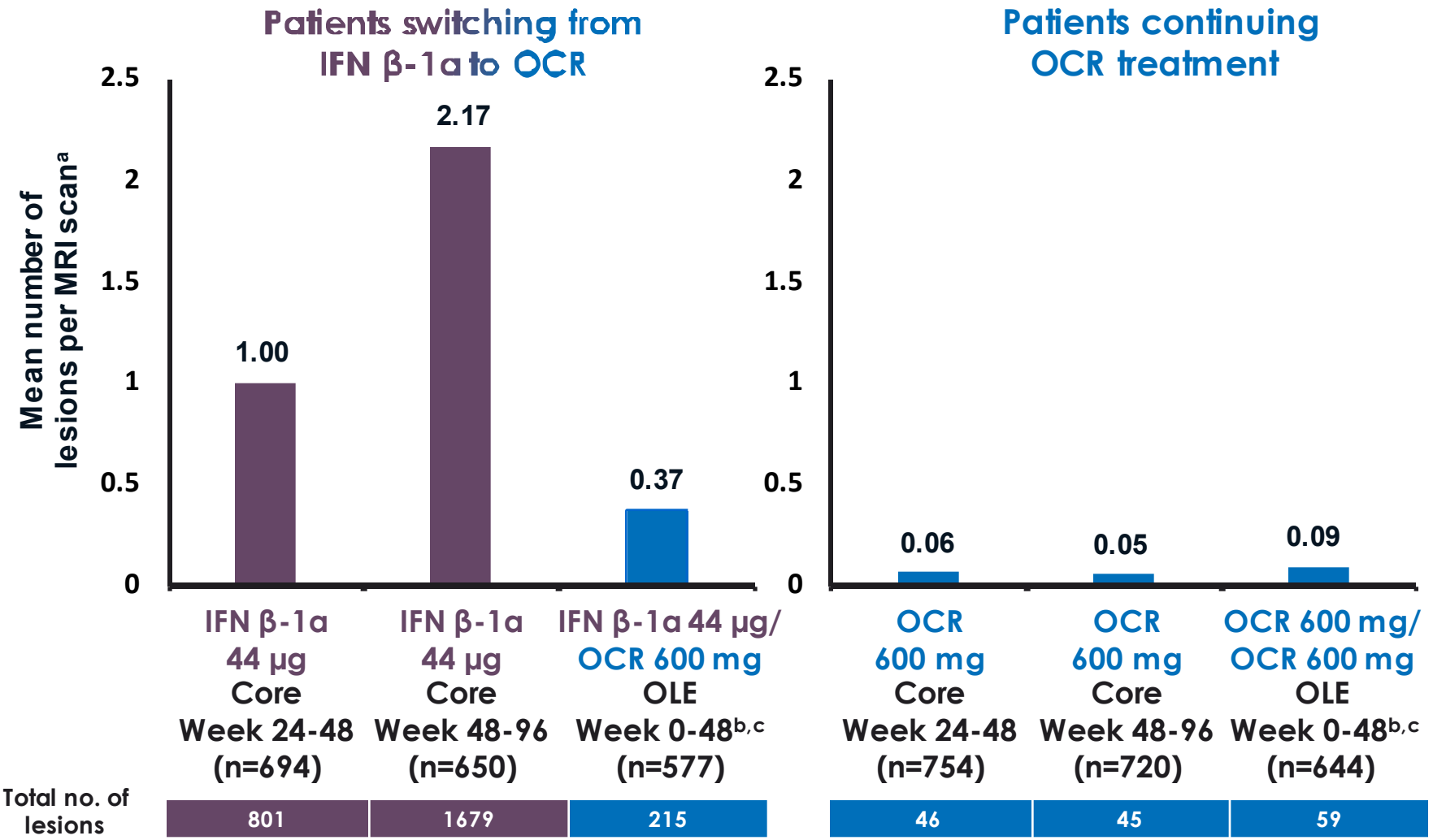
Preliminary data: number of T1 Gd-enhancing lesions in core study at Weeks 48 and 96 and OLE Week 48



[a]Core Week 48 and Core Week 96 data include the ITT population; OLE Week 48 data include the OLE ITT population; [b]Clinical cut off date, January 20, 2016.
Gd, gadolinium; IFN, interferon; ITT, intention to treat; OCR, ocrelizumab; OLE, open-label extension.

Pooled OPERA I and OPERA II

Preliminary data: number of N/E T2 lesions in core study at Weeks 24-48 and 48-96 and OLE Weeks 0-48



[a]Core Week 24-48 and Core Week 48-96 data include the ITT population; OLE Week 0-48 data include the OLE ITT population; [b]Due to lack of Week 24 assessment, OLE Week 0-48 data include initial residual T2 accumulation; [c]Clinical cutoff date, January 20, 2016.

IFN, interferon; ITT, intention to treat; N/E, new or enlarging; OCR, ocrelizumab; OLE, open-label extension.

Conclusions

- More than 94% of patients who completed the double-blind treatment period of the OPERA studies entered the OLE phase and reached the 48-week OLE milestone
- Patients who switched from interferon beta-1a to ocrelizumab in the OLE phase experienced reductions in ARR, T1 Gd-enhancing lesions and new/enlarging T2 lesions
  - These outcomes are consistent with patients who received ocrelizumab in the double-blind treatment period of the OPERA studies
- The beneficial effects of ocrelizumab during the double-blind treatment period persisted in patients who continued on ocrelizumab during the OLE phase, demonstrating the sustained benefit of ocrelizumab treatment
- Additional data from the OPERA I and OPERA II OLE phase are forthcoming, including metrics of disease progression

ARR, annualized relapse rate; Gd, gadolinium; OLE, open-label extension.

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