Supplementary Online Content

Kappos L, Wolinsky JS, Giovannoni G, et al. Contribution of relapse-independent progression vs relapse-associated worsening to overall confirmed disability accumulation in typical relapsing multiple sclerosis in a pooled analysis of 2 randomized clinical trials. *JAMA Neurol*. Published online June 8, 2020. doi:10.1001/jamaneurol.2020.1568

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Relative Contribution of EDSS, T25FW, and 9HPT to Composite RAW and Composite PIRA Events

12-week Composite RAW	**IFN β-1a (N = 829)**	**OCR (N = 827)**	**Combined IFN β-1a/OCR**	**Event as a proportion of patients with composite event (%)**
Patients with event, n (%)	45 (5.4)	24 (2.9)	69 (4.2)	100
Increase in EDSS only, n (%)	30 (3.6)	11 (1.3)	41 (2.5)	59.4
Increase in T25FW only, n (%)	8 (1.0)	7 (0.8)	15 (0.9)	21.7
Increase in 9HPT only, n (%)	2 (0.2)	1 (0.1)	3 (0.2)	4.3
Increase in combination of the above, n (%)	5 (0.6)[a]	5 (0.6)[b]	10 (0.6)	14.5
Increase in all three components, n (%)	0	0	0	0
12-week Composite PIRA	**IFN β-1a (N = 829)**	**OCR (N = 827)**	**Combined IFN β-1a/OCR**	**Event as a proportion of patients with composite event (%)**
Patients with event (%)	174 (21.0)	147 (17.8)	321 (19.4)	100
Increase in EDSS (%)	49 (5.9)	45 (5.4)	94 (5.7)	29.3
Increase in T25FW (%)	79 (9.5)	69 (8.3)	148 (8.9)	46.1
Increase in 9HPT (%)	16 (1.9)	11 (1.3)	27 (1.6)	8.4
Increase in combination of the above (%)	28 (3.4)[c]	21 (2.5)[d]	49 (3.0)	15.3
Increase in all three components	2 (0.2)	1 (0.1)	3 (0.2)	0.9
24-week Composite RAW	**IFN β-1a (N = 829)**	**OCR (N = 827)**	**Combined IFN β-1a/OCR**	**Event as a proportion of patients with composite event (%)**
Patients with event (%)	36 (4.3)	16 (1.9)	52 (3.1)	100
Increase in EDSS (%)	29 (3.5)	7 (0.8)	36 (2.2)	69.2
Increase in T25FW (%)	5 (0.6)	4 (0.5)	9 (0.5)	17.3
Increase in 9HPT (%)	1 (0.1)	1 (0.1)	2 (0.1)	3.8
Increase in combination of the above (%)	1 (0.1)[e]	4 (0.5)[f]	5 (0.3)	9.6
Increase in all three components	0	0	0	0
24-week Composite PIRA	**IFN β-1a (N = 829)**	**OCR (N = 827)**	**Combined IFN β-1a/OCR**	**Event as a proportion of patients with composite event (%)**
Patients with event (%)	136 (16.4)	115 (13.9)	251 (15.2)	100
Increase in EDSS (%)	35 (4.2)	39 (4.7)	74 (4.5)	29.5
Increase in T25FW (%)	65 (7.8)	57 (6.9)	122 (7.4)	48.6
Increase in 9HPT (%)	16 (1.9)	10 (1.2)	26 (1.6)	10.4
Increase in combination of the above (%)[d]	18 (2.2)[g]	9 (1.1)[h]	27 (1.6)	10.8
Increase in all three components	2 (0.2)	0	2 (0.1)	0.8

Abbreviations: 9HPT, 9-Hole Peg Test; EDSS, Expanded Disability Status Scale; IFN, interferon; OCR, ocrelizumab; PIRA, progression independent of relapse activity; RAW, relapse-associated worsening; T25FW, Timed 25-Foot Walk.

Combinations of components: [a] EDSS+T25FW=4, T25FW+9HPT=1; [b] EDSS+T25FW=3, EDSS+9HPT=2; [c] EDSS+T25FW=19, EDSS+9HPT=2; T25FW+9HPT=7; [d] EDSS+T25FW=11, EDSS+9HPT=1; T25FW+9HPT=9;
[e] EDSS+T25FW=1; [f] EDSS+T25FW=3, EDSS+9HPT=1; [g] EDSS+T25FW=14, EDSS+9HPT=1; T25FW+9HPT=3;
[h] EDSS+T25FW=6, T25FW+9HPT=3.

eTable 2. Prognostic Baseline Covariates for Clinical Endpoints in the Pooled Population of the OPERA I and OPERA II Trials (N = 1656)

Covariate	Reference value	Time to protocol-defined relapse (PDR)			Time to composite confirmed disability accumulation (CDA) (12 weeks)			Time to composite progress independent of relapse activity (PIRA) (12 weeks)			Time to composite relapse-associated worsening (RAW) (12 weeks)		
		HR	*P* Value	FDR	HR	*P* Value	FDR	HR	*P* Value	FDR	HR	*P* Value	FDR
Sex	M	1.16	.279	0.511	0.74	.025	0.096	0.67	.010	0.059	0.75	.352	0.764
Duration since MS symptoms onset (days)	≤1781.50	1.06	.673	0.853	1.56	.001	0.020	1.80	< .001	0.006	0.84	.552	0.901
Baseline EDSS	≤2.50	1.36	.018	0.117	1.48	.004	0.024	1.48	.010	0.059	1.21	.516	0.868
Baseline 9HPT	≤22.22	1.09	.504	0.746	1.47	.006	0.029	1.50	.011	0.059	1.17	.606	0.901
PASAT	≤44.00	0.82	.141	0.349	0.68	.006	0.029	0.69	.022	0.094	0.79	.446	0.790
Baseline MSFCS	≤0.08	0.82	.141	0.349	0.65	.003	0.022	0.62	.004	0.038	0.90	.735	0.941
T2 lesion count	≤41.00	1.07	.589	0.820	1.45	.006	0.031	1.62	.002	0.025	0.98	.959	0.966
T2 lesion volume	≤5.78	1.21	.142	0.349	1.51	.002	0.022	1.51	.008	0.057	2.00	.029	0.661
Non-enhancing T1 lesion volume	≤1.08	1.12	.372	0.644	1.53	.002	0.022	1.56	.004	0.038	1.53	.164	0.764
T1 Gd-enhancing lesion category	0	1.47	.003	0.070	1.02	.863	0.945	0.88	.405	0.645	2.38	.004	0.301
Brain volume	≤1503.53	0.95	.720	0.881	0.66	.002	0.022	0.66	.007	0.054	0.71	.253	0.764
Cortical grey matter volume	≤566.32	1.10	.463	0.726	0.64	.001	0.020	0.57	< .001	0.007	0.95	.868	0.946
Total SF36 score	≤89.49	0.76	.038	0.178	0.69	.008	0.035	0.67	.013	0.062	0.64	.140	0.745
SF36 physical summary score	≤44.99	0.72	.015	0.117	0.67	.003	0.023	0.68	.013	0.062	0.66	.169	0.764
FSS: visual	≤0.00	1.37	.016	0.117	1.37	.018	0.076	1.27	.119	0.272	1.07	.823	0.941
FSS: cerebral	≤1.00	1.37	.016	0.117	1.58	< .001	0.020	1.70	< .001	0.007	1.73	.068	0.670
FSS Pyramidal: Gait spasticity score	≤0.00	1.41	.018	0.117	1.57	.003	0.022	1.80	< .001	0.007	0.92	.830	0.941
FSS Pyramidal: Limb/legs spasticity score	≤0.00	1.52	.002	0.068	1.22	.167	0.372	1.21	.232	0.471	1.14	.678	0.938
FSS Pyramidal: Limb strength Hip flexors	<5.00	0.77	.048	0.202	0.73	.026	0.096	0.74	.053	0.182	0.74	.325	0.764
FSS Cerebellar: Gait ataxia score	≤0.00	1.33	.029	0.156	1.71	< .001	0.005	1.89	< .001	0.002	1.39	.282	0.764

FSS Cerebellar: Limb ataxia score lower extremities	≤0.00	1.18	.214	0.444	1.47	.005	0.028	1.34	.056	0.182	1.75	.062	0.670
FSS Cerebellar: Truncal ataxia score	≤0.00	1.02	.904	0.944	1.44	.047	0.152	1.63	.014	0.063	0.87	.777	0.941
FSS Sensory: Vibration sense score LE	≤0.50	1.44	.005	0.081	0.97	.847	0.945	0.88	.409	0.645	1.16	.614	0.901
FSS Bowel and bladder: Urinary hesitancy/retention score	≤0.00	1.68	< .001	0.038	1.15	.407	0.697	1.08	.706	0.800	1.37	.386	0.764

Abbreviations: 9HPT, 9-Hole Peg Test; CDA, confirmed disability accumulation; EDSS, Expanded Disability Status Scale; FDR, false discovery rate; FSS, Functional System Score; Gd, gadolinium; HR, hazard ratio; MSFCS, Multiple Sclerosis Functional Composite Score; PASAT, paced auditory serial addition test; PDR, protocol-defined relapse; PIRA, progression independent of relapse activity; RAW, relapse-associated worsening; SF36, Medical Outcome Study Short Form-36.

Tables includes only variables with a false discovery rate ≤ 0.1 for at least one clinical endpoint. Prognostic effects are estimated as hazard ratios for the respective clinical events in the non-reference subgroup compared with the reference subgroup; cells are colored according to the nominal significance of the respective baseline covariate – endpoint combination: green: P ≤ .05, yellow: P ≤ .20.

eTable 3. Summary of 24-Week Composite Confirmed Disability Accumulation (CDA), Composite Relapse-Associated Worsening (RAW), and Composite Progression Independent of Relapse Activity PIRA by Component (OPERA I and OPERA II Pooled ITT Population)

24-Week Confirmed	Kaplan–Meier Estimates at Week 96,[a] number of events (%)		HR (95% CI)[b]	*P* Value
	IFN β-1a (n = 829)	OCR (n = 827)		
Composite CDA	**170 (22.7)**	**129 (16.2)**	**0.70 (0.55–0.88)**	**.0019**
EDSS	87 (12.0)	57 (7.6)	0.60 (0.43–0.84)	.0025
T25FW	93 (13.5[c])	75 (10.5[d])	0.74 (0.55–1.01)	.058
9HPT	24 (3.5[d])	16 (2.2[e])	0.64 (0.34–1.20)	.16
Composite RAW	**36 (4.8)**	**16 (2.1)**	**0.41 (0.23–0.75)**	**.0025**
EDSS-RAW	30 (4.0)	11 (1.4)	0.34 (0.17–0.69)	.0015
T25FW-RAW	6 (0.9[c])	7 (1.0[d])	1.09 (0.36–3.24)	.88
9HPT-RAW	1 (0.1[d])	2 (0.3[e])	1.98 (0.18–21.90)	.57
Composite PIRA	**137 (18.3)**	**115 (14.4)**	**0.78 (0.61–1.00)**	**.053**
EDSS-PIRA	52 (6.8)	45 (5.3)	0.80 (0.54–1.20)	.29
T25FW-PIRA	85 (12.3[c])	66 (9.2[d])	0.72 (0.52–0.99)	.044
9HPT-PIRA	22 (3.2[d])	13 (1.8[e])	0.56 (0.28–1.12)	.098
48-week Confirmed	**Kaplan–Meier estimates at Week 96,[a] % [number of events]**		**HR (95% CI)[b]**	***P* Value**
	IFN β-1a (N = 829)	**OCR (N = 827)**		
Composite CDA	**108 (13.9)**	**59 (7.0)**	**0.49 (0.36–0.68)**	**< .0001**
EDSS	64 (8.6)	32 (4.2)	0.45 (0.29–0.69)	.0002
T25FW	48 (6.8[c])	26 (3.6[d])	0.51 (0.32–0.82)	.0050
9HPT	14 (2.0[d])	6 (0.8[e])	0.42 (0.16–1.09)	.065
Composite RAW	**15 (2.0)**	**9 (1.0)**	**0.51 (0.21–1.19)**	**.11**
EDSS-RAW	18 (2.3)	9 (1.1)	0.42 (0.18–0.96)	.034
T25FW-RAW	2 (0.3[c])	2 (0.3[d])	0.96 (0.13–6.81)	.97
9HPT-RAW	1 (0.1[d])	1 (0.1[e])	0.99 (0.06–15.80)	.99
Composite PIRA	**83 (10.9)**	**47 (5.7)**	**0.53 (0.37–0.75)**	**< .0001**
EDSS-PIRA	39 (5.1)	20 (2.2)	0.48 (0.28–0.82)	.0062
T25FW-PIRA	43 (6.1[c])	23 (3.1[d])	0.50 (0.30–0.83)	.0063
9HPT-PIRA	11 (1.5[d])	5 (0.7[e])	0.44 (0.15–1.28)	.12

Abbreviations: 9HPT, 9-Hole Peg Test; CDA, confirmed disability accumulation; EDSS, Expanded Disability Status Scale; HR, hazard ratio; IFN, interferon; OCR, ocrelizumab; PIRA, progression independent of relapse activity; RAW, relapse-associated worsening; T25FW, Timed 25-Foot Walk.

[a] Kaplan–Meier proportion of patients with confirmed accumulation at Week 96.

[b] Based on Cox proportional hazards model adjusted by baseline EDSS (<4.0 vs ≥4.0), region (US vs rest of world), and study ID.

Patients included in analysis: [c] n = 770; [d] n = 775; [e] n = 773.

eTable 4. Sensitivity Analyses of Composite Progression Independent of Relapse Activity (PIRA)

	Re-baseline can be < original baseline (ITT)[a]		IID ≥ 12 weeks after onset of relapse (ITT)[b]		Re-baseline ≥60 days after onset of last relapse (ITT)[c]		No relapse during the confirmation period (ITT)[d]		Composite CDA in subgroup of patients without on-study relapses		Composite CDA where patients were censored at onset of the first protocol- defined relapse (ITT)		Composite CDA where patients were censored before any NE T2 lesions[e]		Composite CDA where patients were censored before any NE T2 lesions or first relapse, whichever was earlier[e]	
12-week confirmed composite PIRA	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 590)**	**OCR (n = 682)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**
Total number of events	174	147	174	147	173	147	160	139	130	124	160	144	95	106	72	93
Kaplan–Meier estimates at Week 96, %[f]	23.3	18.5	23.3	18.5	23.0	18.5	21.5	17.5	24.8	19.2	25.1	20.1	27.3	20.9	23.0	19.8
HR (95% CI)[g]	0.78 (0.63–0.98)		0.78 (0.63–0.98)		0.79 (0.63–0.98)		0.80 (0.64–1.01)		0.75 (0.59–0.96)		0.77 (0.61–0.96)		0.71 (0.54–0.94)		0.81 (0.59–1.11)	
***P* value**	.029		.029		.035		.062		.024		.023		.018		.19	
	Re-baseline can be < original baseline (ITT)[a]		**IID ≥ 12 weeks after onset of relapse (ITT)[b]**		**Re-baseline ≥60 days after onset of last relapse (ITT)[c]**		**No relapse during the confirmation period (ITT)[d]**		**Composite CDA in subgroup of patients without on-study relapses**		**Composite CDA where patients were censored at onset of the first protocol-defined relapse (ITT)**		**Composite CDA where patients were censored before any NE T2 lesions[e]**		**Composite CDA where patients were censored before any NE T2 lesions or first relapse, whichever was earlier[e]**	
24-week confirmed composite PIRA	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 590)**	**OCR (n = 682)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**	**IFN β-1a (n = 829)**	**OCR (n = 827)**
Total number of events	136	115	136	115	134	115	119	105	98	94	124	113	75	84	56	76
Kaplan–Meier estimates at Week 96, n (%)[f]	18.2	14.4	18.2	14.4	17.8	14.4	16.1	13.1	18.6	14.4	19.4	15.7	21.6	16.4	18.0	16.2
HR (95% CI)[g]	0.79 (0.61–1.01)		0.79 (0.61–1.01)		0.80 (0.62–1.03)		0.82 (0.63–1.07)		0.76 (0.57–1.01)		0.79 (0.61–1.02)		0.73 (0.53–1.00)		0.86 (0.60–1.22)	
***P* value**	.061		.061		.086		.14		.060		.067		.049		.39	

Abbreviations: CDA, confirmed disability accumulation; EDSS, Expanded Disability Status Scale; HR, hazard ratio; IID, initial increase of disability; IFN, interferon; ITT, intention-to-treat; NE, new or enlarging; OCR, ocrelizumab; PIRA, progression independent of relapse activity.

[a] The re-baseline disability assessment herein can be inferior to the original study baseline value

[b] Restricted to events for which the IID did not occur within at least 12 weeks of relapse.

[c] Relapse re-baselining was defined as the first disability (EDSS/T25FW/9HPT) assessment available ≥60 days after onset of each relapse.

[d] No protocol-defined relapse allowed between baseline/re-baseline and IID and between IID and 30 days after IID confirmation time.

[e] If a new T2 lesion was detected, the patient was censored from the last visit before its detection.

[f] Kaplan–Meier proportion of patients with confirmed progression at Week 96.

[g] Based on Cox proportional hazards model adjusted by baseline EDSS (<4.0 vs ≥4.0), region (US vs rest of world), and study ID..

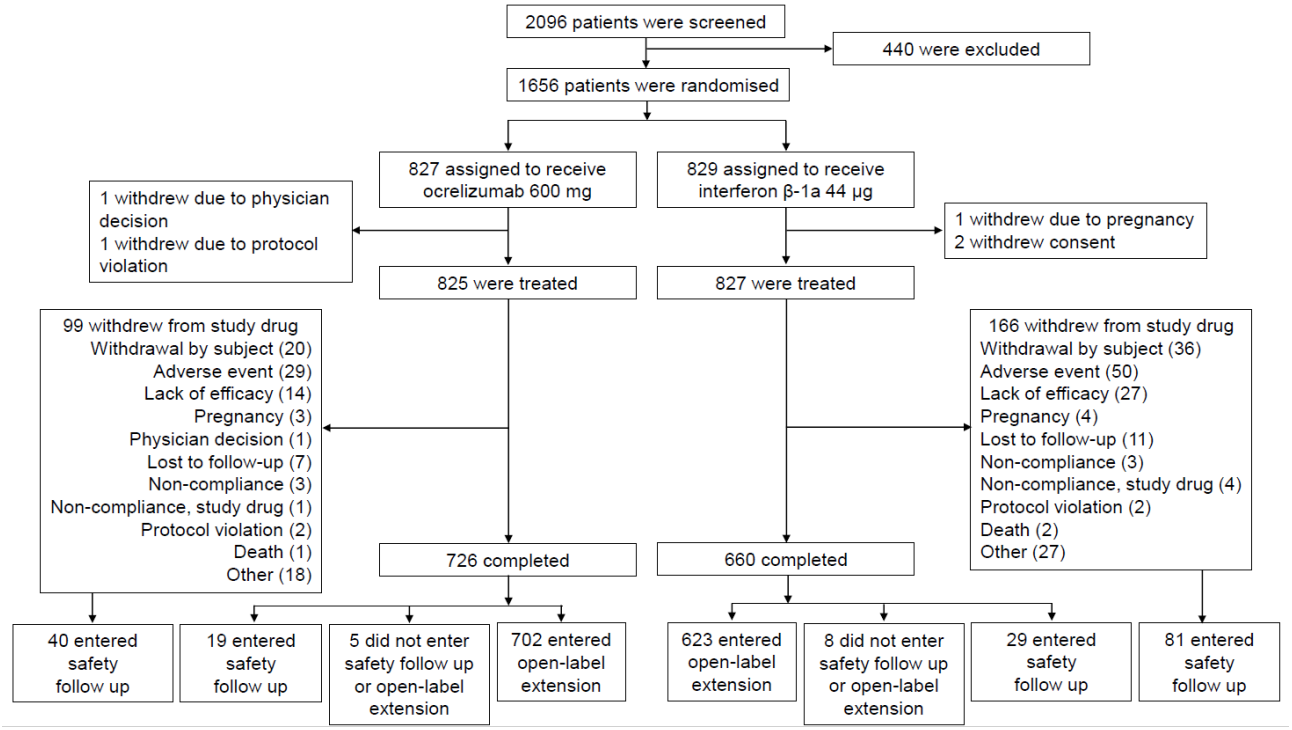
eTable 5. Composite 12- and 24-Week Confirmed Relapse-Associated Worsening (RAW) and Composite Progression Independent of Relapse Activity (PIRA) in Patients at Higher Risk of SPMS[a]

12-week confirmed	**Kaplan–Meier estimates at Week 96,[b] %**		**HR (95% CI)[c]**	***P* Value**
	IFN β-1a (n = 180)	**OCR (n = 175)**		
Composite RAW	**7.9**	**3.8**	**0.46 (0.17–1.24)**	**.12**
EDSS-RAW	6.1	1.9	0.31 (0.08–1.15)	.064
T25FW-RAW	2.8[d]	1.9[e]	0.67 (0.15–2.98)	.59
9HPT-RAW	0.0[d]	1.3[f]	>999.99 (0–NE)	.16
24-week confirmed	**Kaplan–Meier estimates at Week 96,[b] %**		**HR (95% CI)[c]**	***P* Value**
	IFN β-1a (n = 180)	**OCR (n = 175)**		
Composite RAW	**4.7**	**3.1**	**0.67 (0.21–2.13)**	**.50**
EDSS-RAW	4.7	1.3	0.26 (0.05–1.27)	.074
T25FW-RAW	0.0[d]	1.9[e]	>999.99 (0–NE)	.097
9HPT-RAW	0.0[d]	0.6[f]	>999.99 (0–NE)	.31
12-week confirmed	**Kaplan–Meier estimates at Week 96,[b] %**		**HR (95% CI)[c]**	***P* Value**
	IFN β-1a (n = 180)	**OCR (n = 175)**		
Composite PIRA	**28.5**	**18.5**	**0.61 (0.39–0.98)**	**.038**
EDSS-PIRA	7.6	3.0	0.36 (0.13–1.01)	.042
T25FW-PIRA	21.7[d]	14.8[e]	0.65 (0.38–1.11)	.11
9HPT-PIRA	7.8[d]	3.8[f]	0.50 (0.18–1.36)	.17
24-week confirmed	**Kaplan–Meier estimates at Week 96,[b] %**		**HR (95% CI)[c]**	***P* Value**
	IFN β-1a (n = 180)	**OCR (n = 175)**		
Composite PIRA	**25.4**	**16.6**	**0.64 (0.39–1.06)**	**.079**
EDSS-PIRA	6.2	3.0	0.45 (0.15–1.29)	.13
T25FW-PIRA	19.8[d]	13.4[e]	0.67 (0.38–1.18)	.16
9HPT-PIRA	6.4[d]	3.2[f]	0.52 (0.17–1.54)	.23

Abbreviations: 9HPT, 9-Hole Peg Test; EDSS, Expanded Disability Status Scale; HR, hazard ratio; IFN, interferon; NE, not evaluable; OCR, ocrelizumab; PIRA, progression independent of relapse activity; RAW, relapse-associated worsening; SPMS, secondary progressive multiple sclerosis; T25FW, Timed 25-Foot Walk.

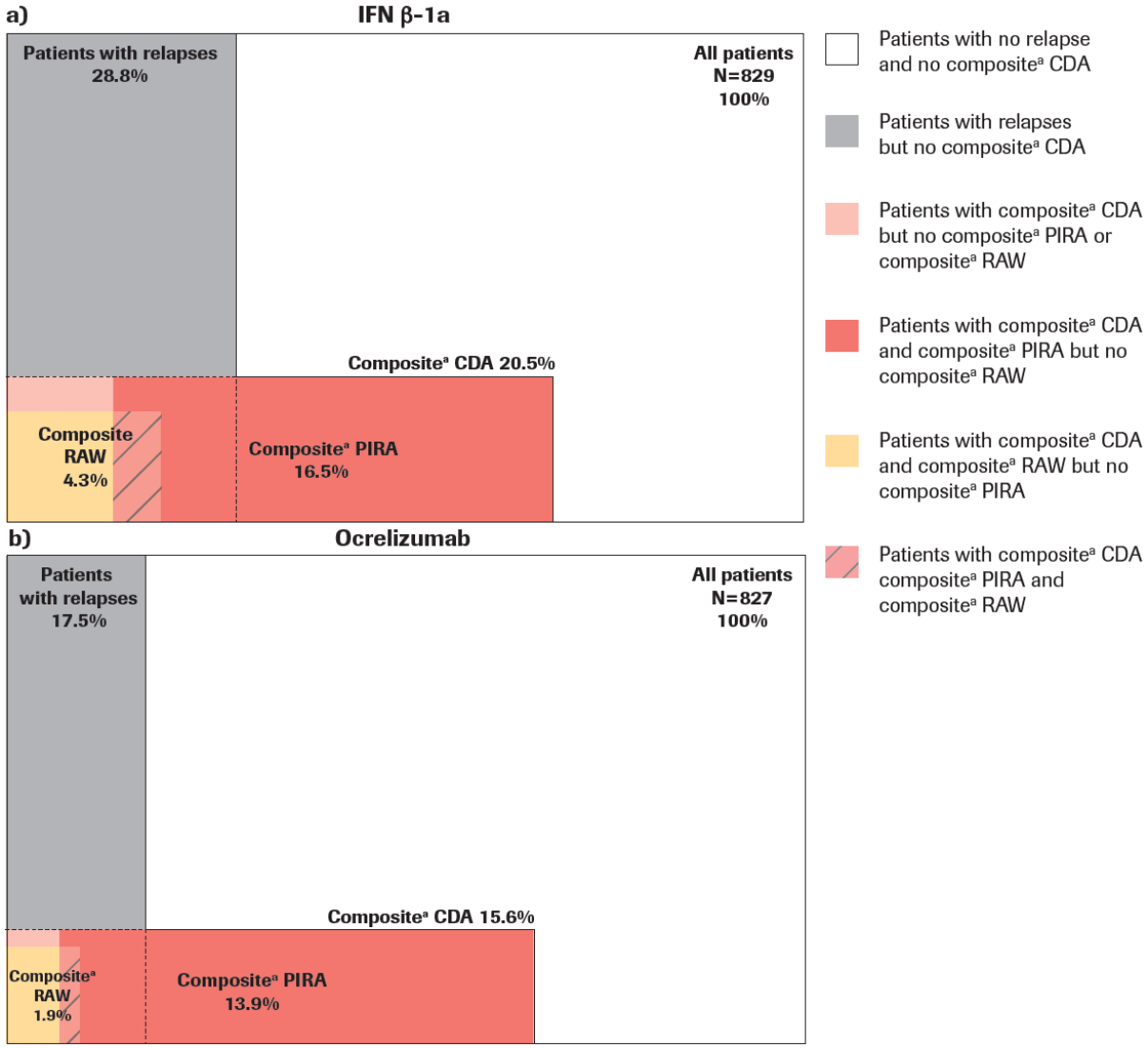
[a] Defined by baseline EDSS ≥4.0 and pyramidal Kurtzke Functional System Score ≥2[11];
[b] Kaplan–Meier proportion of patients with confirmed progression at Week 96;
[c] Based on Cox proportional hazards model adjusted by baseline EDSS (<4.0 vs ≥4.0), region (US vs rest of world), and study ID; Patients included in analysis: [d] n = 163; [e] n = 167; [f] n = 165.

eFigure 1. Patient disposition: Pooled OPERA I and OPERA II Studies



The intent-to-treat population consisted of all randomized patients, including those who prematurely withdrew from the study for any reason and for whom an assessment was not performed for whatever reason; in addition, patients who received an incorrect therapy from that which was intended were summarized according to their randomized treatment. Four patients in total (1 patient in each arm of the two trials, OPERA I and OPERA II) withdrew from study drug due to protocol violation.

eFigure 2. Proportions of patients with all respective combinations for 24-week composite Confirmed Disability Accumulation (CDA), composite Relapse-Associated Worsening (RAW), and composite Progress Independent of Relapse Activity (PIRA) (OPERA I and OPERA II pooled ITT population)



Surface-proportional Venn diagrams for patients receiving A) IFN β-1a and B) ocrelizumab.

Abbreviations: CDA, confirmed disability accumulation; IFN, interferon; PIRA, progression independent of relapse activity; RAW, relapse-associated worsening.

[a]As measured by an increase in EDSS score (≥1.0 if baseline EDSS ≤5.5, or ≥0.5 if baseline EDSS >5.5) or ≥20% increase in T25FW or ≥20% increase in 9HPT.

eMethods. Potential prognostic factor analysis

A univariate analysis of the prognostic effect of all baseline disease and demographic characteristics on clinical outcomes (Supplementary Table XX) was performed in the pooled OPERA I/II population (N = 1656). In the absence of a placebo group in this study, the prognostic effect was estimated based on the ability of the respective baseline covariate to predict the time to the first clinical event across treatment arms, while adjusting for potential covariate–treatment interactions. All patient baseline data (patient demographics, disease history, as well as clinical and imaging-based disease status) collected in the OPERA studies were included in the analysis as potential prognostic factors (total of 72 factors).

All randomized patients were included in the analysis; treatment assignment was based on the actual treatment received. For continuous or ordinal variables, patients were dichotomized at the population median. The prognostic effect of a covariate was estimated from the respective main effect in the Cox model; P values are based on Wald statistics. The false discovery rate (FDR) for the multiple comparisons within each endpoint was controlled with the Benjamini–Hochberg procedure, with an FDR of ≤10% defined as the significance threshold for selection of potential prognostic factors.

List of all patient baseline data (patient demographics, disease history as well as clinical and imaging-based disease status) collected in the OPERA studies and included in the analysis as potential prognostic factors of clinical outcome (Supplementary Table XX). All covariates were treated as continuous except prior MS DMT, sex, T1 Gd-enhancing lesions category, and region that were nominal.

- Age
- Sex
- Weight
- BMI
- Duration since MS symptom onset (days)
- Duration since diagnosis (days)
- Number of relapses in the past 2 years
- Number of relapses in the past year
- Duration since previous relapse (days)
- Prior MS DMT in the last 2 years (y/n)
- Region (US/ROW)
- EDSS
- 9HPT
- T25W
- PASAT score
- MSFC score
- T2 lesion count
- T2 lesion volume
- Non–enhancing T1 lesion volume
- T1 Gd-enhancing lesion count
- T1 Gd enhancing lesion category (y/n)
- Brain volume
- Cortical grey matter volume
- White matter volume
- Modified Fatigue Impact Scale (MFIS) Physical score
- Modified Fatigue Impact Scale (MFIS) Psychosocial score
- Modified Fatigue Impact Scale (MFIS) Cognitive core
- SF-36 Total Score
- SF-36 Mental Summary Score
- SF-36 Physical Summary Score

EDSS Neurostatus components:

- FSS Ambulation
- FSS Visual
- FSS Pyramidal
- FSS Sensory

- FSS Bowel & Bladder
- FSS Cerebellar
- FSS Brainstem
- FSS Cerebral
- FSS cerebral – Decrease in mentation score
- FSS brainstem – Dysphagia score
- FSS brainstem – Dysarthria score
- FSS brainstem – Trigeminal damage score
- FSS brainstem – Extra-ocular movements impairment score
- FSS brainstem – Nystagmus score
- FSS pyramidal – Limb strength Deltoid score
- FSS pyramidal – Limb strength Triceps
- FSS pyramidal – Limb strength Biceps
- FSS pyramidal – Limb strength Wrist/finger flexors
- FSS pyramidal – Limb strength Wrist/finger extensors
- FSS pyramidal – Limb strength Hip flexors
- FSS pyramidal – Limb strength Knee flexors
- FSS pyramidal – Limb strength Knee extensors
- FSS pyramidal – Limb strength Dorsiflexion (feet/toes)
- FSS pyramidal – Limb strength Plantar flexion (feet/toes)
- FSS pyramidal – Gait spasticity score
- FSS pyramidal – Limb/legs spasticity score
- FSS pyramidal – Limb/arms spasticity score
- FSS cerebellar – Gait ataxia score
- FSS cerebellar – Truncal ataxia score
- FSS cerebellar – Limb ataxia score LE
- FSS cerebellar – Limb ataxia score UE
- FSS cerebellar – Romberg Test score
- FSS sensory – Superficial sensation score LE
- FSS sensory – Superficial sensation score UE
- FSS sensory – Position sense score UE
- FSS sensory – Position sense score LE
- FSS sensory – Vibration sense score LE
- FSS sensory – Vibration sense score UE
- FSS bowel and bladder – Urinary hesitancy/retention score
- FSS bowel and bladder – Urinary urgency/incontinence score
- FSS bowel and bladder – Bowel dysfunction score
- FSS bowel and bladder – Bladder catheterization score