Figure e-1

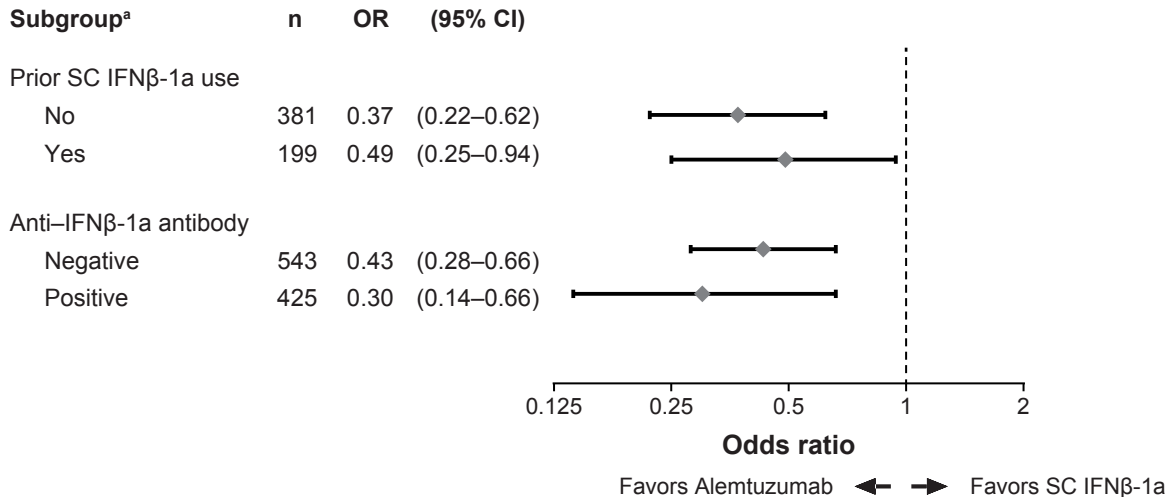| Subgroup[a]	n	OR	(95% CI)
Prior SC IFNβ-1a use			
No	381	0.37	(0.22–0.62)
Yes	199	0.49	(0.25–0.94)
Anti–IFNβ-1a antibody			
Negative	543	0.43	(0.28–0.66)
Positive	425	0.30	(0.14–0.66)

Odds ratio

Favors Alemtuzumab ← → Favors SC IFNβ-1a

Figure e-1 Forest plot of the influence of prior SC IFNβ-1a use and baseline anti–IFNβ-1a antibodies on gadolinium-enhancing lesion activity in CARE-MS II patients.
[a]All patients are stratified for the prior subcutaneous interferon beta-1a (SC IFNβ-1a) use analysis. For the anti–IFNβ-1a antibody analysis, only SC IFNβ-1a–treated patients are stratified by antibody status and compared to all alemtuzumab-treated patients. OR = odds ratio.

Figure e-2

Subgroup[a]	n	OR	(95% CI)
Prior SC IFNβ-1a use			
No	387	0.35	(0.22–0.56)
Yes	203	0.44	(0.23–0.83)
Anti–IFNβ-1a antibody			
Negative	552	0.39	(0.26–0.59)
Positive	433	0.31	(0.13–0.72)

Odds ratio

Favors Alemtuzumab ← → Favors SC IFNβ-1a

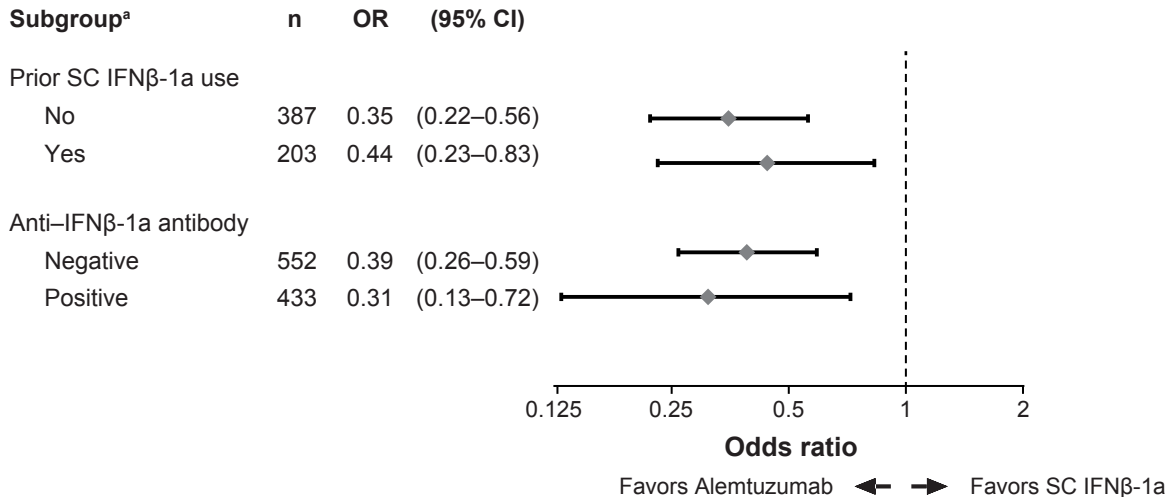**Figure e-2 Forest plot of the influence of prior SC IFNβ-1a use and baseline anti–IFNβ-1a antibodies on new or enlarging T2 lesion activity in CARE-MS II patients.**
[a]All patients are stratified for the prior subcutaneous interferon beta-1a (SC IFNβ-1a) use analysis. For the anti–IFNβ-1a antibody analysis, only SC IFNβ-1a–treated patients are stratified by antibody status and compared to all alemtuzumab-treated patients. OR = odds ratio.

Table e-1 MRI lesion-based outcomes for treatment-naive patients (CARE-MS I) and patients who relapsed on prior therapy (CARE-MS II)

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
New or enlarging T2 hyperintense lesion counts						
Year 0—1						
Patients with data, n	174	370		189	414	
Patients with lesions, %	47.7	40.0		56.1	38.9	
OR (95% CI)		0.70 (0.48–1.02)			0.47 (0.33–0.68)	
Risk reduction, %		30	0.0653		53	<0.0001
Mean (SD)	1.63 (2.68)	1.60 (3.83)	0.4092	4.26 (9.84)	2.16 (7.63)	0.0034
Median (range)	0.0 (0.0–13)	0.0 (0.0–35)		1.0 (0.0–79)	0.0 (0.0–101)	
Years 1—2						
Patients with data, n	175	364		189	404	
Patients with lesions, %	40.6	23.1		52.4	24.3	
OR (95% CI)		0.43 (0.29–0.64)			0.27 (0.19–0.39)	
Risk reduction, %		57	<0.0001		73	<0.0001

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
Mean (SD)	1.61 (3.75)	0.67 (2.62)	0.0006	4.09 (9.07)	1.38 (5.75)	<0.0001
Median (range)	0.0 (0.0–27)	0.0 (0.0–28)		1.0 (0.0–58)	0.0 (0.0–66)	
Years 0—2						
Patients with data, n	172	363		187	403	
Patients with lesions, %	57.6	48.5		67.9	46.2	
OR (95% CI)		0.66 (0.45–0.97)			0.38 (0.26–0.55)	
Risk reduction, %		34	0.0352		62	<0.0001
Mean (SD)	3.15 (5.32)	2.29 (6.05)	0.0288	8.44 (17.5)	3.59 (11.8)	<0.0001
Median (range)	1.0 (0.0–29)	0.0 (0.0–63)		3.0 (0.0–116)	0.0 (0.0–125)	
Gd-enhancing lesion counts						
Year 0—1						
Patients with data, n	176	370		190	412	
Patients with lesions, %	12.5	11.9		23.2	14.1	
OR (95% CI)		0.92 (0.52–1.63)			0.51 (0.32–0.80)	
Risk reduction, %		8	0.7762		49	0.0036
Mean (SD)	0.27 (1.16)	0.41 (1.68)	0.5140	1.04 (4.32)	0.63 (2.80)	0.7663

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
Median (range)	0.0 (0.0–13.0)	0.0 (0.0–18.0)		0.0 (0.0–44.0)	0.0 (0.0–28.0)	
Years 1–2						
Patients with data, n	178	366		190	410	
Patients with lesions %	19.1	7.1		23.2	9.3	
OR (95% CI)		0.30 (0.17–0.53)			0.31 (0.19–0.51)	
Risk reduction, %		70	<0.0001		69	<0.0001
Mean (SD)	0.33 (0.98)	0.16 (0.76)	0.0214	1.11 (4.12)	0.32 (1.46)	0.0087
Median (range)	0.0 (0.0–8.0)	0.0 (0.0–8.0)		0.0 (0.0–44.0)	0.0 (0.0–16.0)	
T2 hyperintense lesion volume						
Year 0–1						
Patients with data, n	174	370		189	414	
Mean change from baseline (SD)	-1.00 (3.50)	-0.69 (2.17)		-0.10 (2.45)	-0.30 (2.60)	
Median change from baseline (range)	-0.2 (-38.5–2.3)	-0.2 (-22.1–8.7)		-0.02 (-15.5–8.1)	-0.07 (-27.3–16.9)	
Mean % change from baseline (SD)	-10.5 (20.8)	-9.0 (19.3)		0.06 (22.3)	-0.82 (22.4)	

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
Median % change from baseline (range)	-8.4 (-72.2–141)	-7.1 (-81.7–166)	0.1636	-0.96 (-82.0–77.9)	-2.22 (-76.9–144)	0.2737
Years 1–2						
Patients with data, n	173	364		189	405	
Mean change from Y1 (SD)	0.20 (1.09)	-0.15 (1.23)		0.15 (1.13)	-0.10 (1.93)	
Median change from Y1 (range)	0.0 (-4.0–7.4)	0.0 (-10.2–7.0)		0.03 (-2.99–6.21)	0.0 (-19.2–5.57)	
Mean % change from Y1 (SD)	2.99 (23.1)	-0.92 (19.0)		3.35 (16.4)	0.46 (18.1)	
Median % change from Y1 (range)	0.0 (-52.1–171)	-1.8 (-83.2–196)	0.0364	0.87 (-58.8–91.8)	0.0 (-55.3–207)	0.0261
Years 0–2						
Patients with data, n	177	364		190	412	
Mean change from baseline (SD)	-0.73 (3.61)	-0.84 (2.31)		0.02 (2.56)	-0.41 (3.25)	
Median change from baseline (range)	-0.2 (-38.8–8.3)	-0.2 (-23.7–6.1)		-0.03 (-15.7–8.06)	-0.04 (-37.3–12.8)	

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
Mean % change from baseline (SD)	-6.7 (32.4)	-10.3 (22.6)		2.41 (26.5)	-1.12 (24.4)	
Median % change from baseline (range)	-6.5 (-74.6–220)	-9.3 (-89.2–143)	0.3080	-1.23 (-82.7–162)	-1.27 (-74.5–155)	0.1371
New T1 hypointense lesions						
Year 0–1						
Patients with data, n	174	370		189	414	
Patients with lesions %	25.3	19.5		28.0	17.1	
OR (95% CI)		0.68 (0.43–1.08)			0.49 (0.32–0.74)	
Risk reduction, %		32	0.1024		51	0.0008
Mean change from baseline (SD)	-0.13 (1.07)	-0.17 (0.98)		0.10 (0.93)	-0.01 (1.21)	
Median volume change from baseline (range)	0.0 (-10.0–3.4)	0.0 (-8.6–3.3)		0.01 (-2.98–6.65)	0.00 (-12.9–7.66)	
Mean % volume change from baseline (SD)	38.9 (423)	-3.36 (117)		18.7 (74.8)	4.08 (62.3)	

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
Median % volume change from baseline (range)	-9.5 (-100–5113)	-15.0 (-100–1503)	0.0464	4.66 (-100–464)	0.00 (-100–429)	0.0300
Years 1—2						
Patients with data, n	176	365		189	404	
Patients with lesions %	18.2	6.8		25.9	7.7	
OR (95% CI)		0.33 (0.19–0.58)			0.21 (0.13–0.36)	
Risk reduction, %		67	0.0001		79	<0.0001
Mean volume change from Y1 (SD)	0.09 (0.55)	0.02 (0.49)		0.09 (1.03)	0.03 (1.01)	
Median volume change from Y1 (range)	0.0 (1.2–3.8)	0.0 (-3.0–3.1)		0.00 (-1.6–13.1)	0.00 (-4.0–9.9)	
Mean % volume change from Y1 (SD)	20.8 (80.2)	20.3 (205)		18.7 (101)	21.4 (111)	
Median % volume change from Y1 (range)	4.1 (-100–472)	0.0 (-100–3146)	0.0387	0.00 (-100–855)	0.00 (-100–1018)	0.7692
Years 0—2						

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
Patients with data, n	177	364		190	412	
Patients with lesions %	31.4	24.0		38.0	19.9	
OR (95% CI)		0.66 (0.43–1.01)			0.37 (0.25–0.55)	
Risk reduction, %		34	0.0545		63	<0.0001
Mean change from baseline (SD)	0.01 (1.27)	-0.20 (1.13)		0.21 (1.51)	0.03 (1.17)	
Median change from baseline (range)	0.0 (-9.7–9.5)	0.0 (-10.1–3.6)		0.01 (-2.97–15.8)	0.00 (7.28–10.0)	
Mean % change from baseline (SD)	68.6 (549)	-4.84 (106)		27.3 (98.7)	17.7 (112)	
Median % change from baseline (range)	-0.1 (-100–6633)	-21.6 (-100–1352)	0.0018	5.08 (-100–518)	0.00 (-100–867)	0.1489
Conversion of Gd-enhancing lesions to T1 hypointense black holes						
Year 0—1[a]						
Patients with data, n	88	170		82	174	
% Conversion from baseline, mean (SD)	19.7 (30.7)	21.2 (32.5)		20.7 (30.8)	18.1 (29.7)	

	Treatment-naive (CARE-MS I)			Relapsed on prior therapy (CARE-MS II)		
	SC IFNβ-1a	Alemtuzumab	*p* value	SC IFNβ-1a	Alemtuzumab	*p* value
% Conversion, median (range)	0.0 (0.0–100)	0.0 (0.0–100)		0.0 (0.0–100)	0.0 (0.0–100)	
OR (95% CI)		0.83 (0.56–1.23)			0.75 (0.50–1.14)	
Risk reduction, %		17	0.3512		25	0.1777
Years 1–2						
Patients with data, n	21	42		38	54	
% Conversion from Y1, mean (SD)	24.9 (40.1)	19.7 (34.0)		27.3 (37.2)	10.7 (25.8)	
% Conversion from Y1, median (range)	0.0 (0.0–100)	0.0 (0.0–100)		0.0 (0.0–100)	0.0 (0.0–100)	
OR (95% CI)		0.55 (0.24–1.22)			0.33 (0.15–0.75)	
Risk reduction, %		45	0.1389		67	0.0078

[a] "Black holes" formed at Year 1 are the result of Gd-enhancing lesions present on baseline scans prior to treatment.

CARE-MS = Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis; CI = confidence interval; Gd = gadolinium; IFNβ-1a = interferon β-1a; OR = odds ratio; SC = subcutaneous; Y = year.