Table e-1. Cumulative Number of New Gadolinium-Enhancing T1 Lesions at Week 12 (PP Population)

Endpoint	Statistic	Placebo[a]	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w	Ofatumumab 60 mg q4w
	n	42	23	22	25	45
Weeks 0–12[b]	Mean rate[c]	1.01	0.37	0.37	0.37	0.37
	Rate ratio (95% CI)	-	0.36 (0.205, 0.638)	0.36 (0.205, 0.638)	0.36 (0.205, 0.638)	0.36 (0.205, 0.638)
Weeks 4–12[b] (post-hoc analysis)	Mean rate[c]	0.85	0.12	0.08	0.08	0.08
	Rate ratio (95% CI)	-	0.14 (0.05, 0.40)	0.10 (0.05, 0.19)	0.09 (0.05, 0.19)	0.09 (0.04, 0.19)

CI, confidence interval; mITT, modified intent-to-treat; MRI, magnetic resonance imaging; PP, per protocol; q4w, every 4 weeks; q12w, every 12 weeks; SD, standard deviation.

Note: The number of patients with an MRI scan showing lesion within the 12 months prior to baseline is shown in Table 1.

[a]Patients randomized to the placebo group received 3 mg of ofatumumab at Week 12; [b]E_{max} model fitted was $E0+E_{max}$*dose/(ED_{50}+dose)+baseline GdE lesion status; [c]rate of the cumulative number of lesions per scan.

Table e-2. Cumulative Volume Analyses of T1 and T2 Lesions at Weeks 12 and 24

Endpoint	Statistic	Pop.	Placebo[a]	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w	Ofatumumab 60 mg q4w
Cumulative Volume (mm^3) of New Gadolinium-Enhancing T1 Lesions at Weeks 12 and 24							
	N	mITT	67	33	30	33	62
Weeks 0–12[b]	Mean rate[d]	mITT	153.14	34.2	75.44	76.69	38.45
	Rate ratio (95% CI)	mITT		0.22 (0.06, 0.84)[h]	0.49 (0.13, 1.86)	0.50 (0.14, 1.78)	0.25 (0.09, 0.71)[g]
Weeks 4–12 (post-hoc analyses)	Mean rate[d]	mITT	120.24	18.54	14.16	3.72	9.43
	Rate ratio (95% CI)	mITT		0.15 (0.02, 1.00)[h]	0.12 (0.02, 0.72)h	0.03 (0.01, 0.18)[h]	0.08 (0.02, 0.34)[e]
Weeks 0–24[c]	Mean rate[d]	mITT	109.58	33.93	44.30	38.22	21.01
	Rate ratio (95% CI)	mITT		0.31 (0.09, 1.02)	0.40 (0.12, 1.41)	0.35 (0.11, 1.15)	0.19 (0.07, 0.51)[e]
Week 4–24 (post-hoc analyses)[c]	Mean rate[d]	mITT	89.43	29.57	10.53	1.84	6.12
	Rate ratio (95% CI)	mITT		0.33 (0.07, 1.54)	0.12 (0.02, 0.57)[g]	0.02 (0.00, 0.10)[e]	0.07 (0.02, 0.24)[e]
Cumulative Volume (mm^3) of Total (New/Persisting) Gadolinium-Enhancing T1 Lesions at Week 12							
	n	mITT	67	32	30	33	62
Weeks 0–12[c]	Mean rate[d]	mITT	251.31	44.19	124.99	116.48	61.35
	Rate ratio (95% CI)	mITT		0.18 (0.05, 0.58)[g]	0.50 (0.15, 1.63)	0.46 (0.15, 1.43)	0.24 (0.10, 0.62)[e]
Weeks 4–12 (post-hoc analyses)[c]	Mean rate[d]	mITT	253.46	25.82	62.11	36.35	28.72
	Rate ratio (95% CI)	mITT		0.10 (0.02, 0.46)[e]	0.25 (0.06, 0.97)[f]	0.14 (0.04, 0.54)[e]	0.11 (0.04, 0.36)
Cumulative Volume (mm^3) of New and Newly Enlarging T2 Lesions at Weeks 4–12 and 4–24							
	n	mITT	67	32	30	33	62
Weeks 4–12 (post-hoc analyses)[c]	Mean rate[d]	mITT	228.36	50.96	13.21	10.71	16.64
	Rate ratio (95% CI)	mITT		0.22 (0.03, 1.46)	0.06 (0.01, 0.37)[g]	0.05 (0.01, 0.28)[e]	0.07 (0.02, 0.33)[e]
Week 4–24 (post-hoc analyses)[c]	Mean rate[d]	mITT	161.21	76.58	9.33	5.87	10.56

	Rate ratio (95% CI)	mITT	0.47 (0.10, 2.17)	0.06 (0.01, 0.28)[e]	0.04 (0.01, 0.17)[e]	0.07 (0.02, 0.23)[e]

CI, confidence interval; mITT, modified intent-to-treat; MRI, magnetic resonance imaging; PP, per protocol; q4w, every 4 weeks; q12w, every 12 weeks; SD, standard deviation.

Note: The number of patients with an MRI scan showing lesion within the 12 months prior to baseline is shown in Table 1.

[a]Patients randomized to the placebo group received 3 mg of ofatumumab at Week 12; [b]E_{max} model fitted was E0+E_{max}*dose/(ED_{50}+dose)+baseline GdE lesion status; [c]statistical model adjusted for treatment and baseline lesion value; [d]rate of the cumulative number of lesions per scan; [e]$P \leq 0.001$; [f]$P=0.002$; [g]$P<0.01$; [h]$P<0.05$.

Table e-3. Summary of Relapses (Safety Population)

Parameter	Placebo[a] (N=67)	Ofatumumab 3 mg q12w (N=34)	Ofatumumab 30 mg q12w (N=32)	Ofatumumab 60 mg q12w (N=34)	Ofatumumab 60 mg q4w (N=64)
Treatment phase: Weeks 0–12, N	**67**	**34**	**32**	**34**	**64**
Number of patients relapsing, n (%)	9 (13)	2 (6)[b]	4 (13)[c]	4 (12)[c]	7 (11)[c]
Total number of relapses	9	2	6	4	7
Absolute risk reduction, % (95% CI)		7.6 (-3.82, 18.92)	0.9 (-13.14, 15.00)	1.7 (-11.90, 15.23)	2.5 (-8.69, 13.68)
Numbers needed to treat, n (95% CI)[d]		13 (NA)	107 (NA)	60 (NA)	40 (NA)
Treatment phase: Weeks 4–12,[e] N	**66**	**33**	**30**	**33**	**62**
Number of patients relapsing, n (%)	7 (11)	1 (3)	3 (10)	1 (3)	3 (5)
Total number of relapses	7	1	3	1	3
Absolute risk reduction, % (95% CI)		7.6 (-1.88, 17.03)	0.6 (-12.45, 13.66)	7.6 (-1.88, 17.03)	5.8 (-3.38, 14.92)
Numbers needed to treat, n (95% CI)[d]		13 (NA)	165 (NA)	13 (NA)	17 (NA)
Treatment phase: Weeks 12–24, N	**65**	**31**	**30**	**33**	**60**
Number of patients relapsing, n (%)	9 (14)	1 (3)	3 (10)	2 (6)	3 (5)
Total number of relapses	9	1	3	2	3

Absolute risk reduction, % (95% CI)		10.6 (0.17, 21.07)	3.8 (-9.78, 17.48)	7.8 (-3.91, 19.48)	8.8 (-1.2, 18.89)
Numbers needed to treat, n (95% CI)[d]		9 (4.7, 584.6)	26 (NA)	13 (NA)	11 (NA)
Treatment phase: Weeks 0–24, N	**67**	**34**	**32**	**34**	**64**
Number of patients relapsing, n (%)	17 (25)	3 (9)	7 (22)	5 (15)	10 (16)
Total number of relapses	18	3	9	6	10
Absolute risk reduction, % (95% CI)		16.5 (2.43, 30.67)	3.5 (-14.21, 21.21)	10.7 (-5.15, 26.49)	9.7 (-3.95, 23.45)
Numbers needed to treat, n (95% CI)[d]		6 (3.3, 41.2)	29 (NA)	9 (NA)	10 (NA)
Follow-Up phase: Weeks 24–48, N	66	31	32	33	59
Number of patients relapsing, n (%)	8 (12)	2 (6)	2 (6)	2 (6)	9 (15)
Total number of relapses	9	2	3	2	9
Absolute risk reduction, % (95% CI)		5.7 (-6.03, 17.37)	5.9 (-5.63, 17.38)	6.1 (-5.27, 17.39)	-3.1 (-15.22, 8.96)
Numbers needed to treat, n (95% CI)[d]		18 (NA)	17 (NA)	17 (NA)	"32"[f] (NA)

CI, confidence interval; NA, not applicable

[a]Patients randomized to placebo group received 3 mg ofatumumab at Week 12; [b]*P*=0.488; [c]*P*=1.000; [d] 95% CI not applicable for the numbers needed to treat when the 95% CI for the absolute risk reduction versus placebo contains 0; [e]post-hoc analysis; [f]Number needed to harm

Table e-4. Summary of Time from Last Active Dose until CD19+ B Cell Count >0.11 GI/L or ≥ to the Subject's Baseline CD19 Value (Safety Population)

	Placebo[a] (N=67)	Ofatumumab 3 mg q12w (N=34)	Ofatumumab 30 mg q12w (N=32)	Ofatumumab 60 mg q12w (N=34)	Ofatumumab 60 mg q4w (N=64)
Subject's CD19 status					
n	65	31	30	33	62
Repleted, n (%)	39 (60)	23 (74)	22 (73)	21 (64)	41 (66)
Did not replete, n (%)	5 (8)	7 (23)	8 (27)	12 (36)	21 (34)
Did not deplete, n (%)[b]	21 (32)	1 (3)	0	0	0
Time (days) to repletion (based on observed events)[c]					
N	39	23	22	21	41
Mean	208.8	292.5	288.1	323.4	355.3
SD	153.70	175.61	153.03	179.91	163.18
Median	168.0	329.0	257.0	253.0	343.0
Min, Max	57, 602	56,750	53, 680	85, 777	101, 713
Kaplan–Meier estimates of days to repletion (accounting for censored data)[d]					
25th percentile	102.0	203.0	214.0	221.09	281.0
Median days	169.5	334.0	329.0	421.0	428.0
75th percentile	429.0	505.0	504.0	777.0	588.0

Max, maximum; Min, minimum; SD, standard deviation.

[a]Patients randomized to placebo group received 3 mg ofatumumab at Week 12; [b]considered to have not depleted if a patient's CD19 value was ≥ their baseline value or above 0.11 GI/L on the dates of their last

active dose and their subsequent evaluable CD19 laboratory test assessment; [c]time to repletion was calculated as the number of days between the last active dose date and the date the CD19 value was ≥ the patient's baseline value or >0.11 GI/L. If a subject withdrew prior to their CD19 value being baseline value or >0.11 GI/L, they have been censored at the date of their last evaluable CD19 assessment; [d]the median, 25th, and 75th percentiles of time to repletion were derived from Kaplan–Meier survival estimates and thus account for censored data

Table e-5. Most Common Adverse Events (≥5% in either the Placebo or Ofatumumab Groups) of Treatment Phase and 24-week Follow-Up Phase

Adverse Event	Placebo[a]	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w	Ofatumumab 60 mg q4w	Total Ofatumumab
Weeks 0–12						
Any infection-related AE	17 (25)	8 (24)	8 (25)	13 (38)	16 (25)	45 (27)
Injection-related reaction	10 (15)	16 (47)	13 (41)	15 (44)	42 (66)	86 (52)
Nasopharyngitis	4 (6)	1 (3)	2 (6)	6 (18)	6 (9)	15 (9)
Headache	4 (6)	1 (3)	1 (3)	3 (9)	3 (5)	8 (5)
Fatigue	7 (10)	0	3 (9)	1 (3)	2 (3)	6 (4)
Weeks 12–24						
Any infection-related AE	19 (29)	5 (16)	6 (20)	6 (18)	9 (15)	45 (21)
Injection-related reaction	9 (14)	6 (19)	3 (10)	6 (18)	5 (8)	29 (13)
Headache	4 (6)	1 (3)	1 (3)	0	4 (7)	10 (5)
Nasopharyngitis	4 (6)	0	2 (7)	1 (3)	3 (5)	10 (5)
Fatigue	7 (10)	0	3 (9)	1 (3)	2 (3)	6 (4)
Back pain	4 (6)	0	1 (3)	0	1 (2)	6 (3)
24-Week Follow-Up phase						
Nasopharyngitis	3 (5)	4 (13)	1 (3)	2 (6)	3 (5)	13 (6)

Urinary tract infection	1 (2)	1 (3)	3 (9)	2 (6)	3 (5)	10 (5)
Fall	2 (3)	2 (6)	1 (3)	2 (6)	0	7 (3)
Pain in extremity	2 (3)	2 (6)	0	0	1 (2)	5 (2)
Sinusitis	0	0	1 (3)	0	3 (5)	4 (2)
Bronchitis	0	0	2 (6)	0	0	2 (<1)

[a]Patients randomized to the placebo group received 3 mg of ofatumumab at Week 12

AE, adverse event; q4w, every 4 weeks; q12w, every 12 weeks

Table e-6. Summary of Injection-Related Reactions (≥5% Incidence in any Dose Group) which Occurred within 7 days following placebo[a] or each dose of Ofatumumab (including pre-conditioning dose[b]) during Weeks 0–24 (Safety Population)

	Placebo (N=67)	**Ofatumumab 3 mg q12w (N=34)**	**Ofatumumab 30 mg q12w (N=16)**	**Ofatumumab 30 mg q12w + CD (N=16)**	**Ofatumumab 60 mg q12w (N=17)**	**Ofatumumab 60 mg q12w + CD (N=17)**	**Ofatumumab 60 mg q4w (N=32)**	**Ofatumumab 60 mg q4w + CD (N=32)**
Week 0 Dose, n (%)	4 (6)	3 (9)	1 (6)	8 (50)	3 (18)	5 (29)	4 (13)	16 (50)
Mild	3	2	0	7	1	3	3	6
Moderate	1	0	1	1	1	2	1	8
Severe	0	1	0	0	1	0	0	2
Week 1 Dose, n (%)	7 (10)	14 (41)	3 (19)	2 (13)	8 (47)[c]	2 (12)	16 (50)	9 (28)
Mild	0	9	3	1	2	2	13	8
Moderate	7	5	0	1	6	0	3	1
Severe	0	0	0	0	0	0	0	0
Week 4 Dose, n (%)	0	1 (3)	1 (6)	0	0	0	2 (6)	1 (3)
Mild	0	0	0	0	0	0	2	0
Moderate	0	1	1	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0

Week 8 Dose, n (%)	0	0	0	0	0	1 (6)	3 (9)	0
Mild	0	0	0	0	0	0	2	0
Moderate	0	0	0	0	0	1	1	0
Severe	0	0	0	0	0	0	0	0
Week 12 Dose, n (%)	9 (13)	6 (18)	1 (6)	1 (6)	3 (18)	3 (18)	3 (9)	1 (3)
Mild	4	2	1	1	1?	1	2	1
Moderate	5	4	0	0	1?	2	1	0
Severe	0	0	0	0	0	0	0	0
Any Dose (Weeks 0–24), n (%)	17 (25)	16 (47)	5 (31)	8 (50)	10 (59)	7 (41)	20 (63)	22 (69)

AE, adverse event; CD, conditioning dose, q12w, every 12 weeks

Note: AEs included in this display were selected based on a clinical review of all injection-related AEs observed in the study. [a]Patients randomized to placebo group received 3 mg ofatumumab at Week 12; [b]to preserve the blind, all randomized patients received a CD of ofatumumab 3 mg or placebo at Week 0. Of all patients, half assigned to the 30 mg arm or either of the two 60 mg arms received a 3 mg CD at Week 0 (1 week prior to the assigned dose), and the remaining patients, including those assigned to the 3 mg dose or placebo arms, received a placebo CD; [c]in addition, 1 subject in the ofatumumab 60 mg q12w dose group reported cytokine release syndrome following the first dose