

Supplemental Tables

Table e-1. Summary of Unadjusted Outcomes at 24-Month Follow-Up in RRMS Patients

	DMF		FTY		p-value
	n= 558		n= 459		
	n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	244	43.7%	148	32.2%	<0.001*
Disease Activity	50	9.0%	46	10.0%	0.640
Intolerability	140	25.1%	73	15.9%	<0.001*
Clinical Relapse ≤ 24 Mo	91	16.3%	62	13.5%	0.243
Relapses per Patient (mean, SD)	0.16	0.37	0.14	0.34	0.210
MRI Available ≤ 24 Mo	409	73.3%	384	83.7%	0.243
MRI Activity ≤ 24 Mo	131	32.0%	115	29.9%	0.578
GdE Lesions	54	13.2%	45	11.7%	0.600
New T2 Lesions	119	29.1%	98	25.5%	0.294
MRI available Between 12-24 Mo	220	39.4%	217	47.3%	0.324
MRI Activity Between 12-24 Mo	41	18.6%	38	17.5%	0.856
GdE Lesions	20	9.1%	13	6.0%	0.296
New T2 Lesions	34	15.5%	33	15.3%	1.000
Absence of Disease Activity†	236	57.7%	238	62.0%	0.248

RRMS: relapsing-remitting multiple sclerosis; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-2. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up in RRMS Patients

Causal effect of treatment	Unadjusted	ATT Weighting
Discontinuation	1.63***	1.62***
OR (95% CI)	(1.26, 2.11)	(1.23, 2.14)
Intolerability	1.77***	1.70**
OR (95% CI)	(1.29, 2.43)	(1.21, 2.38)
Breakthrough Disease	0.88	0.99
OR (95% CI)	(0.58, 1.35)	(0.62, 1.60)
Time to Discontinuation	1.52***	1.52***
Relative Hazard Ratio (95% CI)	(1.24, 1.87)	(1.25, 1.84)
Proportion with Relapses	1.25	1.30
OR (95% CI)	(0.88, 1.77)	(0.90, 1.89)
MRI Activity on DMT ≤ 24 Months	1.10	1.15
OR (95% CI)	(0.82, 1.49)	(0.83, 1.60)
Brain MRI GdE Lesions	1.15	1.62*
OR (95% CI)	(0.75, 1.75)	(1.02, 2.58)
Brain MRI New T2 Lesions	1.20	1.19
OR (95% CI)	(0.88, 1.64)	(0.85, 1.66)
MRI Activity on DMT at 12-24 Months	1.08	1.01
OR (95% CI)	(0.66, 1.76)	(0.60, 1.70)
Brain MRI GdE Lesions	1.57	1.58
OR (95% CI)	(0.76, 3.24)	(0.91, 4.48)
Brain MRI New T2 Lesions	1.01	0.91
OR (95% CI)	(0.60, 1.71)	(0.52, 1.59)
Absence of Disease Activity†	0.84	0.76
OR (95% CI)	(0.63, 1.11)	(0.54, 1.11)

RRMS: relapsing-remitting multiple sclerosis; CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

†Proportion of subjects free of clinical relapses, GdE lesions or New T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001

Table e-3. Summary of Unadjusted Outcomes at 24-Month Follow-Up Stratified by Age

	Age < 40 years-old					Age ≥ 40 years-old				
	DMF n= 200		FTY n= 183		p-value	DMF n= 537		FTY n= 352		p-value
	n	% or SD	n	% or SD		n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	93	46.5%	62	33.9%	0.016*	233	43.4%	124	35.2%	0.018*
Disease Activity	27	13.5%	25	13.7%	1.000	47	8.8%	36	10.2%	0.534
Intolerability	42	21.0%	24	13.1%	0.057	141	26.3%	62	17.6%	0.003*
Clinical Relapse ≤ 24 Mo	50	25.0%	33	18.0%	0.126	61	11.4%	37	10.5%	0.761
Relapses per Patient (mean, SD)	0.25	0.43	0.18	0.39	0.099	0.11	0.32	0.11	0.31	0.679
MRI Available ≤ 24 Mo	153	76.5%	150	82.0%	0.211	379	70.6%	295	83.8%	0.132
MRI Activity ≤ 24 Mo	62	40.5%	58	38.7%	0.831	92	24.3%	69	23.4%	0.860
GdE Lesions	32	20.9%	30	20.0%	0.956	30	7.9%	20	6.8%	0.682
New T2 Lesions	18	23.4%	17	20.2%	0.771	82	21.6%	61	20.7%	0.836
MRI available Between 12-24 Mo	77	38.5%	84	45.9%	0.146	206	38.4%	161	45.7%	0.114
MRI Activity Between 12-24 Mo	22	28.6%	19	22.6%	0.493	26	12.6%	22	13.7%	0.890
GdE Lesions	11	14.3%	8	9.5%	0.490	12	5.8%	6	3.7%	0.496
New T2 lesions	18	23.4%	17	20.2%	0.771	22	10.7%	19	11.9%	0.847
Absence of Disease Activity†	70	45.8%	80	53.3%	0.228	255	67.5%	202	68.5%	0.844

Mo: Month; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-4. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up Stratified by Age

Causal Effect of Treatment	Age < 40 years-old		Age ≥ 40 years-old	
	Unadjusted	ATT Weighting	Unadjusted	ATT Weighting
Discontinuation	1.69**	1.48	1.41*	1.43*
OR (95% CI)	(1.12, 2.56)	(0.95, 2.31)	(1.07, 1.86)	(1.04, 1.95)
Intolerability	1.76*	1.36	1.66**	1.66**
OR (95% CI)	(1.02, 3.05)	(0.76, 2.45)	(1.19, 2.33)	(1.14, 2.43)
Breakthrough Disease	0.99	1.21	0.84	0.92
OR (95% CI)	(0.55, 1.77)	(0.65, 2.27)	(0.53, 1.33)	(0.52, 1.63)
Time to Discontinuation	1.55**	1.39*	1.37**	1.40***
Relative Hazard Ratio (95% CI)	(1.12, 2.14)	(1.02, 1.89)	(1.10, 1.71)	(1.15, 1.69)
Proportion with Relapses	1.51	1.67	1.10	1.09
OR (95% CI)	(0.92, 2.48)	(0.98, 2.86)	(0.71, 1.69)	(0.67, 1.76)
MRI Activity on DMT ≤ 24 Months	1.20	1.02	1.04	1.00
OR (95% CI)	(0.57, 2.54)	(0.62, 1.68)	(0.73, 1.50)	(0.67, 1.48)
Brain MRI GdE Lesions	1.06	1.34	1.18	1.41
OR (95% CI)	(0.61, 1.85)	(0.72, 2.50)	(0.66, 2.13)	(0.73, 2.74)
Brain MRI New T2 Lesions	1.38	1.20	1.06	1.00
OR (95% CI)	(0.86, 2.22)	(0.72, 2.03)	(0.73, 1.54)	(0.65, 1.47)
MRI Activity on DMT 12-24 Months	1.37	1.20	0.91	0.80
OR (95% CI)	(0.67, 2.79)	(0.56, 2.58)	(0.50, 1.68)	(0.42, 1.54)
Brain MRI GdE Lesions	1.58	1.62	1.60	2.11
OR (95% CI)	(0.60, 4.17)	(0.57, 4.61)	(0.59, 4.35)	(0.74, 6.03)
Brain MRI New T2 Lesions	1.20	1.03	0.88	0.73
OR (95% CI)	(0.57, 2.54)	(0.46, 2.33)	(0.46, 1.70)	(0.36, 1.46)
Absence of Disease Activity†	0.74	0.75	0.95	0.99
OR (95% CI)	(0.66, 1.83)	(0.62, 1.79)	(0.76, 1.45)	(0.70, 1.44)

CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001

Table e-5. Summary of Unadjusted Outcomes at 24-Month Follow-Up Stratified by Sex

	Female					Male				
	DMF n= 516		FTY n= 382		p-value	DMF n= 221		FTY n= 153		p-value
	n	% or SD	n	% or SD		n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	238	46.1%	137	35.9%	0.003*	88	39.8%	49	32.0%	0.153
Disease Activity	39	7.6%	46	12.0%	0.031*	35	15.8%	15	9.8%	0.126
Intolerability	155	30.0%	60	15.7%	<0.001*	28	12.7%	26	17.0%	0.308
Clinical Relapse ≤ 24 Mo	78	15.2%	51	13.4%	0.501	33	14.9%	19	12.4%	0.590
Relapses per Patient (mean, SD)	0.15	0.36	0.13	0.34	0.442	0.15	0.36	0.12	0.33	0.491
MRI Available ≤ 24 Mo	362	70.2%	316	82.7%	0.115	170	76.9%	129	84.3%	0.245
MRI Activity ≤ 24 Mo	94	26.0%	92	29.1%	0.407	60	35.3%	35	27.1%	0.169
GdE Lesions	33	9.1%	36	11.4%	0.395	29	17.1%	14	10.9%	0.178
New T2 Lesions	87	24.0%	77	24.4%	0.991	53	31.2%	30	23.3%	0.166
MRI available Between 12-24 Mo	195	37.8%	170	44.5%	0.224	88	39.8%	75	49.0%	0.253
MRI Activity Between 12-24 Mo	32	16.4%	28	16.5%	1.000	16	18.2%	13	17.3%	1.000
GdE Lesions	13	6.7%	10	5.9%	0.927	10	11.4%	4	5.3%	0.276
New T2 lesions	28	14.4%	25	14.8%	1.000	12	13.6%	11	14.7%	1.000
Absence of Disease Activity†	230	63.7%	197	62.3%	0.773	95	55.9%	85	65.9%	0.103

Mo: Month; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-6. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up Stratified by Sex

Causal Effect of Treatment	Female		Male	
	Unadjusted	ATT Weighting	Unadjusted	ATT Weighting
Discontinuation	1.53**	1.55**	1.40	1.60*
OR (95% CI)	(1.17, 2.01)	(1.15, 2.09)	(0.91, 2.17)	(1.01, 2.53)
Intolerability	2.30***	2.17***	0.71	0.76
OR (95% CI)	(1.65, 3.22)	(1.50, 3.13)	(0.40, 1.26)	(0.41, 1.39)
Breakthrough Disease	0.60	0.75	1.73	2.02
OR (95% CI)	(0.38, 0.94)	(0.41, 1.36)	(0.91, 3.30)	(0.99, 4.12)
Time to Discontinuation	1.46***	1.48***	1.35	1.49*
Relative Hazard Ratio (95% CI)	(1.19, 1.81)	(1.22, 1.80)	(0.95, 1.91)	(1.08, 2.05)
Proportion with Relapses	1.16	1.23	1.24	1.39
OR (95% CI)	(0.79, 1.70)	(0.81, 1.86)	(0.68, 2.27)	(0.73, 2.67)
MRI Activity on DMT ≤ 24 Months[#]	0.85	0.94	1.46	1.57
OR (95% CI)	(0.61, 1.20)	(0.65, 1.36)	(0.89, 2.41)	(0.92, 2.67)
Brain MRI GdE Lesions	0.78	1.01	1.69	2.78**
OR (95% CI)	(0.47, 1.28)	(0.58, 1.74)	(0.85, 3.35)	(1.32, 5.82)
Brain MRI New T2 Lesions	0.98	1.03	1.49	1.52
OR (95% CI)	(0.69, 1.40)	(0.70, 1.50)	(0.89, 2.52)	(0.87, 2.64)
MRI Activity on DMT 12-24 Months	1.00	1.00	1.06	1.11
OR (95% CI)	(0.57, 1.73)	(0.56, 1.78)	(0.47, 2.37)	(0.46, 2.67)
Brain MRI GdE Lesions	1.14	1.34	2.28	4.72**
OR (95% CI)	(0.49, 2.68)	(0.54, 3.33)	(0.68, 7.58)	(1.47, 15.19)
Brain MRI New T2 Lesions	0.97	0.97	0.92	1.52
OR (95% CI)	(0.54, 1.73)	(0.53, 1.78)	(0.38, 2.22)	(0.87, 2.64)
Absence of Disease Activity[†]	1.06	1.00	0.66	0.58*
OR (95% CI)	(0.69, 1.29)	(0.71, 1.40)	(0.55, 1.45)	(0.33, 0.95)

CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

[†]Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001

Table e-7. Summary of Unadjusted Outcomes at 24-Month Follow-Up Stratified by Drug Line

	First-Line					Non First-Line				
	DMF n= 63		FTY n= 36		p-value	DMF n= 674		FTY n= 499		p-value
	n	% or SD	n	% or SD		n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	27	42.9%	7	19.4%	0.032*	299	44.4%	179	35.9%	0.004*
Disease Activity	4	6.3%	1	2.8%	0.761	70	10.4%	60	12.0%	0.430
Intolerability	20	31.7%	2	5.6%	0.031*	170	25.2%	84	16.8%	0.001*
Clinical Relapse ≤ 24 Mo	10	16.1%	2	5.6%	0.223	101	15.0%	68	13.6%	0.561
Relapses per Patient (mean, SD)	0.16	0.37	0.06	0.23	0.126	0.15	0.36	0.14	0.34	0.506
MRI Available ≤ 24 Mo	46	73.0%	30	83.3%	0.213	486	72.1%	415	83.2%	0.146
MRI Activity ≤ 24 Mo	15	32.6%	8	26.7%	0.767	139	28.6%	119	28.7%	1.000
GdE Lesions	5	10.9%	0	0.0%	0.163	57	11.7%	50	12.0%	0.964
New T2 Lesions	13	28.3%	8	26.7%	1.000	127	26.1%	99	23.9%	0.479
MRI available Between 12-24 Mo	25	39.7%	19	52.8%	0.090	258	38.3%	226	45.3%	0.323
MRI Activity Between 12-24 Mo	6	24.0%	5	26.3%	1.000	42	16.3%	36	15.9%	1.000
GdE Lesions	2	8.0%	0	0.0%	0.595	21	8.1%	14	6.2%	0.517
New T2 lesions	6	24.0%	5	26.3%	1.000	34	13.2%	31	13.8%	0.953
Absence of Disease Activity†	24	53.3%	20	66.7%	0.363	301	53.5%	262	63.1%	0.763

Mo: Month; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-8. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up Stratified by Drug Line

Causal Effect of Treatment	First-Line		Non First-Line	
	Unadjusted	ATT Weighting	Unadjusted	ATT Weighting
Discontinuation	2.11*	1.63**	1.43**	1.48**
OR (95% CI)	(1.18, 8.15)	(1.23, 3.68)	(1.12, 1.81)	(1.15, 1.91)
Intolerability	1.42	1.71*	1.67***	1.58**
OR (95% CI)	(0.94, 6.85)	(1.12, 3.28)	(1.24, 2.23)	(1.15, 2.17)
Breakthrough Disease	1.37	1.23	0.85	1.01
OR (95% CI)	(0.25, 3.45)	(0.63, 2.56)	(0.59, 1.22)	(0.68, 1.50)
Time to Discontinuation	1.59*	1.11	1.33	1.23
Relative Hazard Ratio (95% CI)	(1.13, 5.93)	(0.76, 2.87)	(0.98, 1.79)	(0.94, 1.62)
Proportion with Relapses	1.27	1.56*	1.12	1.21
OR (95% CI)	(0.67, 3.85)	(1.08, 3.57)	(0.80, 1.56)	(0.85, 1.73)
MRI Activity on DMT ≤ 24 Months	1.33	1.54	1.00	1.05
OR (95% CI)	(0.48, 3.68)	(0.62, 5.38)	(0.75, 1.33)	(0.77, 1.43)
Brain MRI GdE Lesions	1.24	1.36	1.00	1.35
OR (95% CI)	(0.65, 3.21)	(0.54, 3.66)	(0.65, 1.45)	(0.87, 2.11)
Brain MRI New T2 Lesions	1.08	1.58	1.13	1.12
OR (95% CI)	(0.39, 3.04)	(0.62, 5.38)	(0.83, 1.53)	(0.81, 1.55)
MRI Activity on DMT 12-24 Months	1.33	1.54	1.03	1.02
OR (95% CI)	(0.34, 3.49)	(0.35, 6.74)	(0.63, 1.67)	(0.59, 1.64)
Brain MRI GdE Lesions	1.22	1.42	1.34	1.74
OR (95% CI)	(0.42, 4.12)	(0.44, 4.63)	(0.67, 2.71)	(0.82, 3.66)
Brain MRI New T2 Lesions	1.08	1.54	1.00	0.98
OR (95% CI)	(0.39, 3.04)	(0.35, 6.74)	(0.56, 1.60)	(0.50, 1.51)
Absence of Disease Activity†	0.77	0.67*	0.95	0.90
OR (95% CI)	(0.22, 1.49)	(0.48, 0.80)	(0.72, 1.25)	(0.83, 1.49)

CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001

Table e-9. Summary of Unadjusted Outcomes at 24-Month Follow-Up Stratified by Gadolinium-Enhancing Lesions on Baseline Brain MRI

	GdE Lesions on Baseline Brain MRI					No GdE Lesions on Baseline Brain MRI				
	DMF n= 133		FTY n= 115		p-value	DMF n= 604		FTY n= 420		p-value
	n	% or SD	n	% or SD		n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	63	47.4%	32	27.8%	0.002*	240	43.4%	138	36.9%	0.056
Disease Activity	18	13.5%	12	10.4%	0.582	51	9.2%	46	12.3%	0.164
Intolerability	32	24.1%	14	12.2%	0.025*	144	26.0%	65	17.4%	0.003*
Clinical Relapse ≤ 24 Mo	32	24.1%	17	14.8%	0.095	74	13.4%	49	13.1%	0.964
Relapses per Patient (mean, SD)	0.24	0.43	0.15	0.36	0.068	0.13	0.34	0.13	0.34	0.885
MRI Available ≤ 24 Mo	97	72.9%	100	87.0%	0.121	403	72.9%	318	85.0%	0.091
MRI Activity ≤ 24 Mo	41	42.3%	41	41.0%	0.971	100	24.8%	82	25.8%	0.832
GdE Lesions	24	24.7%	21	21.0%	0.649	35	8.7%	29	9.1%	0.943
New T2 Lesions	36	37.1%	34	34.0%	0.758	91	22.6%	69	21.7%	0.847
MRI available Between 12-24 Mo	61	45.7%	64	55.7%	0.197	211	38.2%	164	43.9%	0.453
MRI Activity Between 12-24 Mo	20	32.8%	14	21.9%	0.242	26	12.3%	25	15.2%	0.505
GdE Lesions	12	19.7%	5	7.8%	0.094	11	5.2%	9	5.5%	1.000
New T2 lesions	15	24.6%	12	18.8%	0.565	23	10.9%	22	13.5%	0.545
Absence of Disease Activity†	41	42.3%	53	53.0%	0.172	266	66.2%	206	64.8%	0.756

Mo: Month; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-10. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up Stratified by Gadolinium-Enhancing Lesions on Baseline Brain MRI

Causal effect of treatment	GdE Lesions on Baseline Brain MRI		No GdE Lesions on Baseline Brain MRI	
	Unadjusted	ATT Weighting	Unadjusted	ATT Weighting
Discontinuation	2.33**	1.43*	1.31*	1.43*
OR (95% CI)	(1.37, 3.97)	(1.04, 1.95)	(1.00, 1.71)	(1.07, 1.92)
Intolerability	2.29*	1.66**	1.67**	1.54*
OR (95% CI)	(1.15, 4.54)	(1.14, 2.43)	(1.21, 2.32)	(1.08, 2.21)
Breakthrough Disease	1.34	1.02	0.72	0.93
OR (95% CI)	(0.62, 2.92)	(0.52, 1.63)	(0.48, 1.10)	(0.59, 1.46)
Time to Discontinuation	1.97**	1.85**	1.31**	1.40***
Relative Hazard Ratio (95% CI)	(1.29, 3.02)	(1.24, 2.75)	(1.06, 1.61)	(1.16, 1.69)
Proportion with Relapses	1.83	1.09	1.03	1.08
OR (95% CI)	(0.95, 3.50)	(0.67, 1.76)	(0.70, 1.51)	(0.71, 1.65)
MRI Activity on DMT ≤ 24 Months	1.05	1.00	0.95	1.00
OR (95% CI)	(0.60, 1.86)	(0.67, 1.48)	(0.68, 1.33)	(0.63, 1.30)
Brain MRI GdE Lesions	1.24	1.41	0.95	1.20
OR (95% CI)	(0.64, 2.41)	(0.73, 2.74)	(0.57, 1.59)	(0.68, 2.09)
Brain MRI New T2 Lesions	1.15	1.00	1.05	1.00
OR (95% CI)	(0.64, 2.05)	(0.65, 1.48)	(0.74, 1.50)	(0.64, 1.38)
MRI Activity on DMT at 12-24 Months	1.74	1.06	0.91	1.04
OR (95% CI)	(0.78, 3.87)	(0.53, 2.12)	(0.43, 1.41)	(0.36, 1.28)
Brain MRI GdE Lesions	2.89	2.11	0.95	1.17
OR (95% CI)	(0.95, 8.77)	(0.74, 6.03)	(0.38, 2.34)	(0.44, 3.02)
Brain MRI New T2 Lesions	1.41	1.23	0.93	0.98
OR (95% CI)	(0.60, 3.33)	(0.36, 1.46)	(0.42, 1.46)	(0.33, 1.26)
Absence of Disease Activity†	0.65	0.99	1.06	1.08
OR (95% CI)	(0.48, 1.70)	(0.70, 1.44)	(0.69, 1.28)	(0.67, 1.31)

CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001

Table e-11. Summary of Unadjusted Outcomes at 24-Month Follow-Up Stratified by Baseline MRI Lesion Burden

	Mild MRI Lesion Burden					Moderate-Severe MRI Lesion Burden				
	DMF n= 374		FTY n= 193		p-value	DMF n= 303		FTY n= 289		p-value
	n	% or SD	n	% or SD		n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	169	45.2%	67	34.7	0.021*	127	41.9%	103	35.6%	0.139
Disease Activity	36	9.6%	18	9.3%	1.000	34	11.2%	39	13.5%	0.474
Intolerability	104	27.8%	35	18.1%	0.015*	68	22.4%	45	15.6%	0.043*
Clinical Relapse ≤ 24 Mo	48	12.9%	25	13.0%	1.000	58	19.1%	40	13.8%	0.104
Relapses per Patient (mean, SD)	0.13	0.34	0.13	0.34	0.977	0.19	0.39	0.14	0.35	0.083
MRI Available ≤ 24 Mo	272	72.7%	171	88.6%	0.119	227	74.9%	243	80.2%	0.268
MRI Activity ≤ 24 Mo	70	25.7%	55	32.2%	0.175	71	31.3%	68	28.0%	0.496
GdE Lesions	25	9.2%	13	7.6%	0.684	32	14.1%	37	15.2%	0.830
New T2 Lesions	67	24.6%	48	28.1%	0.489	61	26.9%	55	22.6%	0.338
MRI available Between 12-24 Mo	148	40.0%	95	49.2%	0.135	121	39.9%	130	45.0%	0.574
MRI Activity Between 12-24 Mo	25	16.9%	20	21.1%	0.519	21	17.4%	19	14.6%	0.674
GdE Lesions	12	8.1%	5	5.3%	0.555	11	9.1%	9	6.9%	0.689
New T2 lesions	23	15.5%	18	19.1%	0.580	15	12.4%	16	12.3%	1.000
Absence of Disease Activity†	279	64.9%	125	60.2%	0.172	207	57.7%	199	63.0%	0.285

Mo: Month; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-12. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up Stratified by Baseline MRI Lesion Burden

Causal effect of treatment	Mild MRI Lesion Burden		Moderate-Severe MRI Lesion Burden	
	Unadjusted	ATT Weighting	Unadjusted	ATT Weighting
Discontinuation	1.55**	1.46*	1.30	1.52*
OR (95% CI)	(1.08, 2.22)	(1.00, 2.13)	(0.94, 1.82)	(1.06, 2.18)
Intolerability	1.74**	1.51*	1.57*	1.65*
OR (95% CI)	(1.13, 2.67)	(1.00, 2.39)	(1.03, 2.38)	(1.04, 2.61)
Breakthrough Disease	1.04	1.06	0.81	1.03
OR (95% CI)	(0.57, 1.88)	(0.55, 2.05)	(0.50, 1.32)	(0.61, 1.73)
Time to Discontinuation	1.51**	1.44**	1.26	1.42**
Relative Hazard Ratio (95% CI)	(1.14, 2.00)	(1.14, 1.80)	(0.97, 1.63)	(1.09, 1.85)
Proportion with Relapses	1.00	1.03	1.47	1.59
OR (95% CI)	(0.59, 1.67)	(0.61, 1.75)	(0.94, 2.29)	(0.97, 2.61)
MRI Activity on DMT ≤ 24 Months	0.73	0.78	1.17	1.51
OR (95% CI)	(0.48, 1.11)	(0.51, 1.20)	(0.79, 1.74)	(0.98, 2.33)
Brain MRI GdE Lesions	1.23	1.35	0.91	1.33
OR (95% CI)	(0.61, 2.48)	(0.65, 2.81)	(0.55, 1.52)	(0.75, 2.36)
Brain MRI New T2 Lesions	0.84	0.87	1.26	1.48
OR (95% CI)	(0.54, 1.29)	(0.56, 1.36)	(0.83, 1.91)	(0.93, 2.34)
MRI Activity on DMT at 12-24 Months	0.76	0.77	1.23	1.47
OR (95% CI)	(0.40, 1.47)	(0.40, 1.51)	(0.62, 2.41)	(0.68, 3.14)
Brain MRI GdE Lesions	1.59	1.63	1.34	1.90
OR (95% CI)	(0.54, 4.66)	(0.51, 5.15)	(0.54, 3.37)	(0.69, 5.21)
Brain MRI New T2 Lesions	0.78	0.77	1.01	1.16
OR (95% CI)	(0.39, 1.53)	(0.40, 1.54)	(0.47, 2.14)	(0.51, 2.65)
Absence of Disease Activity†	0.82	0.88	0.81	0.63
OR (95% CI)	(0.73, 1.80)	(0.58, 1.06)	(0.55, 1.16)	(0.52, 2.35)

CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001

Table e-13. Summary of Unadjusted Outcomes at 24-Month Follow-Up in Patients Switching from Natalizumab

	DMF n= 91		FTY n= 139		p-value
	n	% or SD	n	% or SD	
Discontinued Drug ≤ 24 Mo	41	45.1%	57	41.0%	0.638
Disease Activity	15	16.5%	22	15.8%	1.000
Intolerability	19	20.9%	27	19.4%	0.919
Clinical Relapse ≤ 24 Mo	13	14.3%	9	6.5%	0.082
Relapses per Patient (mean, SD)	0.14	0.35	0.06	0.25	0.049*
MRI Available ≤ 24 Mo	77	84.6%	117	84.2%	0.967
MRI Activity ≤ 24 Mo	25	32.5%	36	30.8%	0.927
GdE Lesions	12	15.6%	18	15.4%	1.000
New T2 Lesions	23	29.9%	30	25.6%	0.630
MRI available Between 12-24 Mo	34	37.4%	47	33.8%	0.435
MRI Activity Between 12-24 Mo	8	23.5%	7	14.9%	0.485
GdE Lesions	3	8.8%	5	10.6%	1.000
New T2 Lesions	6	17.6%	6	12.8%	0.769
Absence of Disease Activity†	60	77.9%	100	85.5%	0.407

DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; DMF: dimethyl fumarate; FTY: fingolimod.

*Statistically significant p-value (alpha=0.05)

†Proportion of subjects free of clinical relapses, GdE lesions and new T2 lesions calculated from those with complete data available.

Table e-14. Unadjusted and Adjusted Endpoints at 24-Month Follow-Up in Patients Switching from Natalizumab

Causal effect of treatment	Unadjusted	ATT Weighting
Discontinuation	1.18	1.41
OR (95% CI)	(0.69, 2.01)	(0.79, 2.54)
Intolerability	1.09	1.31
OR (95% CI)	(0.57, 2.11)	(0.63, 2.72)
Breakthrough Disease	1.05	1.19
OR (95% CI)	(0.52, 2.15)	(0.55, 2.59)
Time to Discontinuation	1.16	1.26
Relative Hazard Ratio (95% CI)	(0.75, 1.67)	(0.80, 1.98)
Proportion with Relapses	2.41	1.89
OR (95% CI)	(0.98, 5.89)	(0.66, 5.41)
MRI Activity on DMT ≤ 24 Months	1.08	1.13
OR (95% CI)	(0.58, 2.01)	(0.56, 2.30)
Brain MRI GdE Lesions	1.02	2.15
OR (95% CI)	(0.46, 2.25)	(0.88, 5.29)
Brain MRI New T2 Lesions	1.24	1.22
OR (95% CI)	(0.65, 2.34)	(0.58, 2.55)
MRI Activity on DMT at 12-24 Months	1.76	1.96
OR (95% CI)	(0.57, 5.43)	(0.45, 8.56)
Brain MRI GdE Lesions	0.81	2.45
OR (95% CI)	(0.18, 3.66)	(0.47, 12.89)
Brain MRI New T2 Lesions	1.46	1.54
OR (95% CI)	(0.43, 5.01)	(0.36, 6.63)
Absence of Disease Activity†	0.74	0.79
OR (95% CI)	(0.54, 1.35)	(0.65, 1.47)

CI: confidence interval; DMT: disease-modifying therapy; GdE: gadolinium enhancing; MRI: magnetic resonance imaging; OR: odds ratio; DMF: dimethyl fumarate; FTY: fingolimod.

†Proportion of subjects free of clinical relapses, GdE lesions or New T2 lesions calculated from those with complete data.

*P-value<0.05

**P-value<0.01

***P-value<0.001