

S1 Table

Baseline characteristics of included trials.

Study	Year	Technique	Randomized	Type of DMD	DMD	Number of patients	Sex ratio, f/m	Age, years		EDSS, no		ARR, no		Duration, years	
								mean	SD	mean	SD	mean	SD	mean	SD
BRAVO [1]	2014	SIENA	yes	FLDMD	IFN-B1a	447	2.19	38.20	9.50	2.60	1.20	1.30	0.60	7.00	5.90
				FLDMD	LAQ 0,6mg	434	1.86	37.00	9.30	2.70	1.30	1.30	0.60	6.60	6.00
				Placebo	Placebo	450	2.48	37.50	9.50	2.70	1.20	1.30	0.60	6.90	6.60
FREEDOMS II [2]	2014	SIENA	yes	SLDMD	FIN 1,25mg	370	3.16	40.90	8.90	2.50	1.30	1.50	1.00	10.80	8.20
				SLDMD	FIN 0,5mg	358	3.31	40.60	8.40	2.40	1.30	1.40	0.90	10.40	8.00
				Placebo	Placebo	355	4.30	40.10	8.40	2.40	1.30	1.50	0.90	10.60	7.90
SELECT [3]	2013	SIENA	yes	SLDMD	DAC 150mg	208	2.03	35.30	8.90	2.80	1.20	1.40	0.70	3.00	NA
				SLDMD	DAC 300mg	209	1.78	35.20	8.70	2.70	1.20	1.30	0.70	3.00	NA
				Placebo	Placebo	204	1.70	36.60	9.00	2.70	1.20	1.30	0.60	2.00	NA
Vidal-Jordana [4]	2013	SIENA	no	SLDMD	NTZ 300mg	39	2.55	34.95	8.75	4.00	NA	NA	NA	10.98	NA
CARE-MS I [5]	2012	BPF	yes	FLDMD	IFN-B1a	187	1.86	33.20	8.50	2.00	0.80	1.80	0.80	2.00	1.30
				SLDMD	ALM 12mg	376	1.86	33.00	8.00	2.00	0.80	1.80	0.80	2.10	1.40
CARE-MS II [6]	2012	BPF	yes	FLDMD	IFN-B1a	202	1.86	35.80	8.77	2.70	1.21	1.50	0.75	4.70	2.86
				SLDMD	ALM 12mg	426	1.94	34.80	8.36	2.70	1.26	1.70	0.86	4.50	2.68
				SLDMD	ALM 24mg	170	2.45	35.10	8.40	2.70	1.17	1.60	0.86	4.30	2.77
DEFINE [7,8]	2012	SIENA	yes	FLDMD	BG-12 480mg	176	3.35	38.30	9.30	2.30	1.20	1.30	0.60	8.70	7.10
				FLDMD	BG-12 720mg	184	3.17	38.50	8.60	2.30	1.20	1.30	0.60	8.00	6.00
				Placebo	Placebo	180	3.55	38.30	9.20	2.50	1.20	1.30	0.70	8.60	6.60
ALLEGRO [9]	2012	SIENA	yes	FLDMD	LAQ 0,6mg	550	2.46	38.90	9.20	2.60	1.30	1.20	0.70	8.70	6.90
				Placebo	Placebo	556	1.96	38.50	9.10	2.60	1.30	1.30	0.70	8.70	6.70
Portaccio [10]	2012	SIENA	no	FLDMD	IFN-B	14	3.67	39.00	9.20	1.30	0.40	1.10	0.30	8.60	3.80
				SLDMD	NTZ	12	3.00	37.30	11.90	3.50	1.60	2.30	0.60	8.10	4.70
Rinaldi [11]	2012	CTh	no	FLDMD	IFN-B1 or AG	50	2.21	36.00	8.20	2.00	1.00	0.50	0.50	5.00	2.20
				SLDMD	NTZ	35	1.50	32.60	7.30	3.20	1.20	2.30	1.00	8.70	4.90
				Placebo	Not treated	35	2.50	39.10	11.20	1.30	0.80	1.00	0.90	6.00	4.80
Ruocco [12]	2012	BPFV	no	FLDMD	IFN-B1 or AG	54	2.18	30.00	9.60	2.60	1.20	1.40	1.00	10.00	5.80
Magraner [13]	2012	SIENA	no	SLDMD	NTZ	18	3.50	31.60	9.00	3.10	0.90	2.00	1.10	7.20	5.70
IMPROVE [14,15]	2012	SIENA	yes	FLDMD	IFN-B1a 44µg	120	NA	NA	NA	NA	NA	NA	NA	NA	NA
				Placebo	Placebo	60	NA	NA	NA	NA	NA	NA	NA	NA	NA
TEMPO [16]	2011	BPF	yes	FLDMD	TER 7mg	366	2.30	37.40	9.00	2.68	1.34	1.40	0.70	8.80	6.80
				FLDMD	TER 14mg	359	2.45	37.80	8.20	2.67	1.24	1.30	0.70	8.70	6.70
				Placebo	Placebo	363	3.13	38.40	9.00	2.68	1.34	1.40	0.70	8.60	7.10
FORTE [17]	2011	SIENA	yes	FLDMD	AG 20mg	586	2.55	36.30	9.00	2.20	1.20	1.50	0.70	3.00	4.00
				FLDMD	AG 40mg	569	2.51	36.30	9.00	2.10	1.10	1.40	0.70	3.30	4.80
QUALICORE [18]	2010	BPF	no	FLDMD	IFN-B1a	28	2.50	32.50	NA	1.70	NA	1.70	NA	2.50	NA
SENTINEL [19,20]	2010	BPF	yes	FLDMD	IFN-B1a 30µg	582	2.60	39.10	7.60	2.50	1.10	1.49	0.72	8.00	NA
Van den Elskamp [21]	2010	SIENA	no	Placebo	oral IFN-B1a or Placebo	135	2.65	35.80	8.60	2.00	NA	NA	NA	6.60	5.50
FREEDOMS [22]	2010	SIENA	yes	SLDMD	FIN 1,25mg	429	2.21	37.40	8.90	2.40	1.40	1.50	0.80	8.40	6.90
				SLDMD	FIN 0,5mg	425	2.29	36.60	8.80	2.30	1.30	1.50	0.80	8.00	6.60
				Placebo	Placebo	418	2.48	37.20	8.60	2.50	1.30	1.40	0.70	8.10	6.40
TRANSFORMS [23]	2010	SIENA	yes	FLDMD	IFN-B1a 30µg	435	2.11	36.00	8.30	2.19	1.26	1.50	0.80	7.40	6.30
				SLDMD	FIN 1,25mg	426	2.21	35.80	8.40	2.21	1.31	1.50	0.90	7.30	6.00
				SLDMD	FIN 0,5mg	431	1.89	36.70	8.80	2.24	1.33	1.50	1.20	7.50	6.20
BEYOND [24]	2009	SIENA	yes	FLDMD	AG 20mg	448	2.13	35.20	NA	2.28	NA	1.60	NA	5.10	NA
				FLDMD	IFN-B1b 500µg	899	2.33	35.90	NA	2.33	NA	1.60	NA	5.40	NA
				FLDMD	IFN-B1b 250µg	897	2.33	35.80	NA	2.35	NA	1.60	NA	5.30	NA
ASA [25]	2009	SIENA	yes	FLDMD	IFN-B1a 30µg	60	4.00	28.90	7.10	1.80	0.90	1.80	0.80	4.40	4.20
CAMMS223 [26]	2008	SBV	yes	FLDMD	IFN-B1a	111	1.78	32.80	8.80	1.90	0.83	NA	NA	1.40	NA
				SLDMD	ALM 12mg	112	1.80	31.90	8.00	1.90	0.74	NA	NA	1.30	NA
				SLDMD	ALM 24mg	110	1.82	32.20	8.80	2.00	0.73	NA	NA	1.20	NA
REGARD [27]	2008	SIENA	yes	FLDMD	AG 20mg	378	2.57	36.80	9.50	2.33	1.31	NA	NA	6.55	7.10
				FLDMD	IFN-B1a 44µg	386	2.23	36.70	9.80	2.35	1.28	NA	NA	5.93	6.25
CORAL [28]	2008	CBV	yes	Placebo	Placebo	548	2.70	36.00	7.00	2.00	NA	NA	NA	7.80	6.20
Zivadinov [29]	2007	BPF	no	FLDMD	IFN-B1a	26	1.60	45.00	NA	2.00	NA	NA	NA	13.00	NA
				Placebo	Placebo	28	3.00	47.00	NA	1.00	NA	NA	NA	12.50	NA
AFFIRM [30,31]	2007	BPF	yes	SLDMD	NTZ 300mg	627	2.57	35.60	8.50	2.30	1.20	NA	NA	5.00	NA
				Placebo	Placebo	315	2.03	36.70	7.80	2.30	1.20	NA	NA	6.00	NA
FTY720 D2201 [32]	2006	SIENA	yes	SLDMD	FIN 1,25mg	93	3.00	38.00	NA	2.70	NA	1.30	NA	8.60	NA
				SLDMD	FIN 5mg	92	2.45	38.30	NA	2.50	NA	1.30	NA	9.50	NA
				Placebo	Placebo	92	1.94	37.10	NA	2.60	NA	1.20	NA	8.40	NA
Hardmeier [33]	2005	BPF	no	FLDMD	IFNB1a 30µg or 60µg	386	NA	37.00	7.40	3.50	NA	NA	NA	7.30	5.70
Frank [34]	2004	BV	no	FLDMD	IFN-B1b	30	NA	NA	NA	2.80	2.10	NA	NA	NA	NA
PRISMS [35]	2003	BPV	yes	FLDMD	IFN-B1a 22µg or 44µg	13	2.33	32.00	NA	2.00	NA	NA	NA	4.00	NA
				Placebo	Placebo	7	2.33	32.00	NA	2.00	NA	NA	NA	4.00	NA
Paolillo [36,37]	2002	SBV	yes	FLDMD	IFN-B1a 33µg	57	2.33	30.20	7.70	2.00	1.20	1.60	1.20	5.20	2.80
EUROPEAN / CANADIAN [38,39]	2001	CBV	yes	FLDMD	AG 20mg	113	3.35	34.40	7.40	2.30	1.10	NA	NA	8.00	5.55
				Placebo	Placebo	114	2.68	34.00	7.60	2.40	1.20	NA	NA	8.30	5.58
MSCRG [40,41]	2000	BPF	yes	FLDMD	IFN-B1a	68	NA	36.50	7.20	2.32	0.79	NA	NA	6.60	5.80
				Placebo	Placebo	72	NA	36.40	7.10	2.38	0.91	NA	NA	6.20	5.50
COPOLYMER I [42,43]	2000	BPV	yes	FLDMD	AG 20mg	14	NA	37.10	NA	3.00	NA	NA	NA	5.20	NA
				Placebo	Placebo	13	NA	34.40	NA	2.40	NA	NA	NA	4.20	NA

EDSS: Expanded Disability Status Scale; ARR: Annual Relapse Rate; Duration: disease duration between first relapse or diagnostic; SD: Standard Deviation; SIENA: Structural Image Evaluation, using Normalisation, of Atrophy; BPF: Brain Parenchymal Fraction; CTh: Cortical Thickness; BPFV: Brain Parenchymal Fraction Volume; SBV: Supratentorial Brain Volume; CBV: Central Brain Volume; BV: Brain Volume; BPV: Brain Parenchymal Volume; DMD: Disease Modifying Drug; FLDMD: First-line DMD; SLDMD, Second-line DMD; GA, Glatiramer Acetate; IFN: Interferon; TER: Terifluomide; LAQ: Laquinimod; BG-12: dimethyl fumarate; NTZ: Natalizumab; FIN: Fingolimod; ALM: Alemtuzumab; DAC: Daclizumab; NA: Not Available.

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