

Trial	Comparison	N° patients	Follow-up	Mean Time	Baseline Age	Mean EDSS	ARR Exp.	ARR control	ARR ratio	Rec. ARR ratio	CDP Exp.	CDP control	CDP ratio	Rec. CDP ratio
Achiron et al.	IVIg vs PBO	40	2.00	4.03	34.60	2.86	0.590	1.610	0.366	0.366	0.137	0.171	0.801	0.801
Calabresi et al.	Intf-1A Pegylated 2 weeks vs PBO	1012	0.92	6.60	36.60	2.46	0.256	0.397	0.645	0.645	0.0680	0.1050	0.648	0.648
	INFB-1A Pegylated 4 weeks vs PBO	1000	0.92	6.40	36.35	2.46	0.288	0.397	0.725	0.725	0.0680	0.1050	0.648	0.648
Polman et al.	Natalizumab vs PBO	942	2.30	5.50	36.15	2.30	0.23	0.73	0.315	0.315	0.1700	0.2900	0.586	0.586
Comi et al.	Laquinimod vs PBO	1106	2.00	8.70	38.70	2.60	0.30	0.39	0.769	0.769	0.1110	0.1570	0.707	0.707
Barkhof et al.	Ibudilast 30mg vs PBO	194	1.00	5.55	35.60	3.30	0.90	0.90	1.000	1.000	0.0530	0.0800	0.66	0.663
	Ibudilast 60mg vs PBO	198	1.00	5.75	35.95	3.35	0.70	0.90	0.778	0.778	0.0410	0.0800	0.51	0.513
Baumhackl et al.	Hydrolytic enzymes vs PBO	291	2.00	5.90	36.30	2.90	0.63	0.74	0.851	0.851	0.2800	0.2600	1.077	1.077
O'Connor et al.	INFB-1B 250 µg SC vs GA	1345	2.00	5.20	35.50	2.32	0.360	0.340	1.059	0.667	0.2100	0.2000	1.050	0.714
	INFB-1B 500 µg SC vs GA	1347	2.00	5.25	35.55	2.31	0.330	0.340	0.971	0.611	0.2200	0.2000	1.100	0.748
Vollmer et al.	Laquinimod vs PBO	884	2.00	4.80	37.10	2.50	0.280	0.340	0.824	0.824	0.1000	0.1300	0.769	0.769
	INFB-1A 30 µg IM vs PBO	897	2.00	5.00	38.00	2.50	0.260	0.340	0.765	0.765	0.1100	0.1300	0.846	0.846
CAMMS223	Alemtuzumab 12 mg vs INFB-1A44 µg	223	3.00	1.35	32.35	1.90	0.110	0.360	0.306	0.196	0.1630	0.3270	0.498	0.334
	Alemtuzumab 24 mg vs INFB-1A44 µg	221	3.00	1.30	32.50	1.95	0.080	0.360	0.222	0.142	0.1140	0.2600	0.438	0.294
Cohen et al.	Alemtuzumab 12 mg vs INFB-1A44 µg	563	2.00	2.05	33.10	2.00	0.18	0.39	0.462	0.295	0.0800	0.1112	0.719	0.482
Coles et al.	Alemtuzumab 12 mg vs INFB-1A 44 µg	628	2.00	4.60	35.30	2.70	0.26	0.52	0.500	0.320	0.1271	0.2113	0.602	0.403
Clanet et al.	INFB-1A 30 µg vs INFB-1A 60	802	3.00	6.55	36.80	3.60	0.77	0.81	0.951	0.789	0.2700	0.2700	1.000	0.740

	µg													
Giovannoni et al.	Cladribine 3.5 mg/kg vs PBO	870	1.85	8.40	38.30	2.85	0.14	0.33	0.424	0.424	0.1430	0.2060	0.694	0.694
	Cladribine 5.25mg/kg vs PBO	893	1.85	9.10	38.90	2.95	0.15	0.33	0.455	0.455	0.1510	0.2100	0.719	0.719
Lublin et al.	INFB-1A 30 µg vs GA	509	3.00	1.20	38.30	1.95	0.160	0.110	1.455	0.916	0.2160	0.2480	0.871	0.592
	INFB-1A 30 µg + GA vs GA	758	3.00	1.10	38.05	1.90	0.120	0.110	1.091	0.687	0.2390	0.2480	0.964	0.655
Fox et al.	Dimethyl fumarate 240 mg BID vs PBO	722	2.00	4.85	37.35	2.60	0.224	0.401	0.559	0.559	0.1280	0.1690	0.757	0.757
	Dimethyl fumarate 240 mg TID vs PBO	708	2.00	4.70	37.35	2.55	0.198	0.401	0.494	0.494	0.1300	0.1690	0.769	0.769
	GA vs PBO	713	2.00	4.60	36.80	2.60	0.286	0.401	0.713	0.713	0.1560	0.1690	0.923	0.923
kappos et al.	Daclizumab HYP 150 mg vs INFB-1A 30 µg IM	1841	2.77	6.95	36.30	2.50	0.22	0.39	0.564	0.468	0.1600	0.2000	0.800	0.592
Gold et al.	Dimethyl fumarate 240 mg BID vs PBO	818	1.84	5.70	38.30	2.44	0.170	0.360	0.472	0.472	0.1600	0.2700	0.593	0.593
	Dimethyl fumarate 240 mg TID vs PBO	824	1.84	5.45	38.65	2.42	0.190	0.360	0.528	0.528	0.1800	0.2700	0.667	0.667
Massacesi et al.	AZA vs INFB	150	2.00	6.25	37.35	1.90	0.27	0.41	0.659	0.435	0.0180	0.0800	0.225	0.158
EUPMS	INFB-1B 250 µg SC vs PBO	718	2.75	13.10	41.30	5.15	0.44	0.64	0.688	0.688	0.3890	0.4970	0.783	0.783
Panitch et al.	INFB-1A 44 µg SC vs INFB-1A30 µg	677	0.92	4.05	37.85	2.00	0.54	0.64	0.844	0.700	0.1268	0.1450	0.874	0.647
Fazekas et al.	IVIg vs PBO	148	2.00	7.05	37.00	3.30	0.52	1.26	0.413	0.413	0.1600	0.2300	0.696	0.696
Freedman et al.	MBP8298 vs PBO	513	2.00	9.22	49.75	5.56	0.13	0.14	0.93	0.929	0.3070	0.2780	1.10	1.104
Kappos et al.	Fingolimod 0.5 mg vs PBO	843	2.00	8.05	36.90	2.40	0.180	0.400	0.450	0.450	0.1770	0.2410	0.734	0.734
	Fingolimod 1.25 mg vs PBO	847	2.00	8.25	37.30	2.45	0.160	0.400	0.400	0.400	0.1660	0.2410	0.689	0.689
Calabresi et al.	Fingolimod 0.5 mg vs PBO	713	2.00	10.50	40.35	2.40	0.210	0.400	0.525	0.525	0.2530	0.2900	0.872	0.872

	Fingolimod 1.25 mg vs PBO	725	2.00	10.70	40.50	2.45	0.200	0.400	0.500	0.500	0.2170	0.2900	0.748	0.748
Gonset et al.	Inosine + INFB-1B 250 µg SC	157	2.00	6.35	37.95	2.30	0.580	0.380	1.526	0.992	0.1778	0.1818	0.978	0.567
Havrodva et al.	INFB-1A 30 µg + AZA+ MPRED vs INFB-1A30 µg	123	2.00	5.25	30.65	1.90	0.730	1.050	0.695	0.577	0.1750	0.1680	1.042	0.771
	INFB-1A 30 µg IM + AZA vs INFB-1A 30 µg IM	118	2.00	5.25	29.90	1.85	0.910	1.050	0.867	0.719	0.2070	0.1680	1.232	0.912
Hommes et al.	IVIG vs PBO	318	2.25	14.20	43.50	5.24	0.46	0.46	1.000	1.000	0.4840	0.4400	1.100	1.100
IFNB	INFB-1B 8 mIU SC vs PBO	247	3.00	4.30	35.60	2.90	0.840	1.210	0.694	0.694	0.2000	0.2800	0.714	0.714
	INFB-1B 1.6 mIU SC vs PBO	248	3.00	4.30	35.50	2.85	1.050	1.210	0.868	0.868	0.2800	0.2800	1.000	1.000
Durelli et al.	INFB-1B 250 µg SC vs INFB-1A 30 µg IM	188	2.00	6.30	36.85	1.97	0.50	0.70	0.714	0.593	0.1300	0.3000	0.433	0.321
Johnson et al.	GA vs PBO	251	2.00	6.95	34.45	2.60	0.590	0.840	0.702	0.702	0.2160	0.2460	0.878	0.878
Lenercept	Lenercept 10mg vs PBO	88	0.92	NA	35.55	2.49	1.00	0.98	1.020	1.020	0.7045	0.6744	1.045	1.045
	Lenercept 50mg vs PBO	84	0.92	NA	35.80	2.64	1.64	0.98	1.673	1.673	0.7750	0.6744	1.149	1.149
	Lenercept 100mg vs PBO	84	0.92	NA	35.70	2.50	1.47	0.98	1.500	1.500	0.7750	0.6744	1.149	1.149
Ravnborg et al.	MPRED + INFB-1A 30 µg IM vs INFB-1A 30µg	338	3.00	1.30	37.65	2.00	0.21	0.33	0.636	0.528	0.2573	0.2754	0.934	0.691
Milanese et al.	AZA vs PBO	40	3.00	7.50	29.55	3.29	0.55	0.73	0.750	0.750	0.3800	0.8200	0.463	0.463
Millefiorini et al	Mitoxantrone 12 mg/m2 vs PBO	51	2.00	5.50	29.80	3.55	0.45	1.31	0.340	0.340	0.0700	0.3700	0.189	0.189
Milligan et al.	Isoprinosine vs PBO	26	2.00	8.50	39.75	2.25	0.59	0.72	0.819	0.819	0.2500	0.2222	1.125	1.125
Hartung et al.	Mitoxantrone 12 mg/m2vs PBO	124	2.00	9.95	39.98	4.57	0.35	1.02	0.343	0.343	0.0800	0.2200	0.364	0.364
	Mitoxantrone 5 mg/m2 vs PBO	128	2.00	9.65	39.97	4.67	0.60	1.02	0.593	0.593	0.1400	0.2200	0.636	0.636
Jacobs et al.	INFB-1A 30 µg IM vs PBO	301	2.00	6.50	36.80	2.35	0.61	0.90	0.678	0.678	0.2110	0.3330	0.634	0.634
Panitch et al.	INFB-1B 250 µg SC vs PBO	625	3.00	14.75	46.85	5.15	0.16	0.28	0.571	0.571	0.3200	0.3400	0.941	0.941

	INFB-1B 160 µg SC vs PBO	622	3.00	14.70	47.20	5.10	0.20	0.28	0.714	0.714	0.3900	0.3400	1.147	1.147
Andersen et al.	INFB-1A 22 µg vs PBO	364	3.00	14.30	47.75	4.85	0.25	0.27	0.926	0.926	0.4140	0.3820	1.084	1.084
Sorensen et al.	MPRED + INFB-1A 44 µg vs INFB-1A 44 µg	130	1.85	7.70	38.65	2.70	0.22	0.59	0.373	0.239	0.1600	0.2500	0.640	0.429
O'Connor et al.	Teriflunomide 14mg vs PBO	118	0.69	4.90	39.65	2.25	0.55	0.81	0.679	0.679	0.0740	0.2130	0.347	0.347
Montalban et al.	Cladribine 3.5 mg(kg + INFB vs INFB	172	1.85	10.41	39.30	2.95	0.12	0.32	0.375	0.248	0.1530	0.1250	1.224	0.894
Hauser et al.	Ocrelizumab 600 mg vs INFB-1A 44 µg	821	1.85	6.50	37.00	2.81	0.16	0.29	0.552	0.353	0.0760	0.1220	0.623	0.417
Hauser et al.	Ocrelizumab(600 mg vs INFB-1A 44 µg	835	1.85	6.70	37.30	2.81	0.16	0.29	0.552	0.353	0.1060	0.1510	0.702	0.470
Pöhlau et al.	IVIg vs PBO	231	2.00	14.95	47.95	5.55	0.51	0.59	0.864	0.864	0.4800	0.6300	0.762	0.762
PRISMS	INFB-1A 44 µg vs PBO	371	2.00	5.35	35.10	2.45	0.870	1.280	0.680	0.680	0.2935	0.4118	0.713	0.713
	INFB-1A 22 µg vs PBO	376	2.00	4.85	34.70	2.45	0.910	1.280	0.711	0.711	0.3386	0.4118	0.822	0.822
Mikol et al.	GA vs INFB-1A 44 µg	764	1.84	6.24	36.75	2.34	0.29	0.30	0.967	0.619	0.0870	0.1170	0.744	0.498
Gold et al.	Daclizumab HYP 150 mg SC vs PBO	412	1.00	2.50	35.95	2.75	0.21	0.46	0.457	0.457	0.0600	0.1300	0.462	0.462
	Daclizumab HYP 300 mg vs PBO	413	1.00	2.50	35.90	2.70	0.23	0.46	0.500	0.500	0.0800	0.1300	0.615	0.615
Rudick et al.	Natalizumab + INFB-1A 30 µg vs INFB-1A 30 µg	1171	2.30	7.50	38.95	2.45	0.34	0.75	0.453	0.376	0.2300	0.2900	0.793	0.587
Sorensen et al.	SIMV + INFB-1A 30 µg vs INFB-1A 30 µg	307	3.00	1.25	36.55	1.69	0.19	0.14	1.306	1.084	0.2800	0.2400	1.167	0.863
O'Connor et al.	Teriflunomide 14 mg vs PBO	722	2.07	8.65	38.10	2.68	0.370	0.540	0.685	0.685	0.2020	0.2730	0.740	0.740
	Teriflunomide 7 mg vs PBO	729	2.07	8.70	37.90	2.68	0.370	0.540	0.685	0.685	0.2170	0.2730	0.795	0.795
Confavreux et al.	Teriflunomide 14 mg vs PBO	761	0.92	7.91	38.15	2.70	0.32	0.50	0.640	0.640	0.1189	0.1675	0.710	0.710
	Teriflunomide 7 mg vs PBO	797	0.92	7.91	37.75	2.70	0.39	0.50	0.780	0.780	0.1597	0.1675	0.953	0.953
Cohen et al.	Fingolimod 0.5 mg vs INFB-1A	860	1.00	7.45	36.35	2.20	0.16	0.33	0.485	0.402	0.0590	0.0790	0.747	0.553

30 µg IM

Fingolimod 1.25 mg vs INFB-1A 857 1.00 7.35 35.90 2.20 0.20 0.33 0.606 0.503 0.0670 0.0790 0.848 0.628  
30 µg IM

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**Supplementary table** - Clinical trials used in the analyses

Abbreviations: ARR: annualized relapse rate; AZA: azathioprine; INFB: interferon beta; Rec.: recalculated; CDP: confirmed disability progression; SIMV:

simvastatine; MPRED: methylprednisone