Comparison of the 8-year outcomes of Interferon treatments for relapsing multiple sclerosis

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Introduction. Interferon-β is a safe and effective Disease Modifying Treatment (DMT) for Relapsing-Remitting Multiple Sclerosis (RRMS). However, different Interferon-β formulations have never been compared for their long-term effects and, in particular, for their efficacy in preventing disability accrual.

Figure 1. Patient disposition flow diagram.

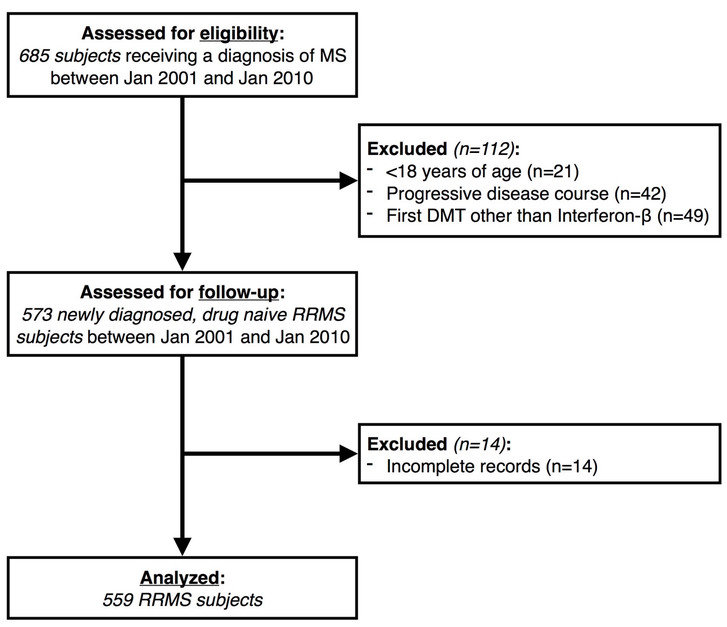


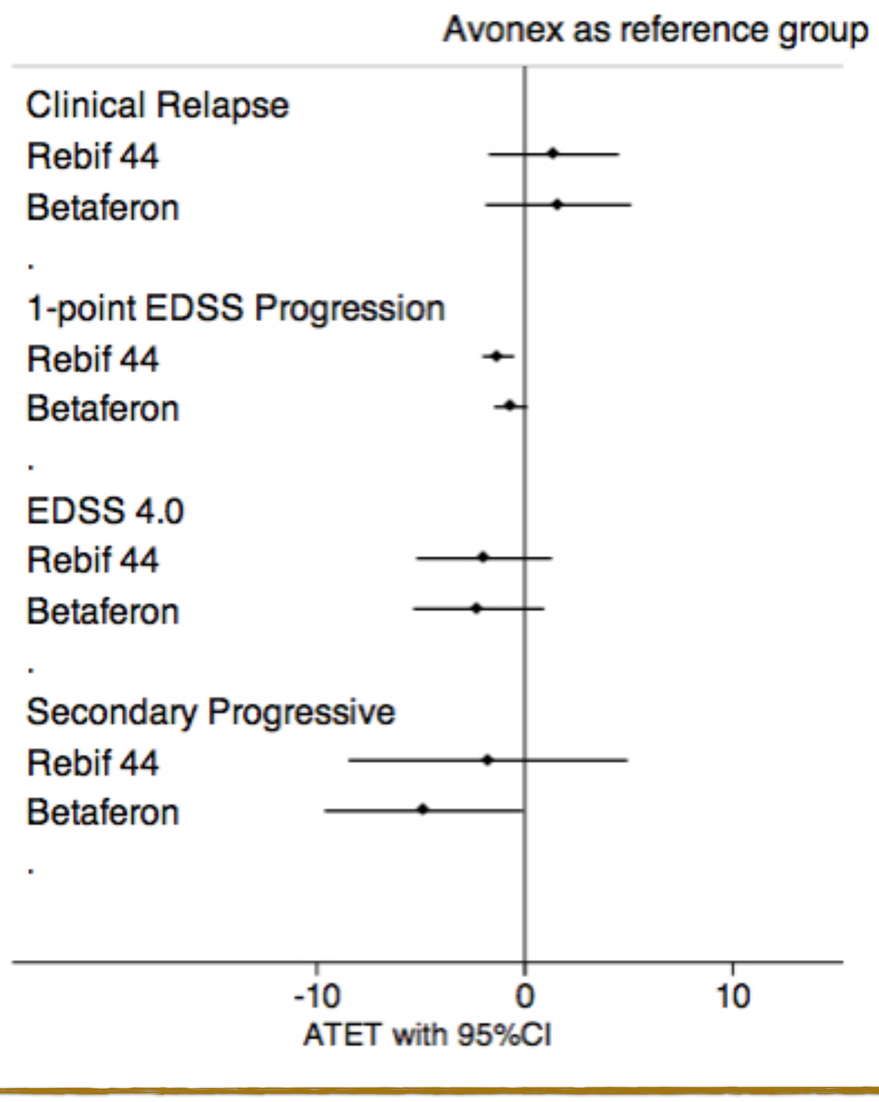
Table 1. Demographic features and clinical findings are reported for different treatment groups. P-values are shown from χ2 test, or analysis of variance, as appropriate (*: p<0.05).

	Avonex (n=202)	Rebif 44 (n=160)	Betaferon (n=148)	*p-values*
Age, *years*	33.40±8.4	31.7±7.9	31.0±8.4	0.018*
Gender, *female (%)*	132 (65.7%)	97 (60.6%)	93 (62.8%)	0.609
Disease duration at diagnosis, *years*	2.7±2.6	2.9±2.7	2.5±2.7	0.493
EDSS at diagnosis	2.0±0.6	2.2±0.6	2.1±0.6	0.094
Relapse occurrence *(%)*	146 (72.3%)	107 (66.9%)	93 (62.8%)	0.166
1-point EDSS progression *(%)*	172 (85.1%)	137 (85.6%)	120 (81.1%)	0.483
Reaching of EDSS 4.0 *(%)*	92 (45.5%)	75 (46.8%)	68 (45.9%)	0.968
Conversion to SP *(%)*	39 (19.6%)	26 (16.2%)	30 (20.7%)	0.631

EDSS: Expanded Disability Status Scale; SP: Secondary Progressive.

Methods. The present retrospective analysis of prospectively collected data included 509 newly diagnosed, drug-naïve RRMS patients (female=322, 62.2%; age 32.1±8.3 years) who received Interferon-β as first DMT during an average period of 8.0±3.9 years. Patients were categorized if receiving low-dose intramuscular Interferon-β1a (Avonex, n=201, 39.6), high-dose subcutaneous Interferon-β1a (Rebif 44, n=160, 31.4%), %), or Interferon-β1b (Betaferon, n=148, 29.0%). Following study outcomes were recorded: relapse occurrence, 1-point EDSS progression, reaching of EDSS 4.0, and SP conversion.
In order to account for possible confounders when assigning the treatment, we employed the propensity score inverse-probability-weighting regression adjustment method accounting for the censoring nature of our dataset. Covariates considered for the latter models were age, gender, disease duration and EDSS at diagnosis. Estimated average treatment effect on the treated (ATET) and 95% confidence intervals (CI) were estimated for relapse occurrence (time to the first relapse), 1-point EDSS progression, reaching of EDSS 4.0, and conversion to SP, in different treatment groups (low-dose intramuscular Interferon-β1a was considered the reference for statistical analyses).

Figure 2. Forest plot showing study outcomes in relation to different treatments (Avonex was utilized as reference group for statistical analyses). ATET: Average Treatment Effect on the Treated; 95%CI: 95% Confidence Intervals.



Results. A lower proportion of patients treated with high-dose subcutaneous Interferon-β1a presented a 1-point EDSS progression, compared to low-dose intramuscular Interferon-β1a (ATET=-1.27; 95%CI=-2.03--0.51). A lower proportion of patients treated with Interferon-β1b converted to SP, compared to low-dose intramuscular Interferon-β1a (ATET=-4.86; 95%CI=-9.62--0.10). No differences were found with regard to relapse occurrence and reaching of EDSS 4.0.

Table 2. Effect of different Interferon-β formulations on clinical outcomes is reported (Avonex group was utilized as reference group for statistical analyses). ATET, 95%CI and p-values are shown (*: p<0.05).

Avonex *(as reference)*	Rebif 44				Betaferon			
	ATET	*95%CI*		*p-values*	*ATET*	*95%CI*		*p-values*
		Lower	*Upper*			*Lower*	*Upper*	
Relapse occurrence	1.38	-1.74	4.50	0.381	1.61	-1.88	5.11	0.360
1-point EDSS progression	-1.27	-2.03	-0.51	0.001*	-0.67	-1.47	0.12	0.099
Reaching of EDSS 4.0	-1.97	-5.22	1.27	0.234	-2.23	-5.38	0.90	0.163
Conversion to SP	-1.77	-8.48	4.92	0.604	-4.86	-9.62	-0.10	0.045*

ATET: Average Treatment Effect on the Treated; 95%CI: 95% Confidence Intervals; EDSS: Expanded Disability Status Scale; SP: Secondary Progressive.

Conclusions. Interferon-β formulations have a comparable efficacy on early inflammatory activity. However, high-dose subcutaneous Interferon-β1a and Interferon-β1b might be able to reduce short and long-term disability accrual, possibly due to an effect at least in part dependent of the dosage and the frequency of administration.

Selected References. Kappos L, Kuhle J, Multanen J, et al. Factors influencing long-term outcomes in relapsing–remitting multiple sclerosis: PRISMS-15. *J Neurol Neurosurg Psychiatry*. 2015;86(11):1202-1207.

Mendes D, Alves C, Batel-Marques F. Benefit-Risk of Therapies for Relapsing-Remitting Multiple Sclerosis: Testing the Number Needed to Treat to Benefit (NNTB), Number Needed to Treat to Harm (NNTH) and the Likelihood to be Helped or Harmed (LHH): A Systematic Review and Meta-Analysis. *CNS Drugs* 2016.

Signori A, Gallo F, Bovis F et al. Long-term impact of interferon or Glatiramer acetate in multiple sclerosis: A systematic review and meta-analysis. *Mult Scler Relat Disord* 2016;6:57-63.