A lesion topography-based approach to refine the value of new active lesions in predicting response to Interferon Beta in multiple sclerosis

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BACKGROUND

Several studies have suggested that the short-term treatment effect on magnetic resonance imaging (MRI) measures may predict the longer-term response to Interferon Beta (IFNB) in patients with multiple sclerosis (MS).

However, none of these studies estimated whether the topography of new lesions occurred early on-treatment may affect their predictive value in assessing the response to IFNB treatment.

PURPOSE

To estimate the predictive value of GD-enhancing and new T2-hyperintense lesions, as evaluated after one year from IFNB start, on the risk of clinical relapses and longer-term disability, by modelling the analysis for lesion topography (supratentorial, infratentorial or spinal cord level).

METHODS

Study design: independent, single-center, post-marketing study.

Participants: Patients starting any formulation of IFNB treatment between 2005 and 2010 as first-line disease-modifying treatment.
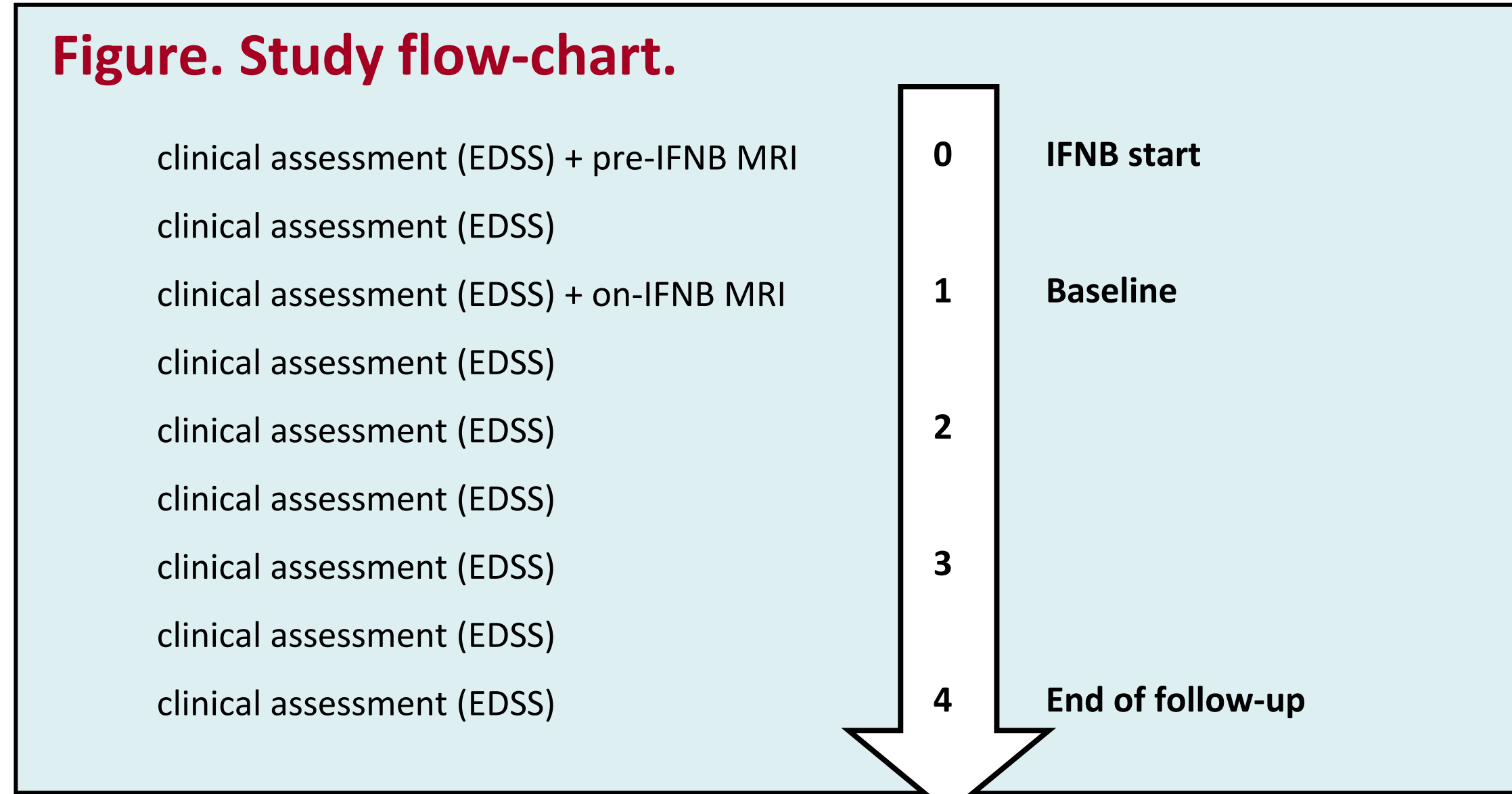
Follow-up: year 1 to 4 from treatment start.

Assessments: demographic data were collected at IFNB start, clinical data were collected every 6 months; MRI data were collected at IFNB start and at 1 year of therapy (see the figure below).

The count and location of gadolinium-enhancing and new T2-hyperintense lesions were performed by two expert operators on the images acquired at 1 year of treatment compared with the pre-IFNB scan. In case of disagreement, the questioned lesion was not included in the lesion count.

Outcomes: occurrence of relapses and sustained disability worsening, i.e. an increase of 1.0 point or more at the Expanded Disability Status Scale (EDSS) score, from year 1 to 4 of follow-up.

Statistical analysis: Cox proportional hazards models (stepwise fashion) were built to investigate the best combination of 1-year demographic, clinical and MRI predictors of relapses and disability worsening. The main time variable was defined as the period in years elapsed between IFNB start and last visit, or therapy discontinuation, or outcome reach, whichever came first. Both models were stratified by IFNB type.

Figure. Study flow-chart.

clinical assessment (EDSS) + pre-IFNB MRI	0	IFNB start
clinical assessment (EDSS)		
clinical assessment (EDSS) + on-IFNB MRI	1	Baseline
clinical assessment (EDSS)		
clinical assessment (EDSS)	2	
clinical assessment (EDSS)		
clinical assessment (EDSS)	3	
clinical assessment (EDSS)		
clinical assessment (EDSS)	4	End of follow-up

RESULTS

Data from 390 patients (269 F, 121 M) with a mean age of 32.5 ± 8.7 years, median disease duration of 2 years (range <1-25), mean number of pre-IFNB relapses of 1.4 ± 0.7 (1-4) and median EDSS score of 1.5 (range 0-3.5) were collected.

One-year data: 48 (12.3%) patients relapsed during the first year of IFNB treatment; 43 (11.1%) patients had gadolinium-enhancement at 1-year MRI scan; when compared with the pre-IFNB scan, 67 (17.2%) patients had new T2 lesions (1 new lesion, n=17; 2 new lesions, n=29; ≥3 new lesions, n=21).

New lesions were observed in either spinal cord, infratentorial and/or supratentorial areas in 28, 18 and 43 patients, respectively.

Four-year outcomes: 160 (41.0%) and 65 (16.5%) patients experienced ≥1 relapses and sustained disability worsening, respectively, from year 1 to 4 of follow-up.

Predictors of clinical relapses (A) and sustained disability worsening (B) from year 1 to 4 are shown in the tables below.

(A) Variables	HR (95% CIs)	p
Age (each year)	0.98 (0.96-0.99)	**0.03**
Relapses 1Y	1.71 (1.11-2.62)	**0.01**
New T2 lesion count 1Y		
0	Ref.	-
1	1.42 (0.73-2.74)	0.29
2	1.67 (0.98-2.83)	0.06
3+	2.64 (1.55-4.49)	**<0.001**

(B) Variables	HR (95% CIs)	p
Male gender	1.9 (1.1-3.3)	**0.02**
EDSS score (each step)	2.1 (1.6-2.8)	**<0.001**
Relapses 1Y	2.9 (1.6-5.2)	**0.001**
New infratentorial lesions 1Y	2.6 (1.2-5.6)	**0.01**
New spinal cord lesions 1Y	2.3 (1.1-4.8)	**0.02**

DISCUSSION

The present study suggests that lesion count at 1 year of IFNB treatment was associated with future relapses, regardless of the lesion topography. By contrast, the lesion location was associated with future disability, regardless of the number of new T2 lesions.

These findings support the notion of a worse prognosis in patients developing new lesions in sites representing anatomical bottle-necks.

Lastly, while the occurrence of clinical relapses in the first IFNB year was associated with both future relapses and disability, the presence of gadolinium enhancement at one-year MRI scan did not contribute to better fit the models.