



Using plasma neurofilament light chain to evaluate response during cladribine treatment in multiple sclerosis



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OBJECTIVE

Cladribine treatment in year 1 and 2 provides high efficacy on multiple sclerosis (MS) outcomes over 4 years. Some patients might have re-emerging disease activity and need additional treatment.

The use of biomarkers of neuro-axonal damage, such as plasma neurofilament light chain (pNfL), might support prognostication and treatment decisions.

This Study aims to:

1. To investigate pNfL variations over time in people with MS treated with cladribine;
2. To compare pNfL levels during cladribine treatment to age- and sex-matched controls
3. To assess pNfL prediction on clinical and radiological outcomes.

METHODS

Retrospective study.

We included 258 people with MS treated with cladribine and 304 age and sex-matched controls.

pNfL was evaluated using Lumipulse™ fully automated chemiluminescent enzyme immunoassay.

For MS cases, we collected evidence of disease activity (EDA3, including relapses, active MRI, and EDSS progression) following pNfL measurement.

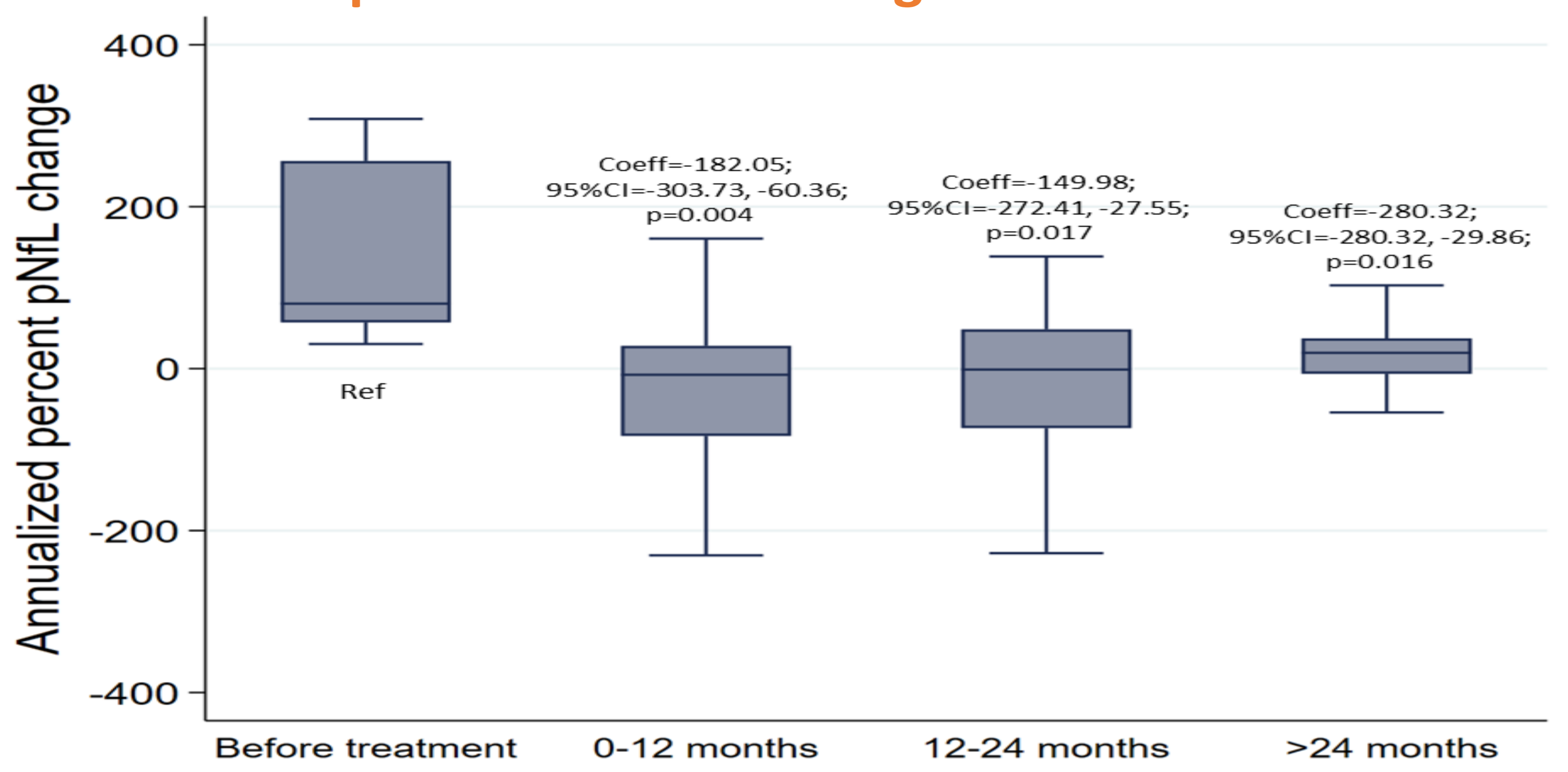
Multivariate linear regression models to investigate pNfL variations over time in people with MS treated with cladribine.

Linear and logistic regression models to compare pNfL levels during cladribine treatment to age- and sex-matched controls for each cladribine timing subgroup.

Cox regression models To assess pNfL prediction of clinical and radiological outcomes

RESULTS

pNfL variations during cladribine



Predictive value of pNfL levels during cladribine

	Adjusted models			
	HR	95% CI		P Value
Baseline pNfL				
Relapse	0.71	0.46	1.09	0.115
MRI activity	2.52	/	/	0.957
EDSS progression	0.95	0.77	1.18	0.675
EDA3	0.91	0.80	1.05	0.190

Table shows hazard ratios (HR), 95% confidence intervals (95% CI), and *p* values from Cox regression models including, in turn, relapses, active MRI, and EDSS progression and evidence of disease activity (EDA3) as independent variable, and pNfL levels as dependent variable; covariates were age, sex, presence of cardiovascular comorbidities, smoking, descriptor of disease progression (relapsing or progressive), EDSS at baseline, and cladribine timing subgroup.

MS cases vs controls

When compared with matched controls, we found higher pNfL in MS cases before cladribine treatment (Coeff= 7.43; 95%CI=2.45, 12.40; *p*=0.004) and similar pNfL in MS cases in the 12 months after year 1 cladribine treatment (Coeff= -1.04; 95%CI=-3.36, 1.28; *p*=0.376); in MS cases in the 12 months after year 2 cladribine treatment (Coeff= 1.48; 95%CI=-0.60, 3.35; *p*=0.162) and in MS cases over year 3 and 4 after cladribine treatment (Coeff= 2.30; 95%CI=-0.47, 5.08; *p*=0.103).

When compared with matched controls, MS cases before cladribine treatment had 7-fold higher probability of pNfL above normality values (OR = 7.22; 95%CI = 1.19, 43.98; *p* = 0.032); no associations were found for MS cases in the 12 months after year 1 cladribine treatment (OR = 0.91; 95%CI = 0.42, 2.04; *p* = 0.840); for MS cases in the 12 months after year 2 cladribine treatment (OR = 1.64; 95%CI = 0.95, 2.82; *p* = 0.076), and for MS cases over year 3 and 4 after cladribine treatment (OR = 2.10; 95%CI = 0.83, 5.27; *p* = 0.115).

CONCLUSIONS

In our real-world study, we showed that pNfL levels decrease during cladribine treatment, until reaching and maintaining for an extended period of time levels comparable to age- and sex-matched controls.

We also confirmed the high efficacy of cladribine, with only a minority of patients having relapses (2.75%), disability progression (1.55%) or MRI activity (0.39%).

During the follow-up of people with MS treated with cladribine, decision of retreatment could be guided by the presence of pNfL above normality values.

In particular, Cladribine reduced pNfL from its first dosing, suggesting reduced neuro-axonal damage, up to levels in line with age- and sex-matched controls. These results confirm the high efficacy of cladribine on inflammatory outcomes (which were reached by a minority of patients in our cohort), while other biomarkers should be considered to predict disability progression.

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