Long-term effect of interferon-β and glatiramer acetate in real-world settings on disability progression: input of time-dependent propensity score

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Background: The long-term effect of beta-interferon (β-IFN) and glatiramer acetate (GA) on multiple sclerosis (MS) disability progression showed controversial results, maybe due to lack of appropriate control of confounding. Indeed, the baseline date, i.e. time of therapeutic decision, is difficult to define when controls are untreated.

Objective: To assess the long-term effect of IFN and GA on disability progression in relapsing-remitting MS patients from the Rennes expert MS centre, France.

Methods: In this retrospective cohort study, we used time-dependent propensity score (PS) using a Cox model to assess the time from MS onset (baseline) to treatment start. The model was adjusted on gender, age, and EDSS score and relapse occurrence as time-dependent covariates. Each IFN/GA-treated patient was matched to a not yet treated patient at the same time and having the same probability to be treated. The restricted mean times (RMTS) to reach an irreversible Expanded Disability Status Scale (EDSS) score of 3 and 6 were compared between the two groups in an intention-to-treat analysis.

Results: Among the 2315 included patients, 1007 were treated. Among them, 904 were matched with a not yet treated patient. The median follow-up duration was 14 years (Interquartile range (IQR): 11–19) for IFN/GA-treated patients and 15 years (IQR: 8-22) for IFN/GA-not yet treated patients. Over 20 years, the time to reach an irreversible EDSS score of 3 was delayed by 1 year in the IFN/GA-treated group (p=0.038). Studying the time to reach EDSS 6, there was no statistical difference between the two groups (p=0.893).

Discussion: Our results showed that IFN and GA delay disability progression at medium-term. Nevertheless, this study does not permit to conclude at long term. Use of the time-dependent PS seems relevant to well balance the two groups over time while conventional PS matching ignores the temporal features of the treatment.