Survival in MS: a randomized cohort study 21 years after the start of the pivotal IFNβ-1b trial.

OBJECTIVE: To examine the effects of interferon beta (IFNβ)-1b on all-cause mortality over 21 years in the cohort of 372 patients who participated in the pivotal randomized clinical trial (RCT), retaining (in the analysis) the original randomized treatment-assignments.

METHODS: For this randomized long-term cohort study, the primary outcome, defined before data collection, was the comparison of all-cause mortality between the IFNβ-1b 250 μg and placebo groups from the time of randomization through the entire 21-year follow-up interval (intention-to-treat, log-rank test for Kaplan-Meier survival curves). All other survival outcomes were secondary.

RESULTS: After a median of 21.1 years from RCT enrollment, 98.4%(366 of 372) of patients were identified, and, of these, 81 deaths were recorded (22.1% [81 of 366]). Patients originally randomly assigned to IFNβ-1b 250 μg showed a significant reduction in all-cause mortality over the 21-year period compared with placebo (p = 0.0173), with a hazard ratio of 0.532 (95% confidence interval 0.314-0.902). The hazard rate of death at long-term follow-up by Kaplan-Meier estimates was reduced by 46.8% among IFNβ-1b 250 μg-treated patients (46.0% among IFNβ-1b 50 μg-treated patients) compared with placebo. Baseline variables did not influence the observed treatment effect.

CONCLUSIONS: There was a significant survival
advantage in this cohort of patients receiving early IFNβ-1b treatment at either dose compared with placebo. Near-complete ascertainment, together with confirmatory findings from both active treatment groups, strengthens the evidence for an IFNβ-1b benefit on all-cause mortality.

CLASSIFICATION OF EVIDENCE: This study provides Class III evidence that early treatment with IFNβ-1b is associated with prolonged survival in initially treatment-naive patients with relapsing-remitting multiple sclerosis.

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