Background: PEGylation can enhance exposure to protein-based therapies while maintaining the safety and tolerability of the parent compound. A PEGylated form of interferon beta-1a (PEG IFNβ-1a) with enhanced in vivo activity, longer half-life, and prolonged exposure is being developed for treatment of MS. Objectives: The primary objective of this phase 3 study is to evaluate the efficacy of PEG IFNβ-1a in reducing relapse rate at 1 year. Secondary objectives include evaluation of magnetic resonance imaging (MRI) efficacy, the proportion of subjects who are relapse-free, quality of life, and disability progression. Methods: ADVANCE is a 2-year, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of subcutaneous PEG IFNβ-1a 125 μg administered every 2 or 4 weeks. Eligible patients must be 18 to 55 years old and have confirmed relapsing multiple sclerosis (MS) (McDonald criteria) with a baseline Expanded Disability Status Scale (EDSS) score of ≤5.0. Patients must have had ≥2 relapses within the last 3 years and ≥1 relapse 12 months prior to randomization. Approximately 1260 patients will be randomized 1:1:1 to receive placebo, PEG IFNβ-1a every 2 weeks, or PEG IFNβ-1a every 4 weeks. Patients on placebo will be rerandomized to PEG IFNβ-1a every 2 or 4 weeks after 1 year. Results: Efficacy of PEG IFNβ-1a versus placebo will be assessed using clinical relapses, MRI (± gadolinium), EDSS, Multiple Sclerosis Impact Scale–29 (MSIS-29) physical score, global impression of change, Multiple Sclerosis Functional Composite score, visual function, and the Symbol Digit Modality Test. Quality of life (QOL) will be assessed using a 12-item short-form health survey, EuroQoL questionnaire, and MSIS. Safety and tolerability will be evaluated throughout the study (physical and neurologic examinations, vital signs, electrocardiograms, clinical laboratory assessments, Beck Depression Inventory, immunogenicity, injection site assessments, adverse event reporting, concomitant medication use). Blood will be collected for population pharmacokinetic (PK) and pharmacodynamic, intensive PK, and other biomarker analyses. Conclusions: PEG IFNβ-1a is being developed to offer patients with MS the proven safety and efficacy of IM IFNβ-1a with improved convenience of administration and, as such, holds promise as a significant addition to the therapeutic armamentarium for MS treatments.

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