Efficacy and safety of peginterferon beta-1a in relapsing-remitting multiple sclerosis: 2-year data from the ADVANCE study

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Objectives

To further evaluate the efficacy and safety of investigational peginterferon beta-1a in patients with RRMS in the ADVANCE study, a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study.

Methods

In Year 1 of the Phase 3 ADVANCE study, patients received placebo or peginterferon beta-1a Q2W or Q4W for up to 12 months, followed by an extension study (ATTAIN) that continued treatment to 24 months. Patients received peginterferon beta-1a Q2W or Q4W from Months 13 to 24 in the ATTAIN study. Patients were randomized 1:1:1 to each of the three treatment groups at Months 0 and 12. Patients received peginterferon beta-1a Q2W or Q4W for up to 24 months. Patients who received peginterferon beta-1a Q2W or Q4W in Year 1 were re-randomized to peginterferon beta-1a Q2W or Q4W in Year 2; patients who received placebo in Year 1 were assigned to placebo, peginterferon beta-1a Q2W or Q4W in Year 2. The primary endpoint was time to sustained 24-week confirmed disability progression. Key secondary endpoints included risk of disability progression and relapse, number of new or newly-enlarging T2 lesions, and multiple other MRI and clinical endpoints.

Results

In Year 2 of the Phase 3 ADVANCE study, patients on placebo were re-randomized to peginterferon beta-1a 125 µg Q2W or Q4W. To further evaluate the efficacy and safety of investigational peginterferon beta-1a in patients with RRMS in the ADVANCE study, a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study.

In Year 1 of the Phase 3 ADVANCE study, patients received placebo or peginterferon beta-1a Q2W or Q4W for up to 12 months, followed by an extension study (ATTAIN) that continued treatment to 24 months. Patients received peginterferon beta-1a Q2W or Q4W from Months 13 to 24 in the ATTAIN study. Patients were randomized 1:1:1 to each of the three treatment groups at Months 0 and 12. Patients received peginterferon beta-1a Q2W or Q4W for up to 24 months. Patients who received peginterferon beta-1a Q2W or Q4W in Year 1 were re-randomized to peginterferon beta-1a Q2W or Q4W in Year 2; patients who received placebo in Year 1 were assigned to placebo, peginterferon beta-1a Q2W or Q4W in Year 2. The primary endpoint was time to sustained 24-week confirmed disability progression. Key secondary endpoints included risk of disability progression and relapse, number of new or newly-enlarging T2 lesions, and multiple other MRI and clinical endpoints.

In Year 2, the number of new or newly-enlarging T2 lesions, Gd+ lesions, and T1 hypointense lesions were significantly lower in patients who remained on peginterferon beta-1a compared to those who changed from placebo to peginterferon beta-1a. Risk of relapse over 2 years was significantly lower among patients who received continuous peginterferon beta-1a compared to patients who received placebo in Year 1 (Q2W, 39% reduction vs patients who received placebo in Year 1 and peginterferon beta-1a in Year 2; PEG-IFN = peginterferon; Q2W = every 2 weeks; Q4W = every 4 weeks; SE = standard error). Over 2 years, patients who received continuous peginterferon beta-1a had a reduced risk of 12-week confirmed disability progression by 35% compared to patients who received placebo in Year 1 (Q2W, 39% reduction vs patients who received placebo in Year 1 and peginterferon beta-1a in Year 2; PEG-IFN = peginterferon; Q2W = every 2 weeks; Q4W = every 4 weeks; SE = standard error). Across treatment groups, 86% to 94% of patients who initiated Year 2 completed Year 2. The majority of hepatic transaminase elevations were <3 times the upper limit of normal. The most common AEs (incidence ≥20% in any treatment group) in the Q2W and Q4W groups were injection site erythema, injection site pain, headache, fatigue, and upper respiratory tract infection.

Conclusions

The efficacy and safety of peginterferon beta-1a in relapsing-remitting multiple sclerosis was evaluated in the ADVANCE study, a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study. The study evaluated the efficacy and safety of peginterferon beta-1a in relapsing-remitting multiple sclerosis in a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study. The study evaluated the efficacy and safety of peginterferon beta-1a in relapsing-remitting multiple sclerosis in a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study. The study evaluated the efficacy and safety of peginterferon beta-1a in relapsing-remitting multiple sclerosis in a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study. The study evaluated the efficacy and safety of peginterferon beta-1a in relapsing-remitting multiple sclerosis in a 2-year, multicenter, randomized, double-blind, parallel-group, Phase 3 study with a 1-year placebo-controlled extension study.

References