Long-term efficacy and safety of ponesimod: Results from randomized phase II core and extension studies in relapsing-remitting multiple sclerosis

Short title: Long-term efficacy and safety of ponesimod

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Abstract

Background

Ponesimod, an orally active, selective sphingosine 1-phosphate receptor-1 (S1P) modulator, showed benefits in clinical and MRI outcomes in a double-blind, placebo controlled, phase 2b Core Study (NCT01006265). Patients rolled-over into an ongoing Extension Study (NCT01093326).

Objective

Evaluate the long-term efficacy and safety of ponesimod in patients with relapsing-remitting multiple sclerosis (RRMS).

Methods

A total of 435 patients with RRMS received ≥1 dose of ponesimod (10, 20, or 40-mg/day) during the Core and/or Extension Study. The 40 and 10-mg doses were subsequently discontinued during Treatment Period 1 (TP1) and TP2 of the Extension Study. All patients received 10 or 20-mg during TP2, followed by open-label 20-mg in TP3. Key efficacy

parameters: annualized relapse rate (ARR), 6-month confirmed disability accumulation (CDA), and MRI outcomes. Safety parameters: frequencies of adverse events (AEs) and serious AEs (SAEs). Results of combined analyses of Core and Extension studies are presented.

Results

As of 31 March 2019, 214 patients were still on ponesimod treatment; median exposure in 20-mg group was 8.02 years; Cumulative exposure across all doses was 2372.47 patients-years. In 20-mg group, ARR (95% CI) for confirmed relapses was 0.154 (0.111–0.214); 64.1% patients remained free of confirmed relapse; Kaplan-Meier estimate of 6- month CDA at Week 432 was 20.4% (13.7–29.7); Mean number of T1 gadolinium enhancing lesions per patient per scan was 0.448 (0.305–0.657); Mean number of new or enlarging T2 lesions per year was 0.718 (0.523–0.985). In ponesimod-treated patients, the most common treatment-emergent AEs were nasopharyngitis (30%), headache (24%) and upper respiratory tract infection (21%). Most SAEs were reported in a single patient, no SAE was reported at an incidence of >1%.

Conclusions

Long-term treatment with ponesimod 20 mg showed consistently low levels of disease activity across relevant clinical and MRI outcomes in patients with RRMS. No new safety signals were identified.