Introduction

Fingolimod 0.5 mg is a once-daily oral sphingosine 1-phosphate (S1P) receptor modulator in development for multiple sclerosis (MS). Therapeutic effects of fingolimod are mediated primarily via functional antagonism of S1P1 receptor signaling, with minimal effects on other circulating lymphocytes, thereby reducing the impact of immune-mediated inflammation.

Patients were randomized 1:1 to oral fingolimod or placebo for 36-60 months5

Rates (95% confidence interval [CI]) of infection-related AEs per 100 patient-years were similar between the overall fingolimod and placebo groups (Table 2), with the exception of respiratory tract infections, which were lower in the fingolimod group (Figure 1).

Objective

The primary aim of this analysis was to examine the relationship between absolute lymphocyte count (ALC) nadirs and the risk of infection-related AEs in patients with relapsing forms of multiple sclerosis (MS) treated with fingolimod 0.5 mg (study NCT00627003) over 36-60 months peri-study baseline and during on-study treatment periods.

Methods

Study design

All patients were aged 18-55 years with a clinical diagnosis of MS, a year of disease progression, and one or more relapses prior to fingolimod initiation (1.6 mg/d). This was a randomized, double-blind, placebo-controlled trial (Study NCT00627003) that recruited patients over 18 months in duration. This report includes data from a post hoc analysis of participants with available data on ALC nadirs.

Analyses

Rates of infection-related AEs were calculated for ALC nadirs ≥0.2 ×10⁹/L, ≤0.2 ×10⁹/L, ≤0.3 ×10⁹/L, ≤0.4 ×10⁹/L, or ≤0.5 ×10⁹/L, as well as for the overall fingolimod and placebo groups.

Results

Patients

In total, 1,007 patients received fingolimod 0.5 mg (mean exposure 18.1 patient-years) and 336 patients received placebo (mean exposure 18.3 patient-years).

Demographics and baseline characteristics were similar between treatment groups (Table 1). Patients had a median (interquartile range [IQR]) age of 45.0 (37.0-53.0) years, median (IQR) number of MS episodes 2.0 (1.0-3.0) episodes, median (IQR) Expanded Disability Status Scale (EDSS) score 3.5 (3.2-4.0), and median (IQR) disease duration since onset 7.0 (4.0-11.0) years.

Conclusions

These data demonstrate that there was no relationship between the magnitude of ALC reduction and risk of infection-related AEs in patients treated with fingolimod 0.5 mg. Further investigations are warranted to better understand the impact of reduced ALC on infection rates.