INTRODUCTION

Studies have shown that antibody-independent B-cell functions play an important role in the pathogenesis of MS, an altered innate immune system also contributes to progression.1  

Evobrutinib is a highly specific, oral inhibitor of Bruton’s tyrosine kinase (BTK) that inhibits B-cell activation and B-cell antigen receptor, decreasing plasma cell formation and auto-antibody production;2 3 it has shown to inhibit MT M-protein release and promote M2 polarization of human macrophages in vitro, and has demonstrated pharmacological efficacy in both B-cell and T-cell dependent mouse models of experimental autoimmune encephalomyelitis.4 5

OBJECTIVES

The objective of this ongoing double-blind, 48-week, phase 2 study (NCT02975349) is to compare the efficacy and safety of three evobrutinib doses with placebo in patients with clinically and radiologically active relapsing MS (RMS). We report the primary analysis of the study, conducted at 24 weeks.

METHODS

The study design is shown in Figure 1. 

Study Population

264 (91.4%) of 291 randomized patients completed 24 weeks of treatment. 

Baseline characteristics were balanced across groups (Table 1).

RESULTS

Primary Endpoint

Evobrutinib 75 mg QD and BID significantly reduced the number of T1 Gd+ lesions per patient per week compared with placebo (Figure 2; evidence of a dose-response relationship was observed (Table 2). 

Other Secondary Endpoints

A trend towards a reduction in ARR was seen with evobrutinib 75 mg QD and BID versus placebo (Figure 3; evidence of a dose-response relationship was observed (Table 3).

CONCLUSIONS

The primary endpoint was met: evobrutinib 75 mg QD and BID significantly reduced the number of T1 Gd+ lesions per patient per week compared with placebo. A trend towards a reduction in ARR was seen with evobrutinib 75 mg QD and BID. 

Treatment with evobrutinib was overall well-tolerated and none of the three doses investigated were associated with serious infections and infestations or lymphopaenia.

We have demonstrated for the first time the reduction in disease activity by BTK inhibitor in a randomized trial for RMS.

The observed benefit-risk profile of evobrutinib supports further clinical development; the 48-week analysis will allow exploration of long-term efficacy and safety.

REFERENCES