Phase 3 REMODEL I/II Trials: Effectiveness, Safety, and Tolerability of Remibrutinib in Patients with Relapsing Multiple Sclerosis

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Objective:
To present the design of the REMODEL I and II Phase 3 trials aimed to evaluate the efficacy, safety and tolerability of remibrutinib versus teriflunomide in patients with relapsing multiple sclerosis (RMS).

Background:
Inhibition of Bruton's Tyrosine Kinase (BTK), a cytoplasmic tyrosine kinase and member of the TEC kinase family, results in reduced activation of B cells and innate immune cells. This offers an alternative mechanism to modulate immune regulatory networks and related neuroinflammation via inhibiting B cells and myeloid cells. Remibrutinib is a potent, highly selective, covalent BTK inhibitor with a short plasma half-life, and a promising pharmacological and safety profile.

Design/Methods:
REMODEL I and II are identical randomized, double-blind, double-dummy, active comparator-controlled, parallel-group, event-driven, multi-center studies in RMS patients. Patients aged 18–55 years having at least one/two relapses within previous one/two years, or one active Gadolinium-enhancing (Gd+) lesion in the 12 months prior to screening with an EDSS of 0.0–5.5 will be enrolled (each 800 participants). The studies consist of an initial double-blind core part for up to 30 months followed by an open-label extension for up to 5 years. The primary endpoint is annualized relapse rate. Key secondary endpoints include, among others, EDSS-based disability progression as measured by 3-month/6-month CDP, number of new/enlarging T2 and Gd+ T1 lesions, reduction in neurofilament light chain concentration, and no evidence of disease activity.

Results:
Both studies are currently open for recruitment and each aim to enroll 800 participants. An interim analysis is planned on pooled 6-month MRI data (new/newly enlarging T2 lesions) from a subset of 200 participants. Further details about study design will be presented at congress.

Conclusions:
The REMODEL I and II studies will investigate the efficacy, safety and tolerability of remibrutinib versus teriflunomide to support regulatory approval worldwide as a potential new oral treatment for patients with this disabling disease.

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