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Efficacy of Delayed-Release Dimethyl Fumarate for Relapsing-Remitting Multiple Sclerosis in Prior Interferon Users with Low Clinical Disease Activity: Integrated Analysis of the Phase 3 Define and Confirm Studies

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Objective: Background/Objectives: The efficacy of delayed-release dimethyl fumarate (DMF) in previously treated patients with low clinical disease activity has not been assessed. In an integrated analysis of Phase 3 DEFINE/CONFIRM, we assessed the effects of DMF on annualized relapse rate (ARR) and MRI measures in RRMS patients treated with 1 prior interferon (IFN) with low clinical disease activity.

Design and Method: Eligible patients were randomized to receive DMF 240 mg twice (BID) or thrice daily, placebo, or subcutaneous glatiramer acetate (reference comparator; CONFIRM only) for up to 2 years. Prior IFN users were treated (>;3 months prior to randomization) with a single IFN. Low clinical disease activity was defined as <;2 relapses in the year before study entry. Outcome measures included ARR and number of new gadolinium-enhancing (Gd+), T1, and T2 lesions on MRI.

Result: The integrated ITT population included 771 and 769 patients receiving placebo or DMF BID, respectively; among them, 112 and 113 were treated with 1 prior IFN and had low clinical disease activity. A subset of these patients (placebo, n=52; DMF BID, n=49) were in the MRI cohort. At 2 years, significant reductions with DMF BID compared with placebo were observed for ARR (55% reduction; P=.0009) and number of new Gd+ lesions (95% reduction; P<;.0001), T1 lesions (80% reduction; P<;.0001), and T2 lesions (91% reduction; P<;.0001).

Conclusion: These findings suggest that DMF BID demonstrated beneficial effects on ARR and MRI outcomes in RRMS patients who were treated with 1 prior IFN and had low clinical disease activity.