Sustained clinically meaningful improvements in walking ability with prolonged-release fampridine: results from the placebo-controlled ENHANCE study.

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Background: A hallmark of multiple sclerosis (MS) is walking disability, affecting 80% of people and detected early in the disease course. Maintaining and improving mobility are high priorities for people with MS (PwMS). While clinical trials, observational studies, and patient reports demonstrate consistent benefits of prolonged-release fampridine (PR-FAM; dalfampridine-ER in US), doubts remain whether these benefits are clinically meaningful.

Objectives: The Phase 3 ENHANCE trial, the largest and longest randomised trial of PR-FAM to date, was a multicentre, randomised, double-blind, placebo-controlled study to evaluate if PR-FAM 10 mg twice daily (BID) provided sustained clinically meaningful benefits vs placebo on patient-reported walking ability and other functional outcome measures.

Methods: ENHANCE enrolled PwMS aged 18-70 yrs, with progressive or relapsing MS, and impaired walking (EDSS 4-7). The primary endpoint was proportion of people with a mean improvement in 12-item MS Walking Scale (MSWS-12) score exceeding a predetermined threshold (≥8-points) from Baseline over 24 wks. Secondary endpoints included: Timed Up and Go (TUG) speed, MS Impact Scale physical subscale (MSIS-29 PHYS), static balance (Berg Balance Scale [BBS]), and upper extremity function (ABILHAND questionnaire). Safety was also assessed.

Results: 646 PwMS from 11 countries were randomised to PR-FAM 10 mg BID (n=323) or placebo BID (n=323); 633 (n=315 PR-FAM; n=318 placebo) had ≥1 dose of PR-FAM and ≥1 post-Baseline efficacy assessment. Baseline characteristics were similar. Significantly more PR-FAM-treated PwMS achieved a clinically meaningful ≥8 point improvement in the MSWS-12 (43.2%) vs placebo (33.6%) over 24 wks (OR:1.61 [95% CI:1.15,2.26];*P*=.006). Significantly more PR-FAM PwMS also achieved a ≥15% mean improvement from Baseline over 24 wks on TUG speed vs placebo (43.4% vs 34.7%; OR:1.46 [95% CI:1.04,2.07];*P*=.030). A greater mean improvement from Baseline in the MSIS-29 PHYS was observed in PR-FAM vs placebo (least square mean difference: -3.31 [95% CI:-5.13,-1.50];*P*< .001). Treatment effects favouring PR-FAM, though not statistically significant, occurred in other secondary endpoints. No new safety risks were observed.

Conclusions: A significantly greater proportion of PwMS treated with PR-FAM vs placebo achieved clinically meaningful benefits on self-reported walking ability, mobility, and balance, sustained over 24 wks. Safety was consistent with the known PR-FAM profile.

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