EP3162 - Prolonged-Release Fampridine Demonstrates Rapid and Sustained Clinically Meaningful Improvements in Walking Ability Over 24 Weeks: MSWS-12 Responders in the ENHANCE Study

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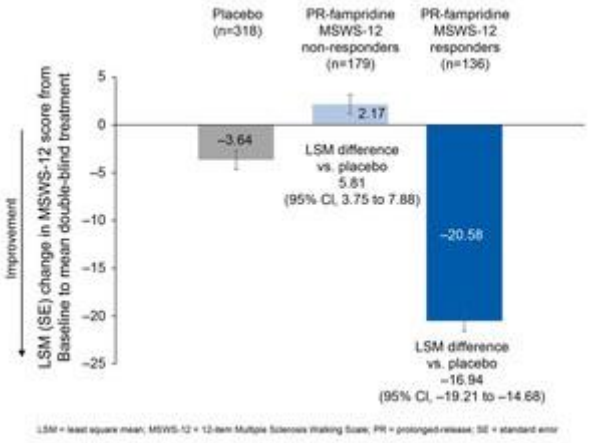
Background and aims:

The international Phase 3, double-blind, placebo-controlled ENHANCE study (NCT02219932) was the largest and longest randomised trial of prolonged-release (PR) fampridine. ENHANCE demonstrated that significantly more subjects had clinically meaningful improvements in walking ability, as assessed by the self-reported Multiple Sclerosis Walking Scale-12 (MSWS-12), with PR-fampridine versus placebo (43% vs. 34%; odds ratio=1.61; *p*=.006) over 24 weeks. This analysis evaluated the magnitude of mean change in MSWS-12 score over 24 weeks, based on clinically meaningful subject-level improvement.

Methods:
An MSWS-12 responder was prospectively defined as an ≥8-point mean reduction (improvement) in MSWS-12 score over 24 weeks; least-square-mean (LSM) analyses used a mixed effects model for repeated measures, adjusted for screening EDSS, baseline MSWS-12, baseline TUG speed, age, and prior aminopyridine as covariates (missing data handled using multiple imputation).

Results:
PR-fampridine–treated MSWS-12 responders demonstrated an LSM improvement of –20.58 points from baseline over 24 weeks; a small mean improvement was observed in the placebo group (–3.64 points), while MSWS-12 non-responders worsened slightly (+2.17 points; see figure). In PR-fampridine–treated MSWS-12 responders, improvements were detected as early as Week 2 and were sustained throughout the treatment period.



Least square mean change (LSM) in MSWS-12 score from baseline over 24 weeks in the placebo group and PR-fampridine–treated MSWS-12 responder and non-responder subjects. LSM, LSM difference, standard error (SE) calculated using mixed effects model for repeated measures.

Conclusion:
Over 24 weeks, PR-fampridine–treated MSWS-12 responders experienced clinically meaningful improvement from baseline—a notable finding given the skewed nature of baseline scores across groups. Whilst the mode of action of PR-fampridine is understood, the pathophysiological

explanation of MSWS-12 responders remains unclear. Therefore, MSWS-12 responders cannot be predicted *a priori*. Nevertheless, the fast-acting nature of PR-fampridine enables quick and efficient identification of MSWS-12 responders in clinical practice.

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