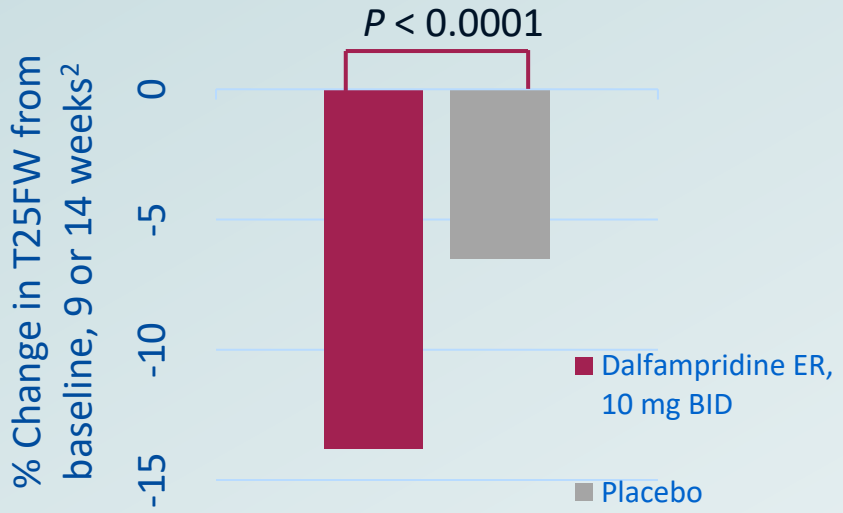
Dalfampridine to Improve Walking: Phase 3 Trial Results

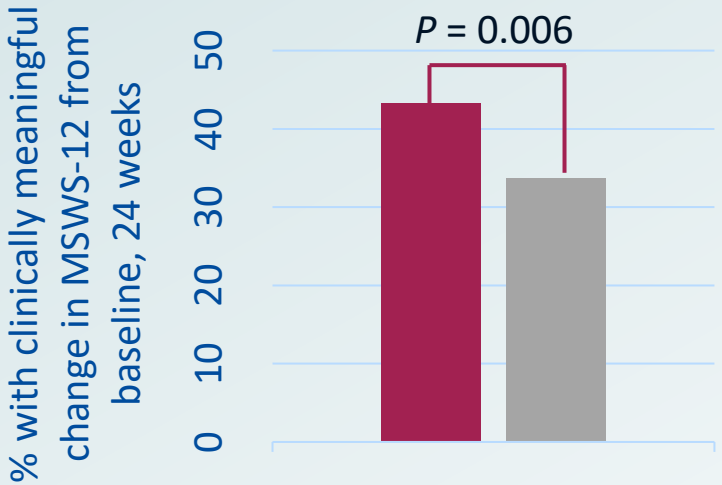
Extended-release **dalfampridine** (US) or **fampridine** (non-US): 4-aminopyridine[1]

- Selective potassium channel blocker; acts on demyelinated axons
- Only approved pharmacologic treatment for poor walking/gait in MS

Improvement in Timed 25 Foot Walk*[2]



Clinically Meaningful Change in MSWS-12†[3]



Additional Significant Effects of Dalfampridine-ER, relative to placebo

% classified as T25FW responders[2]

Change from baseline (24 wks)[3]

- MSWS-12 score
- TUG speed score
- MSIS-29 PHYS score

*T25FW improved for ≥3 of 4 visits during the double-blind treatment period, relative to maximum speed at any of the 5 off-drug visits. † ≥8 points. ER, extended-release; MSIS-29 PHYS, MS Impact Scale, physical impact subscale; MSWS-12, 12-point MS Walking Scale (validated scale for patient self-report of symptoms); TUG, Timed Up and Go.

1. Fernandez O et al. *Expert Rev Clin Pharmacol*. 2012;5:649-665; 2. Goodman AD et al. *Mult Scler*. 2015;21:1322-1331; 3. Hobart J et al. *CNS Drugs*. 2019;33:61-79.

Dalfampridine Safety Analysis

Safety Results from 2 Dalfampridine Phase 3 Trials – Pooled Data[1]	
Serious AEs	• 6.3% in the dalfampridine group; 1.6% for placebo
Treatment-related AEs	• 25.6% in the dalfampridine group; 17.8% for placebo
Discontinuation rates	• 3.2% in the dalfampridine group; 2.1% for placebo
AEs more common in dalfampridine group	• Urinary tract infections, insomnia, dizziness, headache, asthenia, and nausea
Seizures	• One seizure event in each treatment group; neither considered treatment-related • History of seizures was exclusion criterion; immediate-release dalfampridine is associated with an increased risk of seizures[2]

AE, adverse event.

1. Goodman AD et al. *Mult Scler*. 2015;21:1322-1331; 2. Fernandez O et al. *Expert Rev Clin Pharmacol*. 2012;5:649-665.

Functional Electronic Stimulation (FES)

- Stimulation of peroneal nerve in leg and foot
- Increases dorsiflexion – bend in ankle that lifts the front of the foot
- A long-term study found
  - FES associated with clinically significant increases in walking speed; efficacy maintained for 5 years
  - After 5 years, significant improvement in self-report scores for joint pain, spasticity, trips, confidence, and walking effort

Street T et al. *Int J MS Care*. 2018;20:224-230.

Adaptable, Configurable Leg FES (Cionic Neural Sleeve™)

- Wearable functional electronic stimulation (FES) for leg
  - Dorsiflexor muscle stimulation to maintain toe clearance in swing phase and improve heel strike
  - Evertor muscle stimulation to reduce ankle inversion from the swing phase through time load is transferred to leg
- Adaptable, multichannel, with configurable electrodes to allow precise control of appropriate muscles
- Personalizable - adapts across gait speeds
- FDA-approved medical device
- Open-label, single group trial in patients with foot drop: with and without stimulation (32 participants; 8 with MS)*

Dorsiflexion	Inversion (Evertor Stimulation)
93.8% had increased dorsiflexion at heel strike with stimulation	88% had reduced inversion in swing phase with stimulation
Mean change 5.2°	Mean change -3.1°

*Results are from pre-publication, nonreviewed document.
FES, functional electronic stimulation.
Robison J et al. *medRxiv.* 2022.04.27.22273623. https://doi.org/10.1101/2022.04.27.22273623