Background

- Impaired walking is a common complication of multiple sclerosis (MS) that has a substantial adverse impact on patient function, quality of life, andassociated costs. Among patients with MS, 41% report difficulty walking, and more than 70% of those who report difficulty walking said that it is the most challenging aspect of living with MS.

- Sustained-release fampiridine (SR-fampiridine; pridolone)- or modified-release fampiridine in some countries, dalfampridine extended release tablets in the US) is a potassium channel blocker that demonstrated statistically significant improvements in walking 11 persons with relapsing-remitting MS relative to placebo in 2 Phase 3 trials.

- Dalfampridine extended release tablets (moxifampiridine ER- prolonged, modified, or sustained-release fampiridine in some countries) were approved in the US for patients with MS.

- SR-fampiridine tablets are also available for patients with MS in some countries outside the United States.

- The scientific literature suggests that there is a correlation between long-distance walking and endurance, but this has not been assessed in a clinical study with fampiridine-SR.

Objective

- To examine the relationship between performance on the 25-Foot Timed Walk Test (25FTWT) in patients with MS receiving SR-fampiridine.
- The 25FTWT is a standard test of walking speed by measuring how far a patient can walk in 6 minutes.
- The 25FTWT evaluates walking speed by measuring the time it takes to walk 25 ft.

Methods

- During our involvement in MS-P203, a Phase 3, randomized, double-blind, placebo-controlled clinical trial evaluating the impact of SR-fampiridine on walking ability in MS, we recruited 13 patients to our study site.
- Ten patients were randomly assigned to active treatment with SR-fampiridine, 10 mg twice daily, and 3 had been randomly assigned to placebo.
- All 13 participants underwent testing for walking endurance, as measured by the 6MWT (6-Minute Walking Test) and the 25FTWT, over the course of 10 visits.
- These visits included a pre-treatment screening visit (visits 0 and 1). 14 weeks of placebo-controlled, double-blind treatment (visits 2-6) and 3 post-treatment visits (visits 7 and 8).
- A treatment responder was defined as a patient whose walking speed was faster for at least 4 of the 11 visits during the active placebo-controlled treatment period, with the maximum speed during the 5 post-treatment visits (pre-treatment screening and visits 0, 1, 2, 6, and 7).
- The 25FTWT and 6MWT were performed at each pre-treatment screening visit and visit 5 (14 weeks post-randomization) of the placebo-controlled phase of the trial.
- Upper respiratory illness was used to evaluate associations between the 6MWT and 25FTWT.

Results

- Ten of the 13 patients were women, and the average age of the participants was 50 years (Table 1).
- Four participants had relapsing-remitting MS, 8 had secondary progressive MS, and 1 had primary progressive MS (Table 1).
- The average duration of MS was 15 years, and the Expanded Disability Status Scale (EDSS) range among the participants was 3.0 to 9.0 (Table 1).
- Five patients met the responder criteria for the primary outcome of the trial, finding that patients who were taking active treatment and were in the placebo group.
- The patients who were taking active treatment demonstrated improvements from baseline of 25%, 34%, 23%, and 22% in walking speed - 25% in walking speed (Table 2). These improvements were seen in patients in active treatment in the 6MWT, by 24% and by 28%.
- However, 2 of these responders were characterized by a slight deterioration in endurance on the 6MWT, by 7% and 1%

Table 1. Patient Demographics

<table>
<thead>
<tr>
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<th>SR-fampiridine</th>
<th>6MWT</th>
<th>25FTWT</th>
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<tr>
<td>1</td>
<td>13</td>
<td>10 mg twice daily</td>
<td>10 mg twice daily</td>
<td>10 mg twice daily</td>
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<tr>
<td>2</td>
<td>5</td>
<td>Responsive</td>
<td>Non-Responsive</td>
<td>Non-Responsive</td>
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Conclusions

- This case series is consistent with existing literature, which indicates that walking speed correlates well with endurance ability.
- These data provide support for the concept that a walking speed test can be used as a surrogate marker to assess the effect of SR-fampiridine on endurance.
- The clinical observations in these cases suggest further tests to better understand the impact of SR-fampiridine on walking speed.