INTRODUCTION

Lambert-Eaton Myasthenic Syndrome (LEMS) is a rare autoimmune disease with a prevalence of ~3,000 patients in the United States and Canada. The most common clinical presentations of LEMS are proximal weakness, hyporeflexia or areflexia, and cholinergic dysautonomia (dry mouth, impotence, etc.) Ocular bulbar weakness is rare. Symptoms can be life threatening when the weakness involves respiratory muscles. Approximately 50% of LEMS patients have small cell lung cancer.

OBJECTIVES

To evaluate the efficacy and safety, including the long-term safety, of amifampridine (3,4-DAP) phosphate as a symptomatic treatment for patients with LEMS in Phase 3, multicenter, double-blind, placebo-controlled, randomized discontinuation study followed by an open label extension period.

STUDY RATIONALE

The most common clinical presentations of LEMS include proximal weakness, hyporeflexia or areflexia, and cholinergic dysautonomia (dry mouth, impotence, etc.) Ocular bulbar weakness is rare. Symptoms can be life threatening when the weakness involves respiratory muscles. Approximately 50% of LEMS patients have small cell lung cancer.

OVERVIEW OF STUDY DESIGN

Randomized 38 patients randomized, 1:1

STUDY DESIGN

Detailed Study Design

Details of Study Design

Baseline QMG score = 18 patients

Part 2 Double Blinded Treatment Discontinuation Randomization (17 days) – 18 Subjects

- Symptomatic treatment
- Drug withdrawal in Part 2
- Randomization to placebo or no further treatment

Part 1 Open Label Run-in (7 days to 81 days)

- Retreatment
- Drug withdrawal

Part 1 Open Label Extension (81 days)

- Safety and efficacy assessment performed on Day 81 and Day 18

Part 2 Double Blinded Treatment Discontinuation (17 days) – 18 Subjects

- Continue on placebo for 7 days

EFFICACY RESULTS

Change in QMG scores from baseline (Day 1, Part 2 to Day 4, Part 3) in patients with LEMS

- QMG scores at baseline (Day 1, Part 2) in 38 patients: average 18.8
- QMG scores at Day 4 (Part 3) in those patients who received placebo had a greater worsening in QMG and SGI scores than did patients who received amifampridine.
- Statistical analyses using a mixed-effect model of repeated measures (MMRM) demonstrated that patients who received placebo had a greater worsening in QMG and SGI scores than did patients who received amifampridine.

CONCLUSIONS

- This Phase 3 trial in 40 patients with LEMS demonstrated the safety and efficacy of amifampridine phosphate (Firdapse™) in the treatment of patients with LEMS.
- The study was terminated early due to regulatory guidance from the U.S. Food and Drug Administration.
- The study was sponsored by Intercept Pharmaceuticals.