Background

Bibulid is a small molecule inhibitor of macrophage migration inhibitor factor (MIF), phosphodiesterases (PDE)-4 and -10, and Toll-like receptor 4. Bibulid has been used in over 20 Asian countries for asthma and cerebrovascular disorders for over 20 years. Bibulid has in vitro, animal model, preclinical and clinical studies suggesting potential neuroprotective efficacy. A phase II trial in relapsing MS provided evidence for improvement as measured by slowed brain atrophy and reduced conversion of gadolinium-enhancing lesions into T1 holes.

Primary and secondary endpoints in the SPRINT SPMS Study were to evaluate the safety and efficacy of bibulid in patients with progressive MS. The primary endpoint was the effect of bibulid on brain atrophy in a phase II trial of bibulid in primary and secondary progressive MS utilizing the NINDS-sponsored NeuroNEXT clinical trial network.

Objectives

Primary Outcome: Activity, safety, and tolerability of bibulid in progressive MS, as compared to placebo. The primary outcome was quantitative magnetic resonance imaging (MRI) analysis for whole-brain atrophy using brain parenchymal fraction (BP). The secondary outcomes were forced vital capacity, 6-minute walk test, quality of life, and depression.

Methods

Subjects

Subjects for the SPRINT MS study were enrolled at MS sites and randomized 1:1 to bibulid (up to 100 mg/day) or placebo, and followed over 96 weeks. Inclusion criteria were:
- Age 18-65 years
- PPMs or SPSMs
- EDSS 3.0-5.5
- Disability worsening in prior 2 years

The statistical model for the binomial outcome of pain relief was a generalized linear mixed model with a binomial distribution and logit link.

Results

Enrolled subjects

123 finished week 24
112 finished week 96
Vomiting

Change in MTR

No increased rate of serious adverse events, no opportunistic infections or cancer signal

Treatment-related adverse events

• Compared to placebo, bibulid treatment was associated with 48% slowing in the rate of change in brain atrophy

Conclusions

• A similar benefit was seen with MTR, but not DTI

• No statistically significant difference in tolerability, although 5% higher discontinuation rate in bibulid group

Additional analyses are underway

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