OBSERVATIONS ON THE DESIGN OF SECONDARY PROGRESSIVE MS TRIALS UTILIZING PATIENTS WITH AN EDSS SCORE OF 6.0–6.5

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BACKGROUND
We participated in two prospective research trials with patients having secondary progressive multiple sclerosis (SPMS). One was an unblinded, exploratory investigator-initiated trial testing the efficacy of ibudilast in patients with SPMS and inflammatory disease (AMD). The other was a multicenter Phase III, industry-sponsored study testing the effectiveness of ozanimod in patients with relapsing-remitting MS (RRMS) in mitigating fatigue (Friedman et al. 2015). Neither trial produced convincing evidence of treatment benefit.

METHODS
We conducted a retrospective, exploratory analysis evaluating the concomitant use of disease-modifying drugs (DMDs) and ozanimod in patients with SPMS or RRMS. We correlated treatment history with clinical characteristics and outcomes. Patients were divided into two groups based on the presence or absence of DMDs at enrollment for the ozanimod trial. The primary outcome was changes in EDSS scores.

RESULTS
In the AMD trial, patients with lower scores on the extended auditory vertex addition test were more likely to remain in the trial (data not shown). Eight of 15 patients completed at least 5 years of follow-up. The "common treatment time" for ozanimod was 1.2 years. The mean score was 55.4 (p=0.057).

CONCLUSIONS REGARDING FUTURE TRIAL DESIGN
Our 2005-2006 trials were not robust enough to detect significant differences in the two groups in patients with SPMS. In some patients the Ozan Trial appeared to be one of limited benefit, but those findings were not statistically significant and could not be clearly distinguished from treatment benefit in patients with SPMS and inflammatory disease.

OBJECTIVES

1. To determine difference in sensitivity to changes in motor measures.

2. To determine the relationship of changes in motor measures, relapse-related factors and the protocol of the disease-mitigating regimen.

3. To quantify how gains might improve sensitivity to future trials.

RATIONALE
Despite the lack of treatment efficacy that has thus far characterized many studies of agents that may have a beneficial effect on patients with relapsing-remitting MS (RRMS), some studies do show an effect upon motor measures. By controlling for differences in changes in motor measures, relapse-related factors and the protocol of the disease-mitigating regimen, we hope to gain insights that might improve sensitivity to future trials.

OBJECTIVES

1. To determine if there is a difference in sensitivity to changes in motor measures.

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4. To determine if there is a difference in sensitivity to changes in motor measures.

5. To determine if there is a difference in sensitivity to changes in motor measures.

6. To determine if there is a difference in sensitivity to changes in motor measures.

REFERENCES


