TABLE 20.2 Efficacy Data for the Endpoints in the Gold Study

PRIMARY ENDPOINT		
Percent of subjects having a relapse by 2 years	26–27% (study drug)	46% (placebo)
SECONDARY ENDPOINTS		
Number of new or enlarging lesions (mean number of lesions per subject)	2.6–4.4 (study drug)	17.0 (placebo)
Total number of relapses divided by patient-years in the study	0.17–0.19 (study drug)	0.36 (placebo)
Percent of patients that progressed to disability according to EDSS scale	16–18% (study drug)	27% (placebo)

the website of the *New England Journal of Medicine* (113).

Regarding new or enlarging lesions, these are the lesions as measured on T2-weighted images.

Regarding progression to disability, progression of multiple sclerosis in any given patient to a disability was defined as a 1.0-point increase in EDSS in patients with a baseline score of 1.0 or higher, or at least a 1.5-point increase in patients with a baseline score of zero. To trigger this endpoint, the increased score must be sustained for at least 12 weeks.

Table 20.2 discloses the efficacy data from the Gold study. The study drug was actually provided to subjects in two separate study drug arms, not just one arm. The efficacy results from these two arms were similar, and hence are disclosed as a range. As is readily evident, efficacy was dramatically greater in the study drug arm than in the placebo arm. The Gold study demonstrates the use of *clinical response*, which encompassed loss of vision, numbness or tingling sensations, muscle weakness, slurred speech, and *objective response*, which took the form of lesion size and number, as endpoints.

III. FDA'S DECISION-MAKING PROCESS IN EVALUATING ENDPOINTS FOR MULTIPLE SCLEROSIS

Fampridine (Ampyra®), which is also called 4-aminopyridine, improves the symptoms of multiple sclerosis, but does not influence the course of the disease itself. The drug improves conduction of action potentials in demyelinated nerve fibers and increases release of neurotransmitters in synapses and at neuromuscular junctions. Fampridine is fat-soluble and readily crosses the blood–brain barrier. According to articles on fampridine clinical trials, the drug increases in muscle strength and walking speed in a third of patients, as measured by *the endpoint of the 12-Item Walking Scale* (114,115).

[113]Gold R, Kappos L, Arnold DL, et al. Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. New Engl. J. Med. 2012;367:1098–107.

[114]Lugaresi A. Pharmacology and clinical efficacy of dalfampridine for treating multiple sclerosis. Expert Opin. Drug Metab. Toxicol. 2015;11:295–306.

[115]Jensen HB, et al. 4-Aminopyridine for symptomatic treatment of multiple sclerosis: a systematic review. Ther. Adv. Neurol. Dis. 2014;7:97–113.