

proposed that NFL be a useful surrogate marker for testing efficacy of drugs for multiple sclerosis.

Eye pathology is a common initial finding in multiple sclerosis. About 20% of patients with multiple sclerosis have optical neuritis (38). Retinal nerve fiber layer (RNFL) thickness is an objective measure of optic neuritis. Optical coherence tomography (OCT) measures thickness of the RNFL (39). In patients with multiple sclerosis, annual thinning of the RNFL is about 2 $\mu\text{m}/\text{year}$, while in healthy controls, annual thinning is 0.2 $\mu\text{m}/\text{year}$ (40). Data from OCT and from MRI provide complementary information about vision pathology in multiple sclerosis (41). Information on vision impairment in multiple sclerosis is also captured by the quality of life tool, the NEI-VFQ-25 questionnaire.

c. Endpoints for Multiple Sclerosis

Endpoints used in clinical trials for multiple sclerosis include:

- Percent of subjects with relapse at 96 weeks (relapse rate) (42);
- Percent of subjects experiencing relapse per year (relapse rate) (43,44);
- Proportion of subjects who are relapse-free at end of study (45,46);
- Change in EDSS score from baseline to end of study (47);
- Time to 3-month sustained change in EDSS score (defined as time to a sustained increase in EDSS score, of at least 1 point in EDSS score, or an increase of at least 1.5 points, if baseline EDSS score was zero, where sustained increase in EDSS score lasts for at least 3 months) (48,49), or where

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