Supplementary Appendix Materials

Additional Details for NEI-VFQ-25 and NOS-10

The 25-item National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25) includes 25 questions from 11 vision-related subscales (near vision, distance vision, peripheral vision, general vision, color vision, driving, ocular pain, role limitations, dependency, social function, and mental health), and a general health question (1,2). The NEI-VFQ-25 can be expanded up to 39 items using the optional appendix of supplementary questions (2). The appendix items were added to the Near and Distance Activities subscales to improve accuracy. A 5- or 6-point response scale is used, ranging from **1** not affected at all, to **4** severely affected, **5** stopped doing this because of my eyesight and **6** stopped doing this for other reasons. True/false items have a 5-point response scale, ranging from **1** definitely true to **5** definitely false, with **3** indicating not sure. Subscale scores are calculated as the mean of all component item scores (1). The composite score is generated by averaging the subscale scores (excluding general health), as outlined in Mangione et al (2).

The 10-item Neuro-Ophthalmic Supplement (NOS-10) was developed to identify additional characteristics of visual function for patients with neuro-ophthalmologic disorders, such as multiple sclerosis, that may not be captured by the NEI-VFQ-25 alone, and may provide additional value beyond the 39 items in the NEI-VFQ-25 (3). The NOS-10 also is scored on a scale of 0–100 (3). The NOS-10 composite score is calculated as the unweighted mean of the 10 supplement items (3). The combined composite score for the NEI-VFQ-25 and NOS-10 is calculated as the unweighted average of the NEI-VFQ-25 items (excluding general health and the appendix items) and the 10 supplement items.

Additional Results

Pairwise Correlation Analyses of Changes From Baseline to 24 or 32 Weeks Between Patient-Reported Visual Function Outcomes With Retinal Structural and Electrophysiological Outcomes by Treatment Group

Correlations of change from baseline to Weeks 24 and 32 between NEI-VFQ-25 composite score and structure (retinal nerve fiber layer [RNFL] thickness by spectral domain optical coherence tomography) were weak for both treatment groups (Table E4). Correlations of change from baseline to Week 24 between NEI-VFQ-25 composite score and full-field visual evoked potential (FF-VEP) amplitude were weak for both treatment groups. However, for Week 32, correlation was moderate in the placebo group and negligible in the opicinumab group. Correlations of change from baseline to Weeks 24 and 32 between mean NEI-VFQ-25 composite score and mean FF-VEP latency were weak for both treatment groups. Correlations were generally absent between NOS-10 composite score and RNFL thickness, FF-VEP amplitude, and FF-VEP latency for both treatment groups.

Pairwise Correlation Analyses of Changes From Baseline to 24 or 32 Weeks Between HCVA and LCLA Outcomes With Retinal Structural, Electrophysiological, and Patient-Reported Visual Function Outcomes by Treatment Group

Correlations of change from baseline to Week 24 for changes in retinal structure, RNFL thickness, and high-contrast visual acuity (HCVA), 1.25% and 2.5% low-contrast letter acuity (LCLA) were weak to moderate for the placebo group and weak for the opicinumab group (Table E5). Correlations of change from baseline to Week 24 for changes in FF-VEP amplitude and HCVA, 1.25% LCLA, and 2.5% LCLA were absent in placebo and weak or absent in opicinumab. In contrast, consistent weak to moderate correlations were seen for change from

baseline to Week 24 for FF-VEP latency with HCVA and LCLA in the placebo group; remarkably, they were lost in the opicinumab group.

Correlations between changes in NEI-VFQ-25 and NOS-10 composite scores and changes in HCVA and LCLA were mostly absent (NEI-VFQ-25) or inconsistently weak (NOS-10).

Stronger correlations were observed between the 2 LCLA measures than between the LCLA and HCVA measures. Similar correlations were observed for the changes between baseline and 32 weeks for all outcome measures (Table E6). Correlation analyses performed in the intent-to-treat group at Weeks 24 and 32 showed similar results to those presented for the per-protocol population.