<https://doi.org/10.5061/dryad.ck84q23>

**Appendix 2. Statistical Analysis**

The primary efficacy endpoint was the change from baseline in MMDs (weeks 1–12) using an ANCOVA model. Key secondary efficacy endpoints were ≥75% migraine responder rates during weeks 1–4 and weeks 1–12, ≥50% migraine responder rates during weeks 1–12, percentage of patients with a migraine on the day after dosing, reduction in average daily percentage of patients with migraine from baseline to week 4, change in HIT-6 total score from baseline to week 12 (300 mg dose only), and acute migraine medication use from baseline to week 12 (300 mg dose only). A ≥50% or ≥75% migraine responder was defined as a patient who achieved ≥50% reduction or ≥75% reduction in monthly migraine days from baseline, respectively. These reductions were evaluated by comparing the baseline frequency of migraine days to the migraine frequency in 4-week intervals. Results from these 4-week intervals will be combined to produce 12-week responder endpoints. The weeks 1–4, 5–8, and 9–12 change from baseline measures were averaged, and the average value compared to baseline. A percent change from baseline was determined, which was used to determine the responder status. Hypothesis testing was performed for the primary endpoint (change from baseline in MMDs from weeks 1–12). An ANCOVA model with change from baseline as the response variable and treatment, baseline migraine days, and preventive medication use as independent variables were used to test for a difference between treatment arms.

For the key secondary endpoints (migraine responder rates and percentage of patients with a migraine on the day after dosing), testing was based on Cochran-Mantel-Haenszel (CMH)/extended CMH tests. The tests were stratified by the randomization stratification factor. For the HIT-6 and Acute Migraine Medication endpoints an ANCOVA model similar to the one used for the primary endpoint were used for testing. The reduction in migraine prevalence from baseline to week 4 endpoint was based upon the average percent of days with a migraine for each of the first 4 weeks. The treatment effect was tested using a repeated-measures approach.[36](#_ENREF_36) The model specified an unstructured variance/covariance matrix and included the treatment group, week, baseline value of the outcome variable, and treatment group-by-week interaction. The Kenward-Roger approximation was used to estimate the degrees of freedom.