

Statistical Analysis Plan (SAP)

For Protocol: USUHS-20250225

Last Updated: June 5, 2025

1.0 Outcome Measures

- **Co-primary Outcome Measures:**
 - Comparison between TBI and AHI groups in the percent change in migraine headache **frequency** from baseline to peak effect.
 - Comparison between TBI and AHI groups in the percent change in migraine headache **intensity** from baseline to peak effect.
 - Comparison between TBI and AHI groups in the percent change in **HIT-6 score** from baseline to peak effect.
- **Secondary Outcome Measures:** Secondary outcomes include comparing absolute changes in frequency, intensity, and HIT-6 scores; changes in other migraine characteristics; timelines of Xeomin effectiveness; and assessment of residual effects after the treatment has worn off.

2.0 Sample Size and Power

- **Sample Size:** The estimated sample size is 40 patients in the TBI group and 20 patients in the AHI group. This is a convenience sample based on clinic availability.
- **Statistical Power:** With a two-sided alpha of 0.05, the study has a power of 0.8 to detect Cohen's d effect sizes of 0.799 using Mann-Whitney U tests, which is considered a moderate to large effect size.

3.0 Data Analysis Plan

- **Assumptions:** The analysis assumes that the data distributions for the TBI and AHI groups will not be normal; therefore, non-parametric statistical methods will be used.

- **Quantitative Variables:** Medians and 25-75%iles will be calculated. Two-sided Mann-Whitney U tests will be used to compare quantitative variables between the TBI and AHI groups, with Cohen's d calculated to measure effect size.
- **Qualitative Variables:** Frequencies and percentages will be calculated. Chi-squared tests will be used for comparisons between the TBI and AHI groups.
- **Missing Data and Outliers:**
 - **Missing Data:** Missing primary outcome data will be handled with case-wise deletion. Missing secondary outcome data will be imputed using multivariable interpolation, with sensitivity analyses conducted.
 - **Outliers:** Outliers will be examined, and if deemed genuine, they will be retained and noted in the results, as they may be of clinical interest. The non-parametric methods are expected to be robust to outliers.
- **Subgroup Analyses:** Exploratory subgroup analyses based on factors like age, sex, and migraine history may be conducted.
- **Interpretation:** Given this is the first study of its kind, results will require replication and statistical correction for multiple comparisons will not be performed.