Data Analysis -REVISED JULY 2023

Due to the study's pilot study design, sample size was not calculated formally. For both primary and secondary outcomes, descriptive data are presented (i.e., medians and ranges for continuous data, frequencies and percentages for categorical data).

Although the original data plan called for exploratory mixed randomized-repeated measures analysis of variance (ANOVA) to be conducted for the primary and two secondary outcomes, the pattern of missing data across patients at the designated time points was too prevalent (and appeared not to be missing at random) to ensure robust ANOVA results. Therefore, we reported separate non-parametric statistical outcomes when deemed feasible (i.e., adequate and balanced subgroup sample sizes) in an attempt to obtain as much information as possible about data trends and patterns. Because we were unable to capture within-subject correlations over time, as well as the treatment group*time interaction, our results should be interpreted accordingly.

The primary outcome was compliance with HDI and PEG IFN (i.e., percentage of doses taken based on total doses required over 53 weeks, as recorded in patient diaries), with a difference of 30% between groups deemed clinically relevant. We reported frequencies and percentages per week and an overall percentage of doses taken at the end of 53 weeks, with statistical analysis of this outcome.

Secondary outcomes were as follows (with different time points reported depending on the highest outcome frequencies):

- Comparison of the convenience and satisfaction with chemotherapy for patients on standard HDI versus PEG IFN using a chemotherapy convenience and satisfaction questionnaire (CCSQ), summation of items CS1 – GP5, with a 30% between-group difference deemed clinically relevant. Time points of comparison were baseline/week 1, week 3, week 13, week 25, and week 50.

- Item GF7, which assesses contentment with current quality of life, at baseline/week 1, week 3, week 13, week 25, and week 49.

- Item CS10, which assesses satisfaction with current results of chemotherapy, at week 1, week 3, week 13, week 25, week 37, and week 45.

- Items CS11 and CS12, which measure recommendation/choice of chemotherapy regimen, at week 1, week 3, week 13, week 25, week 37, and week 45.

- Item CS13, which rates the chemotherapy regimen overall, at week 1, week 3, week 13, week 25, week 37, and week 45.

- Treatment-related side effects that may impact the patient's health-related QoL (HRQOL) using the Functional Assessment of Cancer Therapy of Biologic Response Modifier (FACT BRM), with a 30% between-group difference in scores deemed clinically relevant. Time points of comparison were baseline/week 1, week 3, week 13, week 25, and week 50.

- The frequency of Grade 3 and 4 adverse events (AEs), according to the National Cancer Institute (NCI) Common Toxicity Criteria for Adverse Events (CTCAE) for patients on standard HDI versus PEG IFN, and the frequency of severe adverse events (SAEs), regardless of grade.

- Patients' reasons for their choice of treatment with HDI versus PEG IFN at the study's conclusion, for those cases in which patients were presented with a choice of either treatment option.

All analyses were conducted using IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.), with $p < .05$ denoting statistical significance.