Advancing Symptom Alleviation With Palliative Treatment (ADAPT)
NCT02713347
IIR 14-346

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ADAPT Data Analysis Plan:

Data from all participants will be included regardless of level of participation using an intent-to-treat approach**.** The primary outcome measure, FACT-G, will be analyzed as a continuous variable, while the secondary outcomes will be either continuous (disease-specific health status, depression, symptom burden, emergency department visits, hospitalizations) or binary (advance care planning communication and documentation; mortality).. Analysis models will adjust for the disease stratification variable used in randomization. Analyses of the repeated measures, including primary and secondary endpoints, will be performed with SAS 9.4 using maximum likelihood estimation (MLE) for incomplete data using linear mixed models for continuous outcomes and generalized linear mixed models with a logit link for binary endpoints. This approach has several advantages: 1) all available data on eligible subjects can be included in the analysis even when there are missing data at follow-up, 2) MLE estimates the correlation between related measures and adjusts test statistics appropriately, 3) time-varying covariates can be incorporated into the model, if desired, and 4) the assumptions about missing data are relaxed from missing completely at random to missing at random (Little RJ. Methods for handling missing values in clinical trials. J Rheumatol 1999;26(8):1654-1656). The primary analyses will not consider the pre-randomization variables, but the effect of these variables on outcomes will be investigated as secondary analyses.

The primary outcome will be the difference between intervention and control in the change in FACT-G from baseline to 6 months. To describe the treatment by disease interaction, we will estimate the treatment effect and its confidence interval within each of the disease groups. Missing data will be reviewed to identify potential patterns and examined to assess how these patterns impact our results. Specifically, we will examine plots of group means over time stratified by the time of the last completed observation to determine if biases are evident due to missing data (Fairclough DL. Design and analysis of quality of life studies in clinical trials. CRC press; 2nd Edn, 2010). When data are missing at random, unbiased results can still be obtained from the likelihood method used in the analysis. If we find evidence of data missing not at random, sensitivity analyses will be performed using pattern mixture models (Little RJ, Wang Y. Pattern-mixture models for multivariate incomplete data with covariates. Biometrics 1996;52(1):98-111) and results will be presented to assess the impact of missing data on the reported conclusions.