

Title: Phenylbutyrate therapy for Maple Syrup Urine Disease

NCT01529060

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MSUD clinical trial methods

Descriptive statistics were calculated using standard methods. Mean, median and the dispersion around the measures of central tendency were calculated for the primary endpoints. The cross-over analysis was carried out following the standard procedures previously described (Piantadosi Steven. *Clinical Trials: A Methodologic Perspective*. 2nd ed. Hoboken, NJ: John Wiley and Sons, Inc). To evaluate the first-order carry-over effect, measured amino acids AUC values from both arms were summated together for each subject. The summated values were compared between the groups that received drug first vs placebo first by two sample t-test. This was performed to test for any carryover effect. The effect of treatment was then calculated by a two-sample t-test to compare the differences in AUC of BCAA over the periods of treatment for the two treatment sequences. To account for the relatedness in the amino acid measurements within each subject during the two treatment periods, linear mixed model was used to account for the non-independence in sequential measurements. For model building, the fixed component was constructed by using amino acid AUC as dependent variable. For the independent variables, the model included treatment and a dichotomized variable defined by whether the first period of treatment is placebo or not. For the mixed effect component, patient ID was used as a grouping factor to estimate random effect arising from the characteristics of each subject.