Study Title: Ketamine for Suicidality in Bipolar Depression

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Statistical methods

The intent-to-treat analysis included all randomized participants. We used R software (r-project.org) and SPSS version 23 (IBM, Armonk, NY, USA). Univariate tests compared groups on baseline characteristics. Histograms were inspected for normality. The primary hypothesis was tested using a linear regression model of day 1 SSI (SSIday1) with baseline SSI (SSIBL) and treatment as the predictors: SSIday1 ~ SSIBL + treatment. Secondary analyses tested treatment effect on response and remission. Effect size calculations used Cohen's d and number needed to treat (NNT). We used regression models analogous to that for SSI to test effects on depression, mania, and anxiety. The POMS was analyzed with a generalized least squares (GLS) model over its three assessment time-points. Since at randomization only one subject was not taking psychiatric medications and only one subject had baseline SSI <8, we did not adjust for the randomization strata. We tested a repeated measures analysis of covariance (ANCOVA) model of SSI, including 230 minute and day 1 assessments, analyzed response to the open-label ketamine infusion, and tested the correlation between change in depressive symptoms and change in SSI. We plotted mean SSI during the 6-week follow-up in those randomized to ketamine and performed paired t tests of the score each week compared to baseline. We investigated infusion effects on neurocognition and explored relationships of clinical variables with CAR, serum BDNF, and post-infusion plasma ketamine, norketamine and dehydronorketamine.31 Safety analyses investigated dissociative, psychotomimetic and cardio-respiratory effects.