Pilot Randomized Clinical Trial of Therapeutic Hypothermia Plus Neuromuscular Blockade vs. Standard of Care in Patients With Moderate to Severe ARDS - the Cooling to Help Injured Lungs (CHILL) Pilot Study

NCT03376854

Statistical Analysis Plan

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Statistical Analysis Plan: This is a pilot study of feasibility to demonstrate feasibility and safety to treat patients with COVID-19 and ARDS with our CHILL treatment protocol (hypothermia to core temperature 34-35°C + NMB for 48h) and to determine whether there are any trends toward benefit in the treated group. The primary outcome will be analyzed using descriptive statistics, the mean ± SD and the median ± IQR of time to reach the target temperature and the percent of total treatment time within the targeted temperature range. Differences in SAEs will be analyzed by Chi square. The group difference on 28-day VFDs will be tested with a permutation test for the difference in group means with alpha = .05 (two-tailed). This test was chosen due to the large number of zero values expected (based on our open-label pilot and retrospective studies). If the difference on a baseline prognostic variable is statistically significant, we will perform a secondary analysis to adjust for this variable using a regression approach. For secondary clinical outcomes t-tests, Wilcoxon, or chi-square tests will be used as appropriate. Mixed model repeated measures ANOVA will be used to test for group differences for physiological and biomarker secondary outcomes over days 0, 1, 2, 3, 4, and 7. We will not include an interim analysis in this small RCT with only 20 subjects.