Statistical analysis plan for KetMo, NCT 05422001

Aarhus. September 15th 2023

The following plan for data analysis was decided upon at a meeting with all members of the steering committee on September 15th, 2023. The plan was made before A and B lists were obtained from the hospital pharmacy.

This study will be undertaken as an equivalence trial with the application of intention to treat analysis.

Missing data are assumed to be missing at random, no imputations.

In brief:

A study enrollment flow diagram in accordance with the CONSORT (Consolidated Standards of Reporting Trials) will be prepared. Patient characteristics and outcome measures will be reported as means, standard deviations (SDs), medians, interquartile ranges (IQRs), and percentages, as appropriate.

Primary outcome will be comparing average change of NRS at 10 minutes between the intervention and control group and analyzed using appropriate test depending on distribution. Primary outcome includes initial analysis of all included patients (n=116) and sub-analysis in two groups (prior opioid use / no prior opioid use). Appropriate test according to potential difference in NRS at T0 in the two groups (prior opioid use / no prior opioid use) will be applied for comparing the differences in NRS between the two groups.

NRS will be reported as median (interquartile range) and compared between groups at the various times using the Mann–Whitney U test. If normal distributed a multilevel mixed effects linear regression will be carried out.

Categorical data (number of patients with Ramsay Sedation Scale Level 2, any adverse events during observation) are reported as numbers (%) with 95% confidence intervals and compared using the $\chi 2$ test. Analysis of other secondary outcomes will be dichotomized and presented for relevant time points, X^2 test.

Secondary outcome concerning Rescue opioid will be evaluated as time to event (opioid) – non parametric – Kaplan Meier estimate will be considered, if appropriate. Alternative rescue opioid yes/no – binary regression if assumptions are fulfilled.

All P-values will be two-sided, and those below 0.05 considered significant.

Detailed statistical plan are written, printed, signed and stored in Trial Master File

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