

Outcomes of Metabolic Resuscitation Using Ascorbic Acid, Thiamine, and Glucocorticoids in the Early Treatment of Sepsis.

ORANGES Trial

NCT#: NCT03422159

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Study end-points:

Primary end-point

- i. Time to vasopressor independence. Defined as the time from starting the active treatment/placebo to discontinuation of all pressors
- ii. Delta SOFA score, defined as the initial SOFA score minus the day 4 SOFA score

Secondary end-points

- iii. 28-day mortality
- iv. Hospital mortality
- v. PCT clearance (PCT-c) calculated using the following formula: initial PCT minus PCT at 96 hours, divided by the initial PCT multiplied by 100. [67,68]
- vi. ICU mortality
- vii. ICU length of stay (LOS) and ICU free days. ICU free days is calculated as the number of days alive and out of the ICU to day 28
- viii. Hospital LOS

Power Calculation:

Based on the results of the preliminary study of Marik et al we project that the combination of hydrocortisone, vitamin C and thiamine could reduce time to vasopressor discontinuation from 54 (+/- 30 hours) versus 30 hours. For the additional primary outcome we projected a greater change of SOFA

score of 4 (+/- 3) versus 2. Assuming a type 1 error of 5% (alpha of 0.05) and a power of 80% (the ability to detect a difference between two groups when a difference exists) would require a sample size of 94 patients. To account for dropouts and patients not requiring vasopressor therapy we will therefore aim for a sample size of 140 patients.

Data analysis:

Summary statistics will be used to describe the clinical data and presented as mean \pm SD, median with interquartile range (IQR) or percentages as appropriate. Chi squared analysis with Fisher's exact test (when appropriate) and Student's t test (Mann Whiney U test for non- normal distributions) were used to compare data between the active treatment group and the placebo group with statistical significance declared for probability values of 0.05 or less.