

25th August, 2022

TAME Cardiac Arrest trial SAP Update

The following should be read in conjunction with the published protocol and statistical analysis plan (SAP) for the TAME Cardiac Arrest trial¹ and the SAP update letter dated 31st May 2022. All amendments to the manuscript, supplemental appendix and planned analyses were made prior to access of any unblinded data. This update was necessary as limitations with data presentation of figures located in the supplemental appendix were identified.

Manuscript – TAME Protocol and SAP – V3

#1 – Statistical analysis plan

Clarification on the handling of missing data

Rationale for update:

- *Original text*

“If more than 5% of missing data are primary or secondary outcomes data, a sensitivity analysis will be performed using multiple imputation conditional on prognostic baseline and post-baseline variables under the assumption that missing data are conditional on observed covariates and were assumed to be missing at random.”

- *Updated text*

“If there are any missing data for the primary or secondary outcomes data, we will perform multiple imputation conditional on prognostic baseline and post-baseline variables under the assumption that missing data are conditional on observed covariates and were assumed to be missing at random.”

#2 – Table 2

Change to the description of the presentation of physiological data

Table 2. Physiological descriptors and process of care measures

- ‘Mean, highest and lowest’ wording changed to ‘Time-weighted mean’ for PaO₂, PaCO₂, pH, and temperature’ to be align with the presentation of data as described in the SAP Supplemental Appendix.

Removal of wording

Table 2. Physiological descriptors and process of care measures

- Removal of the wording ‘and predominant ventilation mode’ to be align with the presentation of data as described in the SAP Supplemental Appendix.

SAP Supplemental Appendix – V3

#1 – Figures

Removed

Figure S2. Forest plot for subgroup of analysis of death from any cause at 6 months

- Duplicated data that is shown in Panel A of Figure 3.

Figure S2. Forest plot for subgroup of analysis of death from any cause at 6 months

- Duplicated data that is shown in Panel B of Figure 3.

Figure S6. Lowest and highest PaCO₂ during intervention period by treatment group

- Analysis not possible as only a single PaCO₂ value was collected per patient per time point.

Figure S8. Mean, lowest, and highest PaO₂ during intervention period by treatment group

- Analysis not possible as only a single PaCO₂ value was collected per patient per time point.

Figure S10. Mean, lowest, and highest pH during intervention period by treatment group

- Analysis not possible as only a single pH value was collected per patient per time point.

Figure S12. Mean, lowest, and highest FiO₂ during intervention period by treatment group

- Analysis not possible as only a single FiO₂ value was collected per patient per time point.

Figure S14. Mean, lowest, and highest PEEP during intervention period by treatment group

- Analysis not possible as only a single PEEP value was collected per patient per time point.

Figure S15. Histogram depicting the ventilator modes used during intervention period by treatment group

- Analysis not possible as no ventilator mode data were collected in the case report form.

Figure S17. Mean, lowest, and highest temperature during intervention period by treatment in Panel B of Figure 3.

- Analysis not possible as only a single temperature value was collected per patient per time point.

Added

Figure S11. Probability of survival until ICU discharge after randomisation by treatment group

- Added to align with text published in the protocol and statistical analysis plan (SAP) for the TAME Cardiac Arrest trial¹ that stated '*survival data, including time to death at ICU, hospital discharge and 180-day*' would be presented.

Figure S12. Probability of survival until hospital discharge after randomisation by treatment group

- Added to align with text published in the protocol and statistical analysis plan (SAP) for the TAME Cardiac Arrest trial¹ that stated '*survival data, including time to death at ICU, hospital discharge and 180-day*' would be presented.

Figure S13. Probability of survival until 180-days after randomisation by treatment group

- Added to align with text published in the protocol and statistical analysis plan (SAP) for the TAME Cardiac Arrest trial¹ that stated '*survival data, including time to death at ICU, hospital discharge and 180-day*' would be presented.

General items

Addition of text “Panel B” to the text of ‘Figure 3. Subgroup analysis of death from any cause and favourable GOSE score at 6 months’ as this was unintentionally omitted at the time of the last update.



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Trial registration:

ClinicalTrials.gov: NCT03114033; and,
Australian and New Zealand Clinical Trials Registry: ACTRN12617000036314p

References

1. Nichol A, Bellomo R, Ady B, et al. Protocol summary and statistical analysis plan for the Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest (TAME) trial. *Crit Care Resusc* 2021;23(4):374-385. <https://doi.org/10/51893/2021.4.OA2>