



FREQUENTLY ASKED QUESTIONS

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Screening & Enrolment

Q. Do I include all out-of-hospital cardiac arrest admission the present to my hospital on the screening log?

A. Yes, please complete and submit a screening form for all out-of-hospital cardiac arrest patients admitted to your hospital. Please submit this form monthly or upload the data shortly after screening has been completed. Please note that for patients who are not eligible because they fall outside the '180 minutes from ROSC' criteria it is important to document the amount of time that had elapsed. Such data will provide guidance on when or if a protocol amendment is required to reduce the number of eligible non-randomised patients based on the tight time window.

Q. Who can screen and enrol patients?

A. Any clinical staff member appropriately trained or delegated by the site principal investigator can screen and enrol patients into TAME.

Q. Can I enrol a patient with a 'known' non-cardiac case of cardiac arrest?

A. Excluded known non-cardiac causes of cardiac arrest are those that would include asphyxia (e.g. hanging), aspiration (e.g. drowning), anaphylaxis or drug overdose (e.g. illicit drug overdose). These non-cardiac causes are a small proportion of the overall reason for admission to hospital following cardiac arrest. Such patients are being excluded as the mechanism of injury is defined, there is intervention specific treatment for each, and the likelihood of survival is poor and for those who do survive they often have significant poor neurological outcome.

Q. What is meant by 'eligible for ICU admission without restriction'?

A. At the time of screening if the patient is for full active treatment and the plan is for the ongoing care of the patient to occur in the intensive care unit then the patient can be enrolled. Should the goals of care change in the hours/days after enrolment because of medical information becoming available then this is okay. Patients are being enrolled on an intention-to-treat basis and as such all study procedures should be performed.

Q. What is meant by 'Within 3 hours of ROSC'?

A. Return of spontaneous circulation for the purposes of TAME is defined as the first ROSC that occurs that is sustained for equal to or greater than 20 minutes without the need for chest compressions. Initial efforts to achieve ROSC are considered as being 'active resuscitation'. A failure to reach a ROSC of equal to or greater than 20 minutes would not fulfil this criterion. Assessing the emergency medical services (e.g. ambulance notes) for the first eligible ROSC is required. The effective time window following identification of the first eligible ROSC is 160 minutes (180 minutes less the 20 minutes required to fulfil sustained ROSC).

Q. Can I enrol a witnessed cardiac arrest that has an initial rhythm of asystole?

A. Yes, a *witnessed* cardiac arrest that has an initial EMS identified rhythm of asystole can be enrolled. Such events are likely to have immediate bystander CPR provided in the time between the cardiac arrest event and the arrival of EMS personnel. Patients who experience an *unwitnessed* arrest with an initial asystolic rhythm are not to be enrolled. Asystole is a non-shockable rhythm with a known probability of a very poor outcome and the actual time from arrest to identification to bystander CPR is unknown.

Q. I've identified that the patient has COPD but there is no documentation of home oxygen, can I enrol this patient?

A. Yes, as long as there is no documentation or record of the patient requiring home oxygen therapy then the patient can be enrolled. Information on the use of supplemental home oxygen may become known in the hours/days afterwards. However, using information available at the time of screening and enrolment if the use of home oxygen is required then enrolment is allowed.

Q. Can the patient be enrolled pre-ICU?

A. Enrolment can occur on arrival to hospital, pre-ICU admission while the patient is still in the emergency department.

Q. What happens if a patient has a coronary angiogram or CT before coming to ICU?

A. We are aware that some participants will be admitted to the ED and have a coronary angiogram and/or CT prior to admission to the ICU. Enrolment under these circumstances it would be reasonable to enrol, commence CO₂ targeting using ETCO₂ and then once in ICU use ABG-derived PaCO₂ to tailor therapy.

Q. The patient has been transferred from another hospital to our ICU?

A. The patient is not eligible for enrolment in TAME. It is also likely that the 3-hour enrolment window from an eligible ROSC will have expired.

Randomisation

Q. Am I able to randomise a patient who has been transferred from another hospital to our ICU?

A. The patient is not eligible for enrolment in TAME.

Q. How will I know which treatment allocation the patient has received?

A. The treatment allocation will be displayed on the randomisation screen on the TAME electronic randomisation portal once all eligibility criteria and consent questions has been answered.

Consent

Q. When do I need to get consent?

A. Consent from the person responsible (legal surrogate / medical treatment decision maker) is to occur in accordance with all relevant ethical and regulatory approvals at your site. In the first instance consent from the person responsible to continue to participant's participation in the trial is likely to occur. The timing of the initial consent conversation will vary on a patient-by-patient and site-by-site basis.

Q. Why is there a 'Waiver of Consent Form' for Australian sites?

A. The waiver is for the collection of data in the event that the participant dies within 7 days of enrolment. Consent to continue (from either the participant or their person responsible) would be sought if deemed appropriate during the early period but recognise that the prognosis is often uncertain and consent discussion would be an undue/unwarranted burden or stressor for family members

Specifically, in section C of the Waiver of Consent request form we state:

"All participants in the study will be unconscious at the time of enrolment and the timing of enrolment must commence as soon after admission to the ED/ICU as possible and as such it is not possible to obtain informed consent prior to enrolment. The ethical issues associated with non-consent randomisation of unconscious patients have been previously considered by the Austin Health Human Research Ethics Committee in our very successful Phase II trial. This request for a waiver of consent is to apply for a period of 7 days from the enrolment of the participant into the study. This duration of time is deemed appropriate as i) the severity of the cardiac arrest event is initially unclear, ii) the treatment interventions are applied rapidly and rapidly completed (including the trial interventions, which last for 24 hours following randomisation, thus there will not be any ongoing intervention between day 1 and day 7), iii) this period is advised based on national and international guidelines prognostication of neurological, and iv) the burden of distress associated with the pursuit of consent following the death of a participant during the early post-resuscitation period is considered."

Study treatment

Q. What are the study treatments in mmHg or kPa and which one do I use?

A. For the purposes of TAME the targeting of either targeted normocapnia (TN) or targeted therapeutic mild hypercapnia (TTMH) is to occur based on the unit of measurement that is routinely used at each site. There are two units of measurement available: millimetres of mercury (mmHg) or kilopascals (kPa).

For patients allocated to targeted normocapnia (TN) the PaCO₂ target is:
= 35-45 mmHg or 4.6 – 6 kPa

For patients allocated to targeted therapeutic mild hypercapnia (TTMH) the PaCO₂ target is
= 50-55 mmHg or 6.6-7.3 kPa

Q. There is a large discrepancy between the end-tidal carbon dioxide (ETCO₂) value on the monitor and the arterial carbon dioxide (PaCO₂) value on the arterial blood gas (ABG). What should I do?

A. Assess the patient for safety. Please make clinical decisions and respiratory rate adjustments based on arterial blood gas data.

Q. There are 4-hourly ABGs requested as a part of the protocol. Can I do extra ABGs?

A. Yes, the 4-hourly ABGs are being performed and requested as a safety/monitoring approach as well as for treatment evaluation. Additional arterial blood gases may be performed based on the clinical need as determined by the patients treating clinical staff.

Q. My patient has been allocated to 'TTMH' and there is initial severe metabolic acidosis, what do I do?

A. This is an important safety consideration and has been included as a means to potentially avoiding worsening of the acidotic state. For patients who have been allocated to TTMH and are initially experiencing severe metabolic acidosis (pH <7.1 and base excess <-6 mmol/L) the initiation of the TTM protocol will occur when the acidosis has been corrected. The time it takes to correct the acidosis is to be deducted from the 24-h intervention window. For example, if the patient has been enrolled at 10:00 am and the acidosis only resolves at 14:00 then a further 20 hours of the TTMH targeting is to occur. The 24-hour window commences at the time of enrolment and occurs once.

Q. What do we do if the patient has been extubated before 24 hours?

A. This will be recorded as a protocol deviation as the allocated intervention has not been delivered. Remembering that the clinical care of the patient will take precedence over trial procedures and as such allows for the withdrawal of life-sustaining therapies or shifting alternate goals of care as directed by the patient's treating clinician.

Q. Why are arterial blood gases measured at 37°C (alpha-stat)?

A. Alpha-stat is the process of blood sample measurement in which that results are adjusted to 37°C. The alternate method is pH-stat, which is the actual temperature of the patient at the time the arterial blood sample is taken. The majority of arterial blood gases that are analysed are done so using the alpha-stat approach. For consistency and standardisation across sites the alpha-stat approach is being performed.

Case Report Form (CRF)

Q. What data do I need to collect at site in the case report form?

A. Data collected by research coordinator/site personnel are to include all pre-hospital, emergency department, intensive care admission and hospital admission data. This includes data related to eligibility, the intervention period, daily data in the ICU and data on the neurological assessment & prognostication of enrolled participants. Outcome data that will include day-30 data, 6- month data and 2-year follow-up data is likely to be collected centrally as the assessments are to be performed by an outcome assessor trained in the administration of the multiple and varied assessments.

Long-term follow-up

Q. Who will perform the follow-up?

A. Follow-up's will be performed by the coordinating centres in Australia and New Zealand. For all other sites the local/regional coordinating centre will conduct the follow-up in accordance with local legislation on privacy and use of health data.

If you have addition questions please email them to anzicrc-tame@monash.edu

Thank-you.