

SOS Screening & Eligibility Training



This training should be completed by medically qualified clinicians who will be assessing and confirming patient eligibility but have not completed full protocol or GCP training.

Please document that you have completed this training by signing the Investigator Training Log.

Contact details:

- Chief Investigator – Prof. Gavin Perkins
- Sponsor – University Hospitals Birmingham NHS Foundation Trust and University of Warwick
- Coordinating Centre – Warwick Clinical Trials Unit

If you have any questions, please do not hesitate to contact the trial team on:

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Trial Summary:

- Design: Multi-centre, open label, phase III randomised controlled clinical and cost-effectiveness trial with internal pilot
- Population: Adult patient >16 with severe TBI and raised ICP requiring ICU
- Intervention: Mannitol or Hypertonic Saline
- Outcome: Extended Glasgow Outcome Scale (GOS-E) at 6 months post-TBI
- Sample size: 638 patients in 36 months

Eligibility Criteria

Inclusion Criteria

- ✓ Adult >16
- ✓ Admission to ICU with TBI
- ✓ ICP > 20mmHg for more than 5 mins despite stage 1 measures
- ✓ < 10 days from initial TBI
- ✓ Abnormal CT scan consistent with TBI*

Exclusion Criteria

- ✗ Devastating brain injury with withdrawal of treatment anticipated in the next 24 hours
- ✗ Pregnancy**
- ✗ Severe hyponatraemia (serum Na < 135mmol/L)

**This relates to the initial CT scan at the first hospital that the patient was admitted to as part of routine care (not a separate scan for the purposes of the trial).*

***Please note, pregnancy is not a contraindication to hyperosmolar therapy, but these patients must be excluded for ethical and regulatory reasons.*

- Do not exclude patients that are given hyperosmolar therapy **prior to** ICU admission.
- Co-enrolment with other Clinical Trials of Investigational Medicinal Products (CTIMP) is **not permitted** (including if they have participated in a CTIMP within the 90 days before randomisation).

Process for confirming eligibility

- All patients admitted to ICU with severe TBI should be screened. This should be a continuous process as patients may become eligible for the trial very quickly. Any member of the team who has been trained can assess eligibility.
- However, eligibility must be confirmed by a **medically qualified doctor only, prior to the patient being enrolled.**
- The paper Screening and Eligibility form must be signed by the doctor who confirmed the patient is eligible to be enrolled in the trial. This can be signed at the time or as soon as practically possible after enrolment. The date and time that eligibility was confirmed also needs to be recorded on the form.
- The justification for the patient meeting **all** of the eligibility criteria must be clearly documented in the patient's medical notes for monitoring purposes. **This includes recording the patient's ICP and serum sodium at the point of confirming eligibility immediately prior to randomisation.**

Good Clinical Practice (GCP)

GCP is an internationally agreed **ethical and scientific quality standard** for designing, conducting, recording and reporting trials that involve the participation of human subjects.

Working to GCP principles provides assurance that the **rights, safety and well-being of trial subjects are protected**, we are working ethically and in accordance with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial **data is credible**.

13 PRINCIPLES

- 1 Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
- 2 Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
- 3 The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
- 4 The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
- 5 Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
- 6 A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.
 - **The trial needs to be conducted as per ethical approval and so there is no flexibility with the eligibility criteria.**
- 7 The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
 - **Eligibility must be confirmed by a medically qualified doctor.**
- 8 Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).
 - **The reason for doing this training!**
- 9 Freely given informed consent should be obtained from every subject prior to clinical trial participation.
- 10 All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
 - **Eligibility must be documented in the medical records, on the paper CRF and online SOS database.**
- 11 The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
- 12 Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.
- 13 Systems with procedures that assure the quality of every aspect of the trial should be implemented.

Principle 3: What is a Serious Adverse Event (SAE)?

An adverse event is considered to be serious if it fulfils one of the following criteria:

- Results in death
- Is life-threatening
- Requires hospitalisation or prolongation of existing inpatients' hospitalisation
- Results in disability/incapacity
- Congenital abnormality/birth defect
- Requires important medical event/medical intervention

Please inform your research team of any possible SAEs as these need to be reported to the trial coordinating centre **within 24 hours** of becoming aware of the event.

- **Serious Adverse Reaction (SAR)** - Serious, and at least possibly related to IMP
- **Suspected Unexpected Serious Adverse Reaction (SUSAR)** - A SAR which is unexpected in nature, severity or frequency as documented in section 4.8 of Reference Safety Information (RSI)/Summary of Product Characteristics (SmPC) .

What is causality?

A medical assessment by a doctor of whether a SAE has a possible causal relationship to the administration of the Investigational Medicinal Product.

What should not be reported as a SAE for SOS?

- Death
- Persistent or significant disability/incapacity
- Organ failure
- Any other events relating to the underlying illness/injury