

Monitoring plan

The Conservative vs. Liberal Approach to fluid therapy of Septic Shock in Intensive Care
(CLASSIC) Trial
A randomised, blinded, placebo-controlled trial

EudraCT-number: 2018-000404-42

Prerequisites

The monitoring plan is based on protocol version 2.1, 3/5/2018, and the risk assessment of the trial according to the SOP I02-16 monitoring plan by the GCP unit.

Extent

This monitoring plan describes the monitoring that is performed by the external monitor (GCP unit or other authorized party).

It may be necessary to perform further quality assurance/quality control, which ought to be described and documented by sponsor.

Monitoring visits

Initiation is done in every centre. When the prerequisites for inclusion of subjects in the centre is met, it will be documented by the monitor through a written approval to start the trial.

First monitoring visit in each trial site is planned to be after inclusion of the first trial participant.

The monitor will hereafter perform monitoring visits in each trial site considering the agreed extent of monitoring, inclusion speed and the needs of individual trial sites. The monitoring frequency is expected to be higher during the inclusion period. As a minimum, the monitor will be in contact with each trial site once per year.

The monitoring is finished on the trial sites when every subject has finished 90 days follow-up and data is registered in the eCRF. Final monitoring visit with sponsor is performed when completion of the trial is reported to the authorities (1 year after the last patient randomised).

Monitoring of Trial Master File

Relevant documents in the Trial Master file will be monitored continuously, as a minimum once yearly.

It will be continuously monitored that data is kept out of reach of unauthorized persons and without risk of change or loss.

Monitoring compliance and data quality

To verify that the trial site has implemented procedures that ensure good compliance with the protocol, it will be monitored that protocol-specific investigations, analyses and procedures are performed as specified in the protocol.

To verify that the trial site has implemented procedures that ensure good data quality, it is monitored that all data are properly registered in the CRF. In addition, it is checked that the CRF is fully completed and that corrections are correctly performed according to GCP. The above-mentioned procedures will be performed for the first 3 included patients on each trial site and hereafter on randomly chosen trial participants until a total of 10% has been monitored.

Monitoring plan version 1.0, 08-10-2018, EudraCT: 2018-000404-42

Since there is no quality in monitoring all "Day forms" for patients with a long ICU admission, data will be monitored for the first 4 "Day forms". Fluid data (D1-13) and protocol violations (D14 – D14a) will be monitored more frequently corresponding to every 10th "Day Form".

Monitoring of informed consent

For all trial participants it will be monitored that

- consent has been obtained according to national regulations
- attempts to obtain consent is properly recorded in patient file or otherwise documented in e.g. consent log
- no protocol-specific actions are performed before informed consent according to national regulations is obtained
- informed consent is only obtained by personnel delegated and trained to do so

Monitoring of selected trial data

Based on the risk assessment of the trial, the following monitoring strategy has been chosen. See also, *Data Verification Plan*.

Inclusion, withdrawal and completion

For all trial subjects the following will be monitored:

- that inclusion of trial participants is performed by personnel trained to do so
- that inclusion and termination of the trial are correctly recorded
- that all inclusion criteria and no exclusion criteria are fulfilled
- that patients withdrawn from the trial fulfil one of the withdrawal criteria and that it is properly documented in patient records and the eCRF

For the first 3 participants included in each trial site and thereafter randomly selected trial participants until approx. 10% withdrawal criteria during ICU admission (patient consent is withdrawn, SAR/ SUSAR, clinical decision or patient is subject to involuntary hospitalization) are monitored. This is done by reviewing the patient file and SAR/SUSAR form if relevant.

Primary outcome

For all trial participants the following is monitored

- primary outcome (90-day mortality) from the patient files.

Examinations

No protocol specific examinations are performed in this trial.

Safety management

Events and side effects

- If a SAR is entered in the eCRF it will be verified in the patient files. This will be done for all day forms from inclusion until 24 hours after last administration or discharge from the ICU to ensure that SARs are correctly registered and reported in the eCRF.
- Sponsor's centre: it will be monitored that all SAR's and SUSAR's are reported without undue delay to the Danish Medicines Agency and the Scientific Ethics Committee and subsequently to the investigators.

Sponsor's monitoring

The coordinating GCP coordinator will monitor at the sponsor's centre, that sponsor documents the following:

Protocol violations

A list of protocol violations on all trial sites will be centrally drawn from the eCRF 4 times a year by Sponsor. The coordinating GCP coordinator that this is documented at Sponsors site in a 'Note to file' in Trial Master File #13 at Sponsors site.

Queries from monitor

Monitor creates queries if potential errors are found in data in the eCRF. Queries from monitor are handled by the centres in question. Sponsors must ensure that the centres correct relevant queries themselves

Initiation

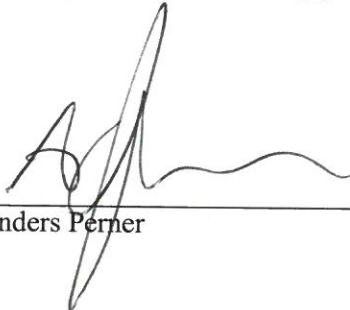
This monitoring plan will take effect from the date of sponsor's acceptance of the monitoring plan.

Evaluation of the monitoring plan

The monitoring plan will be evaluated on a continuous basis and in case of an observed need. If it by the GCP monitoring, central monitoring or audit is observed, that the prerequisites for this monitoring plan have changed, it will result in evaluation and possible revision of the monitoring plan. This may be conditions such as change in the protocol, significant non-compliance, insufficient data quality and significant changes in project staff composition. All changes of the monitoring plan will be in writing

Signatures

13/11/18
Date


Sponsor, Anders Perner

22-10-2018
Date


Primær GCP-koordinator, Pernille Ask Aabo