Monitoring Plan

HOT-ICU

"Handling Oxygenation Targets in the Intensive Care Unit"

EudraCT-no. 2017-000632-34

(Translation of the Danish monitoring plan)

Preconditions for the Monitoring Plan

This monitoring plan is based on protocol version 1.2 and a risk evaluation of the trial according to the Danish GCP units' "SOP I02-16 Monitoreringsplan".

Extent of the Monitoring Plan

This monitoring plan describes the monitoring to take place by designated monitors or qualified personnel contracted by Centre for Research in Intensive Care (CRIC). It may be necessary to carry out additional quality control, which must be described then by Sponsor.

Initiation – and Monitoring visits

An initiation visit is to be conducted at each site. When the conditions for inclusion of the first patient in the trial is fulfilled, an initiation visit report should be forwarded by e-mail to the site (to be kept in the Site Master File) and to the Danish coordinating centre hot-icu@cric.nu. This will be a written approval to initiate patient inclusion.

The first monitoring visit at each site will be arranged as soon as the first patient has been included. All following monitoring visits will be conducted according to the extent of monitoring as described within the plan, as well as the inclusion rate, and the overall needs at the site. The monitoring frequency is expected to be higher during recruitment than during follow-up. A monitoring visit will take place at least once a year.

Final monitoring visit at a site will take place when all included patients have a registered 1-year follow-up and all data has been registered in the eCRF.

Monitoring of Site Master File

Relevant documents in the Site Master File will be monitored regularly for their presence and in up-dated versions when relevant, as a minimum once a year.

Any documents containing patient data including the Site Master File must be kept out of reach for non-authorised personnel, and stored without risk of being modified or lost.

The electronic case report form (eCRF) requires personal login only.

Monitoring of general protocol compliance and data quality

The following will be conducted in the first three patients at each site and hereafter in ten percent of the succeeding patients (randomly selected).

To verify that the site has implemented procedures to ensure protocol compliance and protocol specific examinations, analyses and procedures will be monitored.

To verify that the site has implemented procedures to ensure good data quality, all data in the eCRF will be monitored for correctness. Furthermore, the completeness of eCRF fulfilment, and that all corrections are conducted in compliance with GCP will be ensured.

Monitoring of informed consent

To be monitored for all included patients:

- Presence of informed consent according to national regulatory procedures
- No protocol specific actions have taken place prior to informed consent
- Informed consent is handled by dedicated staff
- The oral or written informed consent is correctly stated in the patient's medical record
- Any attempt to pursue informed consent is documented correctly in the patient's medical record or documented elsewhere

Monitoring of selected data

Based on a risk evaluation of the trial set-up the following strategy for monitoring has been chosen in combination with the "Plan for data verification".

Inclusion, withdrawal and discharge

To be monitored for all included patients

- Inclusion of patients is handled by delegated personnel only
- Inclusion and discharge are correct stated in the patient's medical journal and in the eCRF
- All inclusion criteria and no exclusion criteria are fulfilled
- Correct patient medical records of withdrawal from the trial due to retraction of informed consent, informed consent not given, or SUSAR
- Documented approval of continuation of data collection for patients withdrawn from the trial

Analyses

To be monitored for all included patients

- The values for PaO_2, SaO_2 and FiO_2 are correctly measured at the indicated time and in compliance with the protocol (i.e. interval of 12 hours i.e. 6.00am-6.00pm and 6.00pm-6.00am), and data is correctly stated in the eCRF
- The P(aB)-lactate, or alternatively the P(vB)-lactate, is analysed at the correct time (within 12 hours prior to randomisation) and in compliance with the protocol, and the data is correctly stated in the eCRF

Safety issues

To be monitored for all included patients

- Registration and reporting of SAEs are complete (SAE is defined as new events of shock or myocardial, cerebral, or intestinal ischaemia). Patient medical records are reviewed for the first seven days after admission
- All reported SAEs are evaluated and – if relevant – reported to Sponsor

Date of entry into force

This monitoring plan is applied on the date of sponsors accept.

Evaluation of the monitoring plan

The monitoring plan will be subject to evaluation over time.

If it turns out – during monitoring or audit – that the conditions for this monitoring plan have changed, an evaluation will take place and may result in a revised monitoring plan. Conditions such as i.e. protocol changes, outstanding non-compliance, insufficient data quality, or unfortunate changes in the staff composition are considered reasons to perform an evaluation.

All changes to the monitoring plan will be documented in writing.

28TH OF AUGUST 2017 

Date Sponsors representative

Bodil Steen Rasmussen

Data Verification Plan

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Level I: Data verification in the first three included patients and hereafter in ten percent of succeeding included patients, randomly selected.

Level II: All included patients.

Data	eCRF Code	I	II	Comments
Informed consent		X	X	Compliance with national regulatory standards
Consent stated in medical record		X	X	
Inclusion criteria	S1-S7	X	X	
Exclusion criteria	S8-S19	X	X	
Randomisation	S20-S25	X	X	Tip: S21 check no. 2 before no. 1.
Baseline				Discrepancies must be commented if they affect the SOFA score (Appendix 8.)
General patient information	B1-B6	X		B4: Check only for presence of data
Respiratory support	B7-B7d	X		
Arterial blood gas (ABG)	B8-B11	X	X	
Acute illness	B12-B18	X		B18: Check only for presence of data
SOFA score	B19-B26	X		B19, B20 and B25: Check only for presence of data
Chronic co-morbidities	B27-B30a	X		B28: Check only for presence of data
Daily registration				
Respiration	D1-D7a4	X	X	D1: Intermittent CPAP (less than 1 hour) is not considered respiratory support Registered highest values must be – if possible – from the same time point. Registered lowest values must be – if possible from the same time point
Remaining organ systems	D8	X	X	
Remaining organ systems	D9-D10 and D14	X		
SAE/secondary outcome (Defined as acute myocardial ischemia, ischemic stroke, intestinal ischemia or new episodes of shock)	D11-D13	X	X	Patients' medical records are reviewed for the first 7 days of admission. In case of SAE check eCRF for correct registration
Discharge from ICU	DR1-DR3	X		

Data	eCRF Code	I	II	Comments
Readmission	DR4-DR5	X		Within 90 days after randomisation
Withdrawal	W1-W3b	X	X	Notice: It must be stated in the patients' medical record, if a consent is given to keep up data recording when written consent is retracted or not given
Follow-up on primary outcome after 90 days	F0-F3a	X	X	