Monitoring Plan

HOT-COVID

"Handling Oxygenation Targets in COVID-19"

EudraCT-no. 2017-000632-34

Amendment to the HOT-ICU trial

(Translation of the Danish Monitoring plan version 4.0 of 11. November, 2020)

Preconditions for the Monitoring Plan

This monitoring plan is based on HOT-COVID protocol version 1.2 28. July 2020 and HOT-ICU protocol 2.2 3. July 2020 and a risk evaluation according to the Danish GCP 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 the Collaboration for Research in Intensive Care (CRIC). It may be necessary to carry out additional quality control, which must be described then by Sponsor of the trial.

Initiation – and Monitoring visits

As sites previously have been initiated in the HOT-ICU trial, and the HOT-COVID trial is an amendment, no additional initiation visit is required. The site will be allowed to start once the contract for trial participation is signed.

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 this 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 90-day follow-up and all data has been registered in the electronic case report form (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 eCRF requires personal login only.

Monitoring of general protocol compliance and data quality

The following will be conducted in 5% of the included patients (randomly selected):

- Verify that the site has implemented procedures to ensure protocol compliance for all protocol specific examinations, analyses and procedures that will be monitored.
- Verify that the site has implemented procedures to ensure good data quality, all data in the eCRF will be monitored for correctness. Furthermore, verify 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 *Data verification plan* v. 1.0 of 1. February, 2021.

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 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

To be monitored for 5% of included patients (randomly selected):

- All exclusion criteria are fulfilled

Analyses

To be monitored for all included patients:

- Correct registration of respiratory support (D1) for **the first four days and hereafter every 10th day up to a maximum of 90 days after randomisation**

To be monitored for 5% of included patients (randomly selected):

- Correct registration of respiratory support (D1a-D1c) for **the first four days and hereafter every 10th day up to a maximum of 90 days after randomisation**
- 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. 06.00-18.00pm and 18.00-06.00), and data is correctly stated in the eCRF (D2-D5b) for **the first four days and hereafter every 10th day up to a maximum of 90 days after randomisation**
- Data registered at 90-day follow-up is correctly registered (F1-F7a1)

Safety issues

To be monitored for all included patients for the first four days:

- A registered severe adverse event (SAE) can be verified in the patient's medical records to ascertain that the registration and reporting of SAEs is correct and in due time (SAE is defined as new events of shock or myocardial, cerebral, or intestinal ischaemia)

To be monitored for 5% of included patients (randomly selected) for the first four days:

- Registration and reporting of SAEs are complete. Patient medical records are reviewed for the first four days after admission (SAE is defined as new events of shock or myocardial, cerebral, or intestinal ischaemia)
- 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.

FEBRUARY 1, 2021

Date

Sponsors representative

Bodil Steen Rasmussen