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HOT-ICU newsletter – August 2020

HOT-ICU trial inclusion completed

2928 patients

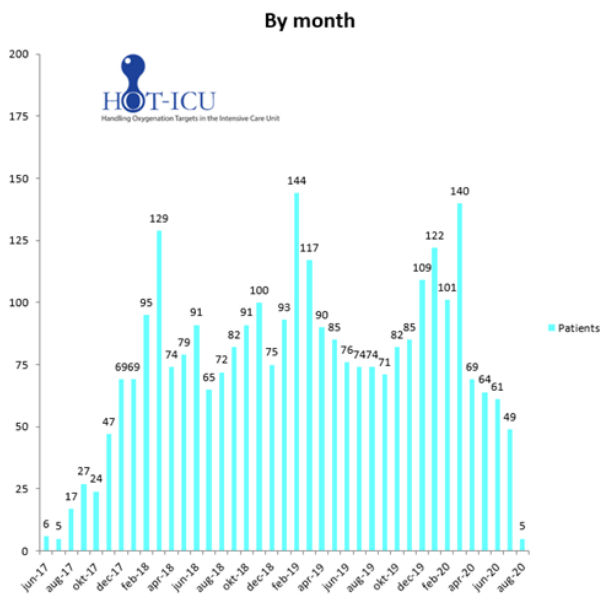
Status

Dear friends and colleagues

We would like to thank you all for your enormous effort in the HOT-ICU trial! Collectively, we have randomised 2928 patient in just three years. This is a fantastic accomplishment. Congratulations to all sites for making it this far. The last patient was randomised in Basel on August 3rd and they will receive a prize to mark the completion of the trial.

Recruitment

A total of 36 sites were initiated in the trial, but due to the COVID-19 pandemic many have been closed this spring, and thus 34 sites managed to randomise patients.



Top recruiters in July and August were:

1. Køge (10) – 8th time number 1!
2. Hillerød and Basel (7 each)
3. ICU 4131 Copenhagen and Aalborg (6 each)
4. ICU North Aarhus (4)
5. Slagelse (3)

Congratulations to all sites.

Work ahead

We know that you have worked hard to get this far, and for this we are very grateful. However, the work is not quite over yet.

Please complete data registration no later than November 2nd, 2020.

In the following we have pinned out the tasks ahead of us in chronological order.
Please read these paragraphs carefully – and do not hesitate to contact us if you have any questions.

Daily until complete 90-day follow-up (November 2nd, 2020)

- Continue trial intervention for already included patients until a maximum of 90 days
- Patients re-admitted to a HOT-ICU trial site within 90 days should be re-admitted in the eCRF and have their intervention resumed as usual
- Please complete data registration as fast as possible, as this is a prerequisite for data validation and the final GCP monitoring visit

Data validation (ongoing)

Data validation has already begun, and you will be involved at the earliest. This process is to ensure as high quality data as possible. We are currently identifying and evaluating the extent of plausible data registration errors.

As local investigators you will receive a list of queries for your specific site. This will contain a list of plausible data registration errors (e.g. extreme values or highly unlikely combinations of registered data, etc.). Please go through this list and send corrections or confirmations of the identified values to the coordinating investigator, as per instructions given.

Days alive without the use of life support (renal replacement therapy, inotropes/vasopressors and mechanical ventilation) within 90 days – a secondary outcome in the trial

This outcome requires data not covered entirely by eCRF data, as life support for some patients may have continued in a non-HOT-ICU trial ICU. Consequently, if a patient has been transferred to a non-HOT-ICU trial ICU, this ICU needs to be contacted in order to register data on potential continued life support.

Local investigators will receive:

- A list of patients (participant IDs) at your site in the eCRF transferred to an ICU not participating in HOT-ICU (as per registered in the eCRF discharge forms)
- A site-specific Microsoft excel document template for registering these data

How to obtain these data will vary from site to site (country to country), e.g. via electronical patient journals or via contact to the receiving ICU.

Closing of sites and final GCP monitoring visit (November 2020 – December 2020)
A site will be *"closed"* by the sponsor when no active patients can be readmitted, i.e. >90 days from last included patient or potentially before if the last included patient(s) is registered as dead in the eCRF.

The mandatory final/closing visits from the respective GCP units require the following:

- Site "closed" by sponsor
- Complete data registration incl. 90-day follow-up
- Complete/signed "*Site Participant List"* (a formal statement of taking responsibility, to the extent possible, for correct inclusion and correct data registration) – this document will be provided by the sponsor to the respective local investigators prior to the final GCP-monitoring visit, and a signed copy should be returned to the coordinating centre

The HOT-COVID trial
The Handling Oxygenation Targets in COVID-19 (HOT-COVID) trial is an amendment to the HOT-ICU trial and will be launched soon. This trial will focus solely on SARS-CoV-2 positive patients admitted to the ICU with acute hypoxaemic respiratory failure but will otherwise follow the HOT-ICU protocol. Already, several sites have agreed to take part in this continuation.

Sites that continue with the HOT-COVID trial will not be closed during the final GCP inspections of the HOT-ICU patients.

If your site wishes to participate, please do not hesitate to contact the coordinating centre. More information on the HOT-COVID trial will be provided separately to those sites interesting in participating and on the HOT-COVID website: cric.nu/hot-covid.

Main paper manuscript (November 2020 – January 2021)
Early drafts are presently being written.

The statistical analyses will be conducted in November (est. Mid-November). Subsequently, a draft will be finalised and sent to all authors (please see below).

Authorships: Please find description of authorship requirements in the HOT-ICU protocol section 13.3.1 (pages 45-46).

The primary local investigator will in soon receive information on the number of authorships granted to the site. This information will include a request from the sponsor to return information on the authors, including correct names, institutions/affiliations, functioning email addresses, ORCID ID numbers if available, and completed ICMJE conflict of interest declarations. Please do also provide names of all site

investigators as these will be presented in 'The HOT-ICU trial investigators' section in the appendix. Please see that all the requested information is returned as quickly as possible.

Patient information of trial results

National regulations on patient information, upon publication of trial results vary. Lists of matching participant IDs and trial allocation can be provided by the coordinating investigator (after publication of the main paper) upon request.

A trial result patient information letter template will be drafted by the coordinating site in Danish and English and offered to the local trial investigators. This information will also be available on the trial website.

In Denmark: The coordinating centre will be responsible for sending out this information letter to those patients included in Denmark who have answered 'yes' to the question "Do you wish to receive information about the trial result?" on the consent form. This information letter will not include patient allocation but contact details will be provided on the coordinating investigator who can pass on this information upon request.

Long-term follow up

One-year follow-up data will be available August 4th, 2021 at the latest. More information on this will come in due time. Please complete follow-up when possible.

In Denmark: Mortality status at one-year follow-up, and contact information will be obtained as per usual practice for the centralised EQ-5D-5L obtainment.

Long term follow-up paper: In order to acknowledge that many investigators have worked hard in the HOT-ICU trial, and some without meeting main paper authorship requirement, the HOT-ICU management committee has agreed to offer one authorship in the long term follow-up paper to each site being 25 patients or less from an authorship (or additional authorship) on the main paper. The local investigator will be informed of this if applicable.

HOT-ICU hotline

If you have any questions do not hesitate to send an e-mail to hot-icu@cric.nu or to contact the HOT-ICU hotline (+45 2118 2543). Please **leave a message and your phone number if the call is not answered** and we will call you back as soon as possible.

Please archive this newsletter in your site master file.

Kindest regards,
Thomas, Olav and Bodil