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SUP-ICU Newsletter – November 2017

SUP-ICU trial inclusion completed
 # 3350 patients

Status

Dear friends

Once again thank you very much for your tremendous efforts in the SUP-ICU trial – 3350 randomised patients in 22 months is truly impressive!

We know that it has taken a lot of hard work to get to this interesting point and for that we are very grateful.

However, the work is not quite over yet.

Please complete (as to the extent possible) data registration no later than December 4th 2017.

Below we have highlighted, in chronological order, the tasks ahead of us.

Please read these paragraphs carefully – and do not hesitate to contact us if you have any questions.

Daily until complete follow-up (January 22nd 2018)

- Continue to administer trial medication for already included patients untill a maximum of 90-days
- Patients re-admitted to a SUP-ICU trial site within 90-days should continue to be re-admitted in the eCRF and have their trial medication resummed
- The majority of trial medication will expire end of november 2017. A minor part, however, is due one more month and will expire end of december 2017. Boxes of trial medication will be centrally inactivated in the medication module at November 30 and December 31, respectively (you should not do anything)
- Re-distribution of IMP may need to continue untill the end of December. We are well aware that this mandates a big effort on you to re-pack and help shipping trial medication between sites, and we are very gratefull for the work you continuosly put into this
- Please complete data registration at the earliest, as this is a prerequisite for data validation and the final GCP monitoring visit

Data validation (ongoing)

This process is to ensure as high quality data as possible.

Data validation has already begun, and you will be involved at the earliest

We are currently identifying and evaluating the extent of:

- Missing data
- Plausible data registration errors

As local investigators you will receive a list of queries for your specific site by email early December.

This will contain:

- A list of missing data - including instructions on potential “logical” imputation, if applicable. Please go through this list and send the applicable data to the coordinating investigator, as per instructions given
- A list of plausible data registration errors (e.g. extreme values or highly unlikely combinations of registered data, etc.). Please go though 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 modalities (RRT, 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-SUP-ICU ICU.

Consequently, if a patient has been transferred to a non-SUP-ICU ICU, we need to contact this ICU in order to register data on potential continued life support.

International local investigators (=NOT in DK) will early December receive:

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

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

We know that this entails an extra workload on you as local investigators; we are very grateful for your help. In some cases this information will be difficult (or even in few cases impossible) to obtain.

In Denmark the above mentioned process will be carried out by the coordinating centre.

Closing of sites and final GCP monitoring visit (December 2017 – January 2018)

A site will be 'closed' by the sponsor when no active (IMP and/or data registration) patients, included at the particular site, 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.

Please note: From the time of closing (we will inform you on this) the SUP-ICU intervention should **not** be continued in case of transfer of an active SUP-ICU patient from another active SUP-ICU site. The dispatching/discharging site should choose 'ICU not participating in SUP-ICU trial' in the discharge form in case of transfer to a 'closed' SUP-ICU site.

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 responsibilty, 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.

Main paper manuscript (January 2018 – March/April 2018)

Early drafts are presently being written.

The independent statistician will conduct the predefined blinded analyses in March (est. mid-March). Subsequently, a draft will be finalised and sent to the authors (please see below).

Authorships: Please find description of authorship requirements in the SUP-ICU protocol section 13.3.1 (page 41-42). The primary local investigator will in December receive information on the number of authorships granted to the particular site. This information will include a request from the sponsor to return information on the authors, including correct names, institutions/affiliations, functioning email addresses and completed ICMJE and Copyright Agreement forms. Please do also provide names of all site investigators as these will be presented in 'The SUP-ICU trial investigators'-section, in the appendix. Please see that all the requested information is returned as quickly as possible.

Drug/IMP accountability and disposal (December 2017 – March 2018)

Residual SUP-ICU IMP at trial sites after January 1st 2018 should be accounted for and disposed as per the following instructions:

- Vial numbers of residual vials are to be registered on the trial document '*Drug disposal Form v.2*' by the local investigators.
- Subsequently the residual vials should be disposed as per local/national regulations. Please note that residual IMP should not be returned to the sponsor.
- A signed copy of the '*Drug Disposal Form v.2'* should subsequenly be returned to the coordinating investigator
- The coordninating center will, depending on the extent of mismatch between actual residual vials and electronically registered vials in the SUP-ICU mediciation module, be in contact to resolve any uncertanties in this regard.

Patient information of trial results

National regulations on patient information, upon publication of trial results and un-blinding of patient allocation, 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 in English and offered to the local trial investigators.

In Denmark: The local investigator will be responsible for sending out this information letter to those relatives/patients included at your site, who have answered 'yes' to the question "Do you wish to receive information about the trial result?" on the consent form. The information letter, to patients included in Denmark, will not include patient allocation, but contact details will be provided on the coordinating investigator, who can pass on this information upon inquiry. The above mentioned solution, for patients included in Denmark, enables the use of email as route of information (- if an email address has been obtained). If no email address is known, the use of regular mailing service is needed.

Long-term follow up

One-year follow-up data will be available January 22nd 2019, at the latest.
More information on this will come in due time. Please complete follow-up when possible.

In Denmark: 1-year mortality data will be collected centrally from the National Patient Registry (CPR-registret). However, follow-up of patients without a Danish social security number included in SUP-ICU in Denmark, must be collected by the local investigators.

Long term follow-up paper:
In order to acknowledge that many investigators have worked hard in the SUP-ICU trial, and some without meeting main paper authorship requirement, the SUP-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.

SUP-ICU hotline

If you have any questions please send us an email (soeren.marker.jensen.01@regionh.dk) or contact the SUP-ICU hotline (+45 3545 7450). If no one answers the phone, please **leave a message and your phone number** and we will call you back as soon as possible.

Please archive this newsletter in your Site Master File.

Best regards

Søren, Mette, Anders and Morten