# Minutes CRIC board meeting, spring 2023

Date: May 9, 2023

Place: Rigshospitalet in Copenhagen and online on Teams

**Attending members (17):** Anders Perner, Bodil Steen Rasmussen, Morten Hylander Møller, Maj-Brit Nørregaard Kjær, Anders Granholm, Olav Lilleholt Schjørring, Morten Bestle, Robert Winding, Thomas Strøm, Jon Henrik Laake, Maria Cronhjort, Theis Skovsgaard Itenov, Johanna Hästbacka, Marlies Ostermann, Eric Keus, Lone Musaeus Poulsen, Praleene Sivapalan

Online: Christian Gluud, Kathy Rowan, Theis Lange, Martin Siegemund, Anne Sofie Andreasen, Christian Ahlstedt, Anne Craveiro Brøchner

Unable to attend: Mette Krag Vogelius, Carmen Pfortmüller, Joerg Christian Schefold, Matthew Morgan, Wojtek Szczeklik, Martin Ingi Sigurdsson, Jacob Hollenberg, Rebecka Rubenson Wahlin, Andreas Barratt-Due and Ashish K Khanna

## Agenda and minutes

**Welcome (Maj-Brit)**
The meeting started with a short presentation of the participants.

**1. Update on CRIC activities (Anders)**
*Ongoing activities:*
The development of the platform trial – INCEPT is ongoing. It will initially start recruiting in Denmark and subsequently expand internationally.
The GODIF trial is currently running – more countries and sites are on the way.
HOT-COVID soon finalizes 90 follow-up (FUP) and next 1-year FUP will be assessed.
The AID ICU 1-year FUP is being analysed.
The CLASSIC 1-year FUP is completed, and the paper is under review.

CRIC has been invited to a world conference in Istanbul -> Nina Ranbjerg-Andersen will represent CRIC and present the AID-ICU trial.

Gitte Kingo Vesterlund has resigned and instead Mette Qviste (non-medical background) will join the CRIC office from 1st of June.

The CRIC network is growing – activities are increasing, and programs are slowly progressing even though the day-to-day activity can be sparse.

Open discussion of how the network should continue and whether we should rotate the meetings. For now, we will continue with the meetings in Copenhagen, but other sites are welcome to take over anytime.

## 2. Ongoing trials (Bodil Steen Rasmussen, Morten Bestle)

HOT-COVID update:

- 726 patients were included and 54 were pending, when the trial stopped March 8, 2023 due to low recruitment even during winter.
- Results pending – last 90-day FUP on June 7, 2023.
- Presenting results in Milano, ESCIM.
- Journal editor contacted for publication.
- Ongoing work for a IPDMA for the HOT-ICU & the HOT-COVID trial

GODIF update:

- Published protocol, statistical analysis plan, systematic review, and results for the first 50 GODIF patients prior to update of the protocol.
- Still low inclusion rates
- New sites needed (awaiting European and Australian sites)
- Challenges: Active substance issues. Problems with pharmacies supplying sufficient documentation regarding the medication -> amendment do it by an unblinded person from shelf-medication as done for COVID-STEROID.
- How to proceed?
    - Maybe motivate that the cost money is used to organize infrastructure and create the research environment and try to increase the personnel's time at the departments.
    - Regular online GODIF meetings have been initiated to accommodate and capture challenges or other issues important to evaluate on for continuing and hopefully improve the inclusion rate.

## 3. Coming trials (Jon H Laake, Eric Keus, Anders Granholm)

**SVALBARD (Jon Henrik Laake):**

Breathing on a ventilator in a control vs. triggered mode – either mode might be harmful. Observational studies point in both directions and guidelines based on low quality of evidence. International survey of clinicians has been conducted

*Most respondents were prepared to randomise patients with moderate ARDS to modes allowing spontaneous breathing vs. controlled ventilation. Most favoured short-term clinical outcomes over patient reported.*

How to proceed?

- Pilot feasibility trial (maybe embedded in a larger trial)
- Pragmatic trial – design and data collection.
- How to handle crossover? Maybe intended controlled vs spontaneous focusing on the first 72 h as there will be cross-over when weaning off -> does the days on the different intervention differ?
- Clinicians should be allowed to choose the optimal ventilator mode for the individual patient independent on allocation.
- Primary outcome? Is it even realistic to hope for a change in mortality? Maybe focus on evaluating safety but include mortality however not powered for this necessary.
- Jon will reach out to colleagues to discuss trial design.

**Thromboprophylaxis (Eric Keus):**

Motivation from a network meta-analysis. Intermediate dose prophylaxis might have beneficial effects on patients with VTE compared with lower dose.
Results from the survey presented (still open on request):

- 40% local variation vs. 80% national variation
- Categorized by the hospital: 13% low, 87% intermediate dose. The definition of intermediate dose included e.g., Fragmin 5000 IEx1, which is considered as low dose thromboprophylaxis in some ICUs.
- Willingness to randomization on:
    - Dose: intermediate vs low (type and dose varies in practice)
    - Guided by weight
    - Placebo is not possible
    - Once or twice daily dosing
    - Based on individual risk assessment (unsure on which model?)
- How to proceed?
    - Fast, simple observational study?
    - Definition on low, intermittent and high dosing?
    - Compare clinical protocol/guidelines from different sites?
    - Intermediate vs. weight-based and maybe even third arm with low as well.
    - Availability to use the same drug? – not always equivalent?

**EMPRESS (Anders Granholm):**

- Updated systematic review
- Internal unofficial pilot trial for INCEPT.
- Start early, learn from it and adapt later
- Design presented incl. Bayesian framework with stopping rules and max. sample size
- Focus: high probability of a conclusive result.
- Consider subgroup according to geography.
- Could one include without prior consent if you have equivalent treatments?

**4. Intensive CarE Platform Trial (INCEPT) (Morten Hylander, Maj-Brit N Kjær)**

**Challenges and possibilities** with Morten were skipped due to the time limit.

**External validation of a Danish Core Outcome Set (COS) (Maj-Brit N Kjær)**

- A Danish COS is being developed (protocol published https://doi.org/10.1111/aas.14024)
- No golden standard of how to extend a COS to other countries, why the COMET group with their expertise was consulted.
- Issues to discuss:
    - Is it needed? Should it be a priority?
        - Not a re-invention, but external validation to see if the COS are good enough outside our environment in Denmark.
        - Main objective: Acceptable main core outcomes set– whether it exactly match is not the question.

    - Challenges arise about variables not included in the COS, however specific variables for each trial can be added

- How we decide to validate the COS for other countries should be explained by an amendment to the existing protocol.
- Research panels has been initiated across Denmark to help inform the development of the COS, but also in many other ways as e.g. ethical questions, face validity of flyers, documents, website, guidelines, research questions where ever patients, relatives, clinicians and researchers different perspectives could be of interest.
- Suggest a research panel in every country being a part of CRIC/INCEPT.

If no objections the upcoming meetings will be with only physical participation.

Dates for upcoming meetings

- *Online CRIC board meeting is 24 August 2023 from 3:30 pm to 4:30 pm*

- *CRIC board meeting is 6 November 2023 from 4pm with following dinner all in Copenhagen (only physical participation).*

- *All stakeholder meeting is 7 November 2023 from 9am to 3pm (only physical participation) in Copenhagen.*