

Meeting minutes of CRIC

Scientific Steering Committee Meeting

Date: October 9th, 2015

Time: 11am-1pm

Place: CRIC facilities, Dept. 7831, 3.floor, Tagensvej 22, 2200 Copenhagen N

Invited members: Bodil Steen Rasmussen (BSR), John A. Myburgh (JAM), Ville Pettilä (VP), Ingrid Egerod (IE), Jakob Kjellberg (JK), Jan Bonde (JB), Christian Gluud (CG), Morten H Bestle (MHB), Hans-Henrik Bülow (HHB), Robert Winding (RW), Theis Lange (TL), Helle L. Nibro (HN), Morten H. Møller (MHM), Jens Winther (WIN), Jørn Wetterslev (WET), Anders Perner (AP).

Invited non-members: Irene Bang Møller, Innovationsfonden (IBM), Lars Winther, Innovationsfonden (LW), Birgit Agerholm Larsen, CRIC project manager, (BAL), Helle Birgitte Kjeldsen, CRIC clinical research assistant (HBK)

Participants: BSR, IE, JB, CG, MHB, HHB, RW (on Skype), TL (on Skype), MHM, WET, AP, LW, BAL, HBK

Declined: JAM, VP, JK, HN, WIN, IBM (no longer working at Innovationsfonden)

Minutes according to agenda.

1) Welcome (AP)

2) Presentation (all, short)

3) HHB presentation (and discussion in plenum)

- a) An initiation visit for the SUP-ICU trial (by Mette Krag) at Holbæk Hospital inspired HHB to present the overall scientific and financial outcome of their research collaboration with Rigshospitalet within clinical trials.
- b) Discussion regarding trials, number of patients included and the number of involved clinicians

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- i) Number of clinicians involved may depend on turnover of employment at the department.
- ii) How to involve clinicians: Benefits, obliged to be involved in research at this department.
- iii) Agreement on: “keep the trial set-up as simple as possible”; if the goal is to make it a part of “daily work”, then make it easy to include patients in research.

4) Status of programs (all)

a) **HOT-ICU (BSR)**

- i) Focus of HOT-ICU on the tendency of “the more oxygen, the better”.
- ii) Big gap in the clinic between lower and upper target level (examples presented by BSR)
- iii) Respiratory data (from other source) and a statistical evaluation of the data will be performed and presented ultimo 2015.
- iv) Olav Schjørring starts as a PhD Student December 15th 2015.
- v) Stratification needed for: *Site* and *COPD* (maybe more). In general it was suggested to go easy on stratification since lack of balance of risk factors between intervention groups will be minimized when including large number of patients.

b) **SUP-ICU (MHM)**

- i) Challenges regarding SUP-ICU placebo (§39 permission, the Authorities, distribution, blinding).
- ii) E-CRF almost ready.
- iii) Monitoring plan is in progress.
- iv) Status for inclusion: Weeks (maybe 1-2 months) before SUP-ICU is ready to include the first patient at Rigshospitalet, Mette Krag is visiting Danish Sites (initiation meetings).

c) **Specific challenges on placebo-production regarding §39 permission**

The SSC agreed on making a summary of the process to create a focus on the challenges and consequences of all the “unnecessary” obstacles and delays for clinical trials in general and in specific for independent clinical trials, covering the mess/ambiguity regarding the §39 permissions.

§39 permission: § 39 is in general required for import, export, production, storage and distribution of medicine both national and when doing business with foreign countries. The Danish Pharmacies have a special arrangement in that respect – a permission in the legislation similar but not quite equal to a §39 permission as they do not have the permission to “export” to foreign countries.

The Danish Health and Medicines Authority* approved the SUP-ICU trial protocol stating that the RegionH Pharmacy should provide the placebo-production for later distribution to foreign countries though they must have overlooked that the Pharmacy of RegionH do not have a §39 permission and only have permission to national production and distribution by law.

* Danish Health and Medicines Authority changed October 8th 2015 to: *Danish Medicines Agency*

d) **AID-ICU (AP)**

- i) **TOD-ICU has changed program name to AID-ICU** (Agents Intervening against Delirium in Intensive Care Unit).
- ii) Ph.D student Marie Oxenboell-Collet is working on focus group interviews and an observation study.

- iii) The protocol (to the cohort study) is estimated to be final during next week.
- iv) Meeting with all participants for the AID-ICU at October 20th to schedule the randomized trial.

e) **CTU (WET)**

- i) PhD student Marija Barbateskovic is working on systematic reviews of pharmacological interventions in delirium in the ICU, oxygen trials, and a methodology study (the University of Copenhagen has just – the 12th of October- approved the enrolment of PhD student Marija Barbateskovic).

f) **Statistics (TL)**

Lining up the statistical work package; statisticians introduced to work package but not yet all integrated in working on the statistical tasks.

5) Sub-studies

- a) It was questioned whether an author – within the present terms – may experience to have a sub-study publication declined for publication by the trials management committee. It was argued, however, that data are in the hands of the management group and partners for only two years, after which the data is given free for public access. The terms will be unchanged.
- b) Multi-site trials may have the potential of a number of sub-studies. It was suggested that each of the individual trial steering committees may invite partners/collaborators/sites to join a meeting dedicated to potential sub-study titles.

6) Economy

- a) All should be aware of documenting used time/ hours as it may be enforced to do so by hospital administrations in near future.
- b) Rigshospitalets Forskningspulje has granted AP 900.000 Dkr. for operating expenses to SUP-ICU. ESICM has granted MHM an award of 20.000 Euro to the SUP-ICU (salary).
- c) Svend Andersen foundation has declined an application from HOT-ICU.
- d) Innovationsfonden (LW) recommends a strategic plan for funding (approved by SSC)
 - i) Framework set-up to show the next potential investor that CRIC will be worth an investment.
 - ii) Also to show and communicate progress as appetizers for possible additional investors.
 - iii) And be specific on what the investor's opportunity is to profile itself.

7) In general SSC will be pro co-enrolment

- a) The SUP-ICU trial team (MHM) have planned a sub-study analyzing data from the trial regarding the potential influence of co-enrolment on the primary and secondary results.

8) Opening new research programs

- a) More resources (especially on data management) are needed to be able to allocate persons to potential new projects/studies.
- b) Terms and procedures need to be discussed; do we prefer well known partners, new partners?
- c) Common agreement that already active sites would be awkward to refuse on collaboration.
- d) Transparency of the collaboration terms is important –
 - i) Prefer studies with focus on “best for the patient”.
 - ii) Collaboration is based on economy; transparency in research process is important (would be encouraged by CRIC)

- iii) CRIC may not have the capacity – at present – to take on more clinical programs for the time being.
- e) Focus on small regional hospitals – which also has political focus.
- f) Success is depending on ongoing CRIC studies.
- g) This subject will also be discussed at the next SSC meeting (April 29th 2016).

9) Conflicts of Interests

- a) All SSC members were asked to fill out a Conflict of Interest Form. Those SSC members not physically present at the meeting will receive the form by mail (and when filled out, please return it by e-mail to hbk@cric.nu).

10) Terms of Reference

- a) The Terms of Reference has been shortened since the last SSC meeting in April.
- b) The Terms of Reference should reflect some overall considerations about the role of CRIC (to be discussed at the next SSC meeting in spring 2016).

11) CRIC office update

- a) New locations – moved to the third floor, but still Tagensvej 22, dept.7831, DK-2200 Copenhagen N, same e-mail and phone numbers.

12) ICNARC – Intensive Care National Audit & Research Centre

SORRY, we missed this business on the agenda – we will discuss this at the next SSC meeting April 29th 2016.

13) Any other business

RW approves skype, but/ and recommends Tandberg as a strategic investment of CRIC as it provides a much better net/quality on picture and sound.

The next Scientific Steering Committee Meeting is to be held at CRIC facilities the 29th of April 2016 (All Stakeholder meeting is planned to be held at the same date).