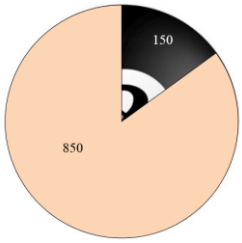


Place in Site Master File #13

AID-ICU newsletter – January/February 2019

Thank you for your commitment to the AID-ICU trial

STATUS

We have currently reached inclusion of **150 patients** in the AID-ICU trial. The beginning of 2019 has shown inclusion rates of **11 patients** per week, which so far is the fastest inclusion in AID-ICU – thank you for all your efforts in this regard.
We hope to reach and maintain a steady number of **13 patients** per week in the following months by welcoming new Danish and European sites and hope to see continuous inclusion from active sites.

Remember to stay updated on your recruitment at **Cric.nu/aid-icu**. The graphs are updated two or three times a week.

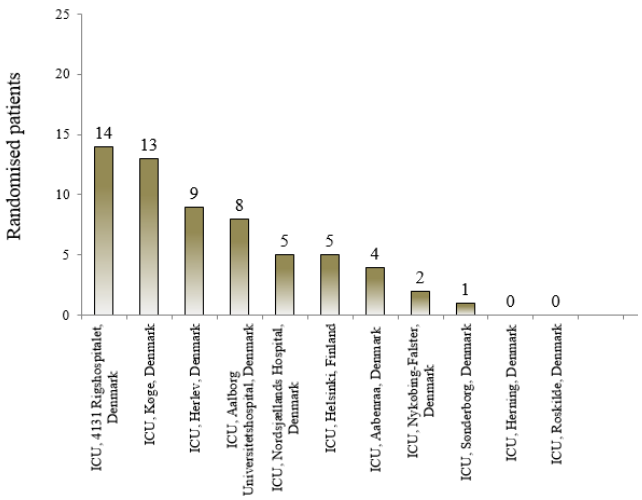
Welcoming new sites in AID-ICU

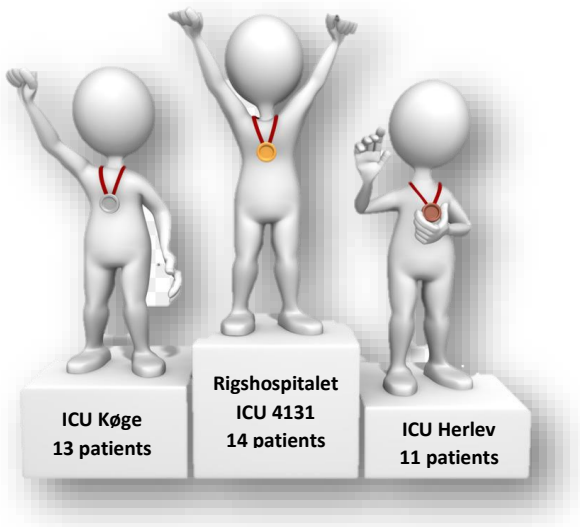
We are at the moment 12 active sites in the AID-ICU trial and in the following months we are looking forward to welcome

- Intensive Care Unit at **Odense University Hospital, Denmark** with primary investigator Louise Gramstrup Nielsen
- Intensive Care Unit at **Turku University Hospital**, Finland with primary investigator Outi Inkinen

Looking forward to collaborate with you in the AID-ICU trial.

Top Recruiters January and February (combined)





IMPORTANT NOTICE

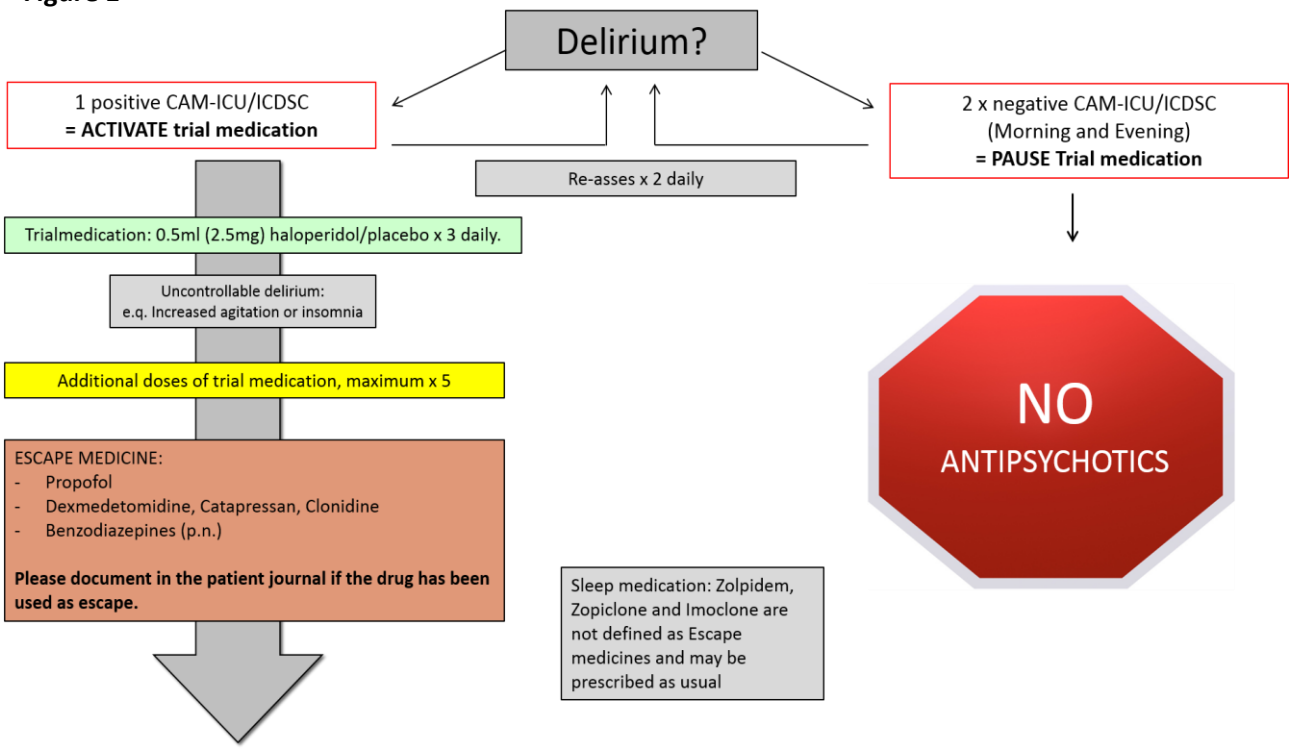
News from the coordinating centre

1. **When do I pause trial medication?**
   Pausing criteria: When a patient has 2 consecutive negative CAM-ICUs or ICDSC < 4 on the **same day** the patient is termed delirium free and trial medication is paused. However, a single positive CAM-ICU or ICDSC ≥ 4 will reactivate the trial medication. A common example of this is a patient who is screened negative for delirium during dayshift and evening shift. This patient meets pausing criteria after the second negative screening, however if this patient turns delirious during night shift trial medication shall re-activate. Also see figure 1 below.
   This may cause some confusion (or even delirium? ☺), and therefore we recommend to check for the pausing criteria in the morning. Check if ALL delirium-screenings of the previous day were negative, if so then pause trial medication. For further instructions on pausing criteria check our Standard Operating Procedure: http://www.cric.nu/aid-icu-sop-trial-medication/

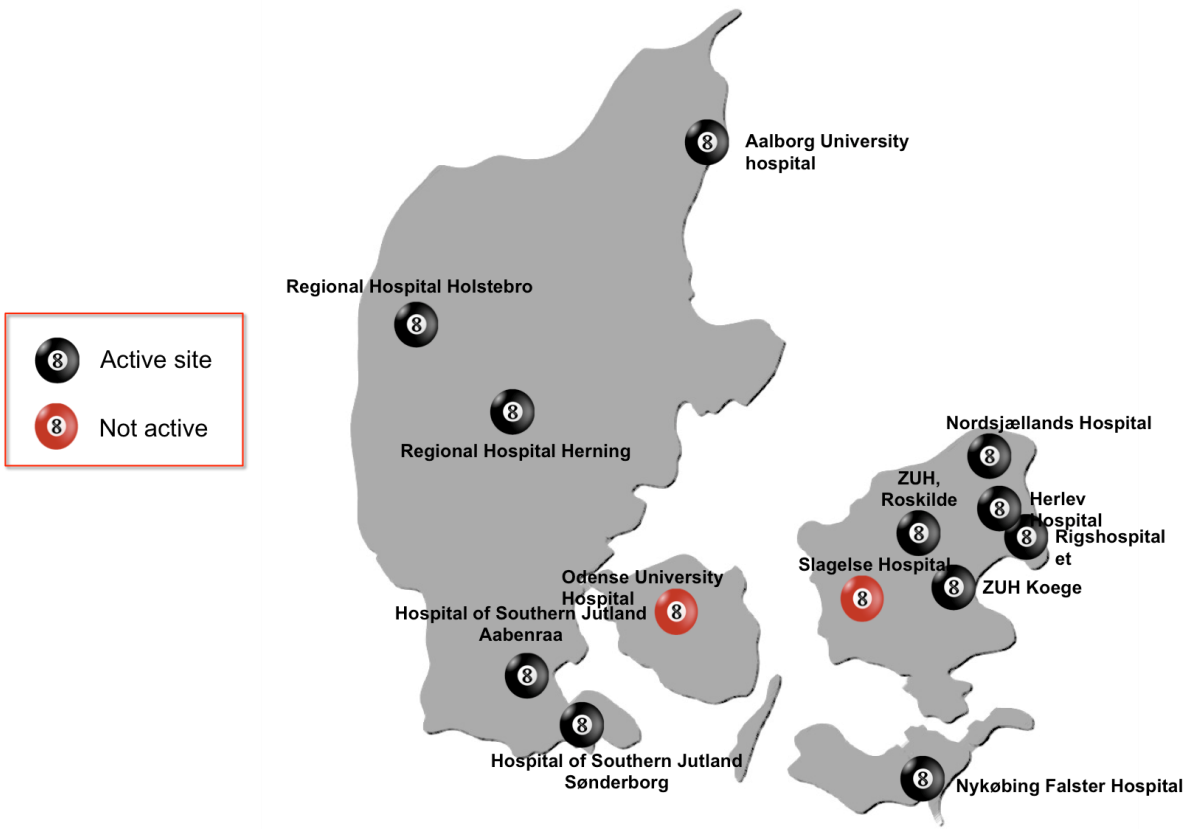
2. Attached to this newsletter you will find the **safety report of 2018**. No SAR or SUSAR have been reported in the AID-ICU trial so far. Please print and place in Site Master File under **section 4f**.

3. In this month however, the coordinating centre was informed of a serious adverse event (SAE) that following judgement of the local investigator and sponsor was classified as a suspected unexpected serious adverse reaction (SUSAR). In accordance with our protocol the trial participant was unblinded. Interestingly, we found that the patient had received PLACEBO. The SAE was hereby not related to the intervention and NO SUSAR was reported.

Figure 1



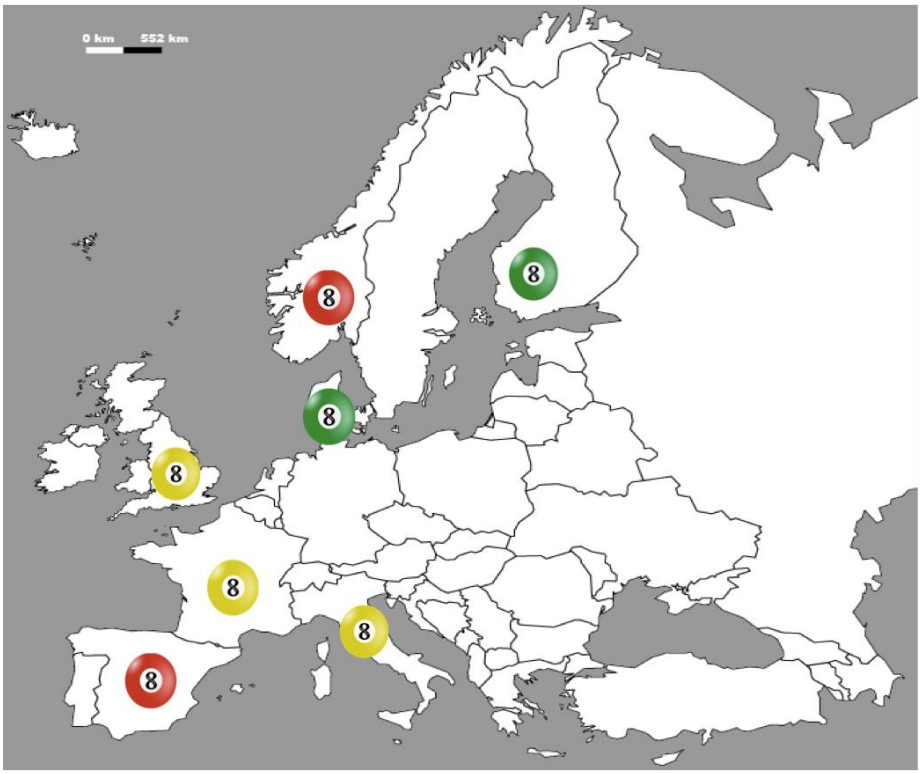
Friends of the AID-ICU trial – Denmark



Friends of the AID-ICU trial – Europe

National Investigators:

- Finland: Johanna Hästbacka
- Italien: Giuseppe Citero
- Frankrig: Lara Zafrani
- England: Matthew Morgan
- Norge: Hans Flaaten
- Spanien: Jesus Caballero



Remember the Coordinating center is always available to answer any questions concerning the AID-ICU trial (24-7) on:

AID-ICU HOT-LINE: +45 93 57 77 50

Kind Regards from the AID-ICU team
Lone (sponsor) and Nina (Coordinating Investigator)