icnarc intensive care national audit & research centre

Napier House
24 High Holborn
London WC1V 6AZ
tel +44 (0)20 7831 6878
fax +44 (0)20 7831 6879
email icnarc@icnarc.org

Niklas Nielsen, MD, PhD
Department of Anesthesiology and Intensive care
Helsingborg Hospital
Department of Clinical Sciences
Lund University
S Vallgatan 5, 25187 Helsingborg
Sweden

04 October 2019

Dear Niklas

Re: Targeted Hypothermia Versus Targeted Normothermia After Out-of-hospital Cardiac Arrest (TTM-2) trial

I write to you in your role as Chief Investigator for the TTM-2 trial.

As you are aware, the Data Safety Monitoring Committee (DSMC), which I independently chair, met on 26 September 2019 for both an Open and Closed Session. In the Closed Session, the DSMC members reviewed analysis of data for the pre-planned, formal interim analysis scheduled to be conducted when 600 TTM-2 participants had reached 180-day follow-up.

In total, in the Closed Report (updated and rapidly re-circulated to DSMC members following the formal meeting), 1185 participants had reached 30 days and 745 participants had reached 180 days in the trial. The DSMB noted that the formal interim analysis was later than planned (i.e. it included 745, rather than 600, participants who had reached 180 days in the trial) and that every effort should be made to avoid this situation in future, in this or other trials.

As set out in the Charter, the DSMC reviewed: the primary outcome measure of all-cause mortality at 180 days; the secondary composite outcome measure of all-cause mortality and poor functional outcome (modified Rankin Scale 4 to 6) at 30 days and at 180 days; and serious adverse events. The DSMC also noted recent results published in NEJM for the Hyperion Trial (Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm by Lascarrou J-B et al.).

On behalf of the DSMC, I can confirm that, based on the supplied analyses, there are no safety concerns that require modification of the TTM-2 trial and that the TTM-2 trial should continue in its current form.

As before, the DSMC congratulate the TTM-2 trial team and sites on the excellent recruitment to the trial and noted the efforts made to ensure that missing data were minimised and encourage that such efforts must continue to trial end.

Yours sincerely

Professor Kathy Rowan
Chair, Data Safety Monitoring Committee, TTM-2 trial