Monday 8 June 2020

Chair of the Executive Group of the Solidarity Trial
to the National Principal Investigators of the Solidarity Trial

Subject: 5 June 2020 statement on hydroxychloroquine from the UK RECOVERY trial of this and other treatments for hospitalised COVID-19 patients

Dear Solidarity Trial Principal Investigator,

The UK-based RECOVERY trial has randomised large numbers of high-risk hospitalised patients between various treatments, and (because of a request for information from the UK drug regulators) has released its interim mortality findings on hydroxychloroquine in a press statement (https://www.recoverytrial.net/files/hcq-recovery-statement-050620-final-002.pdf). This will shortly be followed by submission of a full report for peer-reviewed publication, which will provide far more detailed information. The RECOVERY investigators conclude in their press statement that there is no beneficial effect of hydroxychloroquine and have therefore decided to stop enrolling participants to the hydroxychloroquine arm of the RECOVERY trial.

In parallel, the Solidarity trial Data and Safety Monitoring Committee (DSMC) reported to the Executive Group of the Solidarity trial on 5 June 2020 that the joint Solidarity/Discovery interim trial results reinforce the conclusion from the RECOVERY results of no benefit of hydroxychloroquine. Hence, the Executive Group provisionally agreed the following points:

1. Based on this evidence It is disappointing that hydroxychloroquine is not effective.

2. More detailed analyses of Solidarity / Discovery and of RECOVERY trail data need to be conducted as soon as possible.

3. If as is probable, the RECOVERY press release will be followed up shortly by a peer-reviewed publication and detailed examination of the evidence, allocation in Solidarity of further patients to hydroxychloroquine would be unlikely to alter the conclusion from RECOVERY of no clinical benefit from this treatment.

4. A short report on the Solidarity/Discovery interim data on hydroxychloroquine will be drafted as soon as possible. In Solidarity, all outcomes should be reported to the study website promptly, as soon as trial patients die or are discharged. Given the need for interim results to be as reliable as possible, **please check over the next few days that all deaths or discharges of included patients have been reported.**

5. After follow-up of most of those randomised but not yet reported on, a meta-analysis of the detailed findings on hydroxychloroquine from both trials (Solidarity/Discovery and Recovery) will be needed.

6. The Executive Group expects that the RECOVERY trial will soon report comparably reliable large-scale randomised evidence on Lopinavir/ritonavir, on Dexamethasone, and on Azithromycin. (The RECOVERY trial does not evaluate Remdesivir or Interferon.)

Solidarity is now the most promising trial globally in terms of recruitment rate in areas with high COVID-19 incidence. It was conceived as an adaptive trial, so it has an opportunity and responsibility to contribute to other key public health questions that have not yet been reliably answered. Hence, adjustment of the Solidarity randomisation rules to concentrate on assessing the effects of Remdesivir on mortality is being urgently considered. This is driven by the fact that the trial has access to significant quantities of Remdesivir and there is not yet robust data on the effect of Remdesivir on mortality. If sharper focus on Remdesivir increases recruitment rates, then Solidarity will soon yield new, therapeutically relevant results.

At its next regular meeting, the Solidarity Executive Group will discuss how best to adapt the trial to generate internationally relevant evidence that would not otherwise be generated, and when clear recommendations have been agreed these will be shared promptly with all of you. We look forward to your continued collaboration as Solidarity re-focuses on these and other unanswered questions.

Until then, collaborating investigators who choose not to allocate patients to hydroxychloroquine can avoid doing so by answering "no" when the program at the time of randomization asks whether hydroxychloroquine is available.

Thank you for your continued collaboration.

John-Arne Røttingen

The Executive Group of the Steering Committee of the SOLIDARITY trial is John-Arne Røttingen (Chair), Quarraisha Abdool Karim, Marissa M. Alejandria, César Hernández García, Marie-Paule Kieny, Reza Malekzadeh, Srinivas Murthy, Srinath Reddy, Mirta Roses Periago, Richard Peto (observer from the DSMC) and Soumya Swaminathan (on behalf of WHO)