NEXT OF KIN-INFORMATION – ENGLISH – HOT-COVID

This document is a translation of the Danish "Skriftlig deltagerinformation, HOT-COVID, patienten" version 1.0, June 2nd 2020. It has been prepared according to Danish regulations. As you may require additional or different information according to your national regulations please feel free to change the document.

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FOR THE NEXT OF KIN

We would like to ask if your next of kin can participate in a medical research project dealing with critically ill patients admitted to an intensive care unit due to respiratory failure caused by corona virus disease 2019 (COVID-19)

Your next of kin has been/is seriously ill and has been/is in need of immediate treatment in the intensive care unit. On these grounds we would like to ask your permission for his/hers participation in a clinical trial during the admission. This is necessary since we are not able to inform and ask your next of kin directly due to his/hers condition. The trial was initiated as part of the immediate treatment. Participation is voluntary and you can at any time point and without any reason withdraw your permission. Declining participation or withdrawal will not have any influence on the overall treatment of your next of kin.

Before you can decide whether your next kin is permitted to participate in the trial you need to completely understand how and why the trial is conducted. Therefore, we kindly ask you to read the description below. Further, you will be offered a conversation with a person from the research group where you will be given a more in-depth understanding of the trial and you can ask questions. You are welcome to bring a family member, a friend, or an acquaintance to this conversation.

If you decide to permit participation in the trial for your next of kin, we will ask you to sign the attached consent form. Remember that you have the opportunity to consider your decision before signing.

It is voluntary to participate in the trial. You may at any time without further explanation withdraw your consent. When your next of kin will be asked directly for his/hers acceptance of participation when their medical condition allows it.

Background
Critically ill COVID-19 patients acutely admitted to an intensive care unit with respiratory failure have a life threatening condition due to the reduced ability of the lungs to absorb oxygen. Therefore, the patients are treated with supplemental oxygen to ensure adequate oxygen supply to the tissues. Oxygen, which is a medical drug, is given through the airways and absorbed via the lungs into the blood. Oxygen, however, is also harmful, especially for the affected lung tissue when it is given in concentrations that exceeds the atmospheric oxygen content (21%). The fear of not getting enough oxygen to the body's cells in acute lung failure causes oxygen to be administered very liberally and therefore patients admitted to intensive care units often have high levels of oxygen in the blood.

The optimal range of oxygenation in the blood critically ill COVID-19 patients in an intensive care unit is unknown. Very low concentrations of oxygen in the blood lead to higher mortality, but more and more studies show a tendency towards several serious side effects and perhaps an increased mortality when a

high level of oxygen in the blood is targeted. Studies have shown that it is safe to aim for lower values of oxygenation in critically ill patients than the values used up until now.

It is unresolved whether lower oxygenation in the blood overall is beneficial or harmful to mechanically ventilated critically ill patients in intensive care units with COVID-19, and there is thus a great need of a trial that clarifies this.

Purpose of the trial

The purpose of the trial is to assess whether a lower level of oxygenation in the blood has beneficial effects in critically ill COVID-19 patients admitted to an intensive care unit with COVID-19 requiring mechanical ventilation.

Course
Your next of kin were admitted to the intensive care unit and mechanical ventilation was initiated because his/hers condition required it. In relation to the research project, your next of kin was randomly treated with oxygen equivalent to a lower level of oxygenation in the blood or similar to the usual standard, from the time of initiated mechanical ventilation in the intensive care unit.

Before trial inclusion, an independent physician not involved in the trial approved your next of kin's participation. As soon as possible after trial inclusion we have sought to inform you and yet another physician not involved in the trial was also contacted and informed. Both you, as relatives, and this physician have to provide written consent for the trial to continue. Aside of the trial medication (oxygen) your next of kin will also receive the usual treatment for his/hers medical condition.

The trial duration is from admission to the intensive care unit until discharge from the intensive care unit and will continue if your next of kin is re-admitted in a participating intensive care unit up until a maximum of 90 days after having entered the trial. After one year, we will contact your next of kin again to ask about his/hers quality of life. After one year, your next of kin will also be invited to participate in an examination of his/hers lung function and his/hers cognitive function (the examination is done at selected sites).

In addition to the physician in charge of the trial (as stated in this information letter), doctors and nurses working in the intensive care unit contribute by practical implementation of the trial.

Discontinuation of the trial
As next of kin, you can at any time without justification withdraw your relative from the trial. Withdrawal will not affect your relations to the physicians in the intensive care unit or the given treatment. Your next of kin will continue to receive the treatment that is standard for his/hers medical condition.

Advantages of the experiment
Participation in the trial is beneficial for your next of kin because the oxygen treatment will be followed closely in both groups. Also, by participating your next of kin can help to ensure that we acquire information on whether it is beneficial for critically ill COVID-19 patients to receive lower levels of oxygen supplementation. Thus, the collected data will result in an improved treatment of COVID-19 patients in the intensive care unit.

Disadvantages of the experiment
There are no disadvantages in your next of kin's trial participation.

Side effects, risks and complications
Oxygen is the most commonly used drug in an intensive care unit. Very few adverse reactions of oxygen have been recorded. These include pneumonia, collapse of lung tissue and acute lung failure. The two first mentioned are often transient and mild, while the last mentioned is a rare but serious adverse reaction. All patients admitted acutely to the intensive care unit with COVID-19 and respiratory failure have these changes, and it is therefore not possible to distinguish these from adverse effects directly triggered by oxygen therapy.

All patients admitted to intensive care unit will be continuously monitored with measurement of their oxygen saturation in the blood and be treated by well-trained staff with extensive experience in treatment of critically ill patients. In both groups of patients, the aim is to keep the oxygen level in the blood above critical low values. Therefore, no risks are related to trial inclusion.

Patient Compensation
Damage caused by the study drugs is very unlikely in this study. However, if an injury occurs because of the study drug (oxygen) you are covered by the public patient insurance. If you want to complain about anything related to your participation in this trial, you can obtain instructions from the research group or from the patient counsellor in your country or region.

Privacy and confidentiality
All information will be treated confidentially. When reporting results and when publishing the results of the trial, you will remain anonymous. The research group and the Good Clinical Practice monitoring group have access to your entire medical record to ensure that the trial is carried out as described within the protocol. From your medical records, we will use information about past medical history, surgical procedures during this hospitalisation, blood test results, medication, treatment and events in the intensive care unit. Anyone with access to the journal is subject to confidentiality.

Economy
The idea for the trial comes from Professor Bodil Steen Rasmussen, Aalborg University Hospital. Together with PhD student Thomas Lass Klitgaard and PhD student Frederik Mølgaard Nielsen, Aalborg University Hospital, Bodil Steen Rasmussen is responsible for the planning and conducting of the trial. The responsible investigators are employed at Aalborg University Hospital and have no financial interests in the study. The study is funded by 4.997.300 DKK from the Danish Ministry of Education and Research. Principal Investigator, professor Bodil Steen Rasmussen, is unrelated to the contributor. The money represents a research fund administered by Professor Bodil Steen Rasmussen, which is subject to external audit.

Access to study results
When the trial is completed, we will determine survival and occurrence of adverse events among participants. The results will be published in an international scientific journal as well as on the website of Aalborg University Hospital and on the trial website (http://www.cric.nu/hot-covid/). If you want to know the results of the project and any consequences for you, you can tick this off on the consent statement.

Contact

We hope that you with this information feel sufficiently informed and able to make a decision on your next of kin's potential participation. For further information, please feel free to contact one of the investigators below.

Sincerely

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Name
Title
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Institution
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Phone
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Sponsor and Principal Investigator
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