**REMAP-CAP**

**Patient Information Sheet and Informed Consent Form**

**For patients with capacity or now recovered capacity**

**Invitation to the study**

We are inviting people admitted to hospital with a respiratory tract infection (an infection that affects the nose, throat, airways or lungs) such as pneumonia, to participate in our research study. This can be caused by bacteria or viruses like flu (influenza) and COVID-19. This study is trying to find the best treatments for these health problems. This form provides information about the study, the treatments we are using, and risks and benefits of taking part. We understand that having an infection can be very stressful. Take your time to read this information and feel free to discuss it with your partner, friends or family.

**What is the purpose of this study?**

A respiratory tract infection is an important health problem. Although there are many different treatments currently used to treat patients with this, often doctors are unsure which option is best. As new treatments become available more research is also needed to see whether they work better. The aim of this study is to find out which treatments are best for patients who are seriously ill with this type of infection, to improve their chances of survival and recovery. REMAP-CAP is a worldwide study that has been active since 2016.

**What treatments are being investigated?**

When there is an infection, the immune system responds to fight the bacteria or virus (called ‘inflammation’). Sometimes, the immune system responds too much and this can lead to organ damage. We are studying the following treatments in patients who have been admitted to a hospital ward and/or an intensive care unit (ICU). Some of these treatments fight the bacteria or viruses directly, and the ‘anti-inflammatory’ treatments reduce an overactive immune response.

**Antibiotics** are medicines that fight bacterial infection and different antibiotics may work best for different bacteria. Sometimes combinations of different antibiotics may be needed and different doctors may give different antibiotics. The following antibiotics are being compared: ceftriaxone and a macrolide, piperacillin-tazobactam and a macrolide, amoxicillin-clavulanate and a macrolide, moxifloxacin, or levofloxacin. These medications are given through a tube into your vein (drip) or as a tablet or liquid to swallow.

**Macrolides** are a type of antibiotic which may also help reduce inflammation if they are given for longer. We are comparing a long-course of macrolides (14 days) compared to a short-course (3-5 days) or no macrolide. The following different macrolides are being compared: azithromycin, clarithromycin, erythromycin, or roxithromycin. These medications are given through a tube into your vein (drip) or as a tablet or liquid to swallow.

**Corticosteroids** are a type of anti-inflammatory medicine. The following treatments are being compared: dexamethasone (for up to 10 days), hydrocortisone (if you have septic shock, which is when your infection is causing organ failure), or no corticosteroids. These medications are given through a tube into your vein (drip) or as a tablet to swallow.

**Influenza (flu) antivirals** are medicines that fight flu viruses. The following treatments are being compared: oseltamivir (a short or long course), baloxavir, the combination of both oseltamivir and baloxavir, or no antiviral. These medications are given as a tablet or liquid to swallow.

**Immune modulators** are medicines which help your immune system work properly andare found to be effective in infections such as COVID-19. They might work against flu but we do not know for sure. The following treatments for influenza (flu) are being compared: baricitinib, tocilizumab, or no immune modulator. These are given through a tube into your vein (drip) or as a tablet to swallow.

**Immunoglobulin therapy** contains antibodies which fight infection in the liquid part of blood (convalescent plasma), taken from patients who recovered from COVID-19. These antibodies could help fight the virus in people who have not yet recovered from COVID-19. We are comparing convalescent plasma with no convalescent plasma treatment. A blood sample requiring about a teaspoon of blood may be needed from you to find out what your blood type is. The treatment is administered by an injection (known as a transfusion).



*(please delete domain(s) and/or treatment(s) that the site is not participating in, in both text and chart above)*

Your doctor will know which set of treatments are suited to you in the study. We may use a combination of these treatments because it is important to understand which combinations are best. Many of these treatment comparisons also include a ‘no additional treatment’ option, so you may not receive any of these treatments but you will still receive standard of care at your hospital.

**Who will be included in the study?**
Patients who have been admitted to hospital or to ICU, who have or are suspected to have a respiratory tract infection (an infection that affects the nose, throat, airways or lungs) such as pneumonia, flu, or COVID-19. Only patients who meet the study requirements and their doctor believes they are suitable will be included. The treatments available depend on how serious the condition is and whether the different treatments are suitable for you.

**What does participation in this study involve?**

Your doctor will always first decide if the study is best for you and will always provide the healthcare you require.

It is important to start treatment of these conditions as quickly as possible. This is why some treatments may already have started before you were given this consent form. If you were not able to give your consent straight away, we asked your family member/friend or doctor for their consent to include you in the study. This will only happen if your family member/friend or doctor is not aware of any previous reason that you may not wish to participate in the trial. If a family member/friend is not available, an independent doctor or independent senior nurse can be asked to provide consent on your behalf. An independent doctor/senior nurse is not involved in the study. We always check if you are happy to continue in the study once you are able to give your own consent.

Participation is entirely voluntary. If you agree to participate, we will ask you to sign a consent form. We will enter some details about you and answer some medical questions on a computer. You will then be randomised by a computer to one or more of the above treatment options. Randomisation is a process like tossing a coin, and you will have a chance of receiving one of the above treatment options in each group, which allows us to compare your treatment to others. The study looks at the results on an ongoing basis and uses these results to make some changes to the randomisation process with the aim of increasing the chances of getting treatments that are looking better for new patients in the study, but there is no guarantee.

Once you have been randomised, depending on the treatment, a nasal swab and/or a blood sample (about a teaspoon of blood) will be taken. Nasal swabs will also be collected 3 and 7 days later, while blood samples will be collected weekly until hospital discharge. The doctor, nurse or researcher will explain the study to you, but no one can choose which treatment you will get. Even if you are participating in the study, the study treatment will be adjusted or stopped if your doctor thinks it should be.

During the study, further information about your health will be entered on to a computer. Once you are discharged from hospital, no further visits are required by you. We will contact you 6 months later to complete a questionnaire about your wellbeing, by telephone. To learn whether the treatments worked, we will collect information about you from your medical records from before you joined the study and up to 6 months later. We will also request information about you from the following research databases: Intensive Care National Audit & Research Centre (ICNARC), NHS Digital, UK Health Security Agency, and genetic or other research databases (if you have provided your information/samples to them). We will keep this information for up to 25 years after your discharge. All data collected from you will be pseudonymised, which means that your name and other identifiers will be replaced by a reference number (code), so you cannot be directly personally identified by this.

**Are there any benefits in taking part?**

This study will tell us if some treatments are better than others, but we cannot guarantee that taking part in the study will benefit you directly. The findings may help improve treatment for people with a respiratory tract infection such as pneumonia pneumonia, flu, or COVID-19 in the future.

If there is little difference between the treatments, then the benefit of being in the study will be less, but the disadvantages will still be minimal.

**Are there any risks in taking part?**

All medical treatments can have side effects, and these range from mild to serious. The side effects known for the treatments used in this study are described later in this form. The risks and side effects are similar whether you choose to be in the study or not. Your doctor will know what treatment you are receiving at all times and will be looking out for any side effects.

**Pregnancy**

Women who are pregnant or breastfeeding may be included depending on the treatment. Some treatments (e.g., baloxavir and baricitinib) have not been tested on pregnant women before, and the effect on unborn babies is uncertain, so these treatments may not be available if you are pregnant. We have an expert group who review our safety results closely, and if there are any issues, your treatment will be stopped immediately.

**Can I stop/change my mind?**

Whether you take part in the study is up to you. If you no longer wish to be part of this study, this is not a problem and you will not lose out. No further information will be collected about you, and the doctors will continue to provide you with standard medical treatment. You will have the option to allow us to continue to collect information about you. Pseudonymised (coded) data about you and samples that were already collected up to your withdrawal will still be analysed by the study team unless you tell us that you do not want the data or samples already collected, to be used.

**What if I have a problem or a question?**

If you have any questions about the study, please reach out to your medical team in the first instance. Their details are below:

|  |  |
| --- | --- |
| **Contact Name**  | **Contact Number** |
|   |   |

Further information about the study can be found on our study website:

https://remapcap.co.uk/patients, via email: ukremap-cap@icnarc.org, or telephone: 0207 594 5906.

For independent research advice, please see the contact information below:

***England/Wales sites only (delete if not applicable)***

If you have any questions about being in a research study, you can contact the Trust’s Patient Advice Liaison Service (PALS). They will give you advice about who you can talk to for independent advice.

|  |  |
| --- | --- |
| **Local PALS office telephone number**  | **Local PALS office address**  |
|   |   |

 ***Northern Ireland sites only (delete if not applicable)***

If you have any questions about being in a research study, you can contact the person listed below. They will give you advice about who you can talk to for independent advice.

|  |  |
| --- | --- |
| **Local Contact** | **Local address** |
|   |   |

***Scotland sites only (delete if not applicable)***

If you have any questions about being in a research study, you can contact [*insert full name*] (contact details below) who is not involved in the study and will be able to give you independent advice.

[*insert independent contact telephone number/email address/postal address*]

You can also find more information about the study by searching for REMAP-CAP on the website [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

The trial sponsor is University Medical Center Utrecht (UMCU), who holds an insurance policy for this study (Allianz Global Corporate & Specialty, policy number: GBL00716220B). In the unlikely event that you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that UMCU is at fault. Not all damage is covered. This does not affect your legal rights to seek compensation. If you are harmed due to someone’s negligence, then you may have grounds for legal action.

**How do you use information about me and how do you keep it private?**

All information about you, your health, and your participation will be kept private. The only people who will have access to this information are the doctors and nurses looking after you and employees of the Sponsor UMC Utrecht, Imperial College London, and ICNARC who have authorisation. More information is available in our privacy notice, which can be downloaded from our website: https://remapcap.co.uk/patients. If you prefer, you can ask for a copy of it from your medical team.

**End of study**

Your participation in this study will stop if:

• The follow-up period for the study has been completed. This is either 90 days or 180 days after your participation in the study (once you have been contacted by the research team to complete a questionnaire about your wellbeing for the 6-month follow-up)

• You decide to not take part anymore

• The Ethics Committee, government, or UMC Utrecht (study sponsor) decides to stop the study

The doctor or researcher will let you know if there is any new information about the study that is important to you. They will then ask you if you want to continue in the study, if you are still receiving study treatment.

**How do I find out the results?**

You will not be personally told about the results of the study. The results of this study will be presented at medical meetings and published in scientific journals. This will only involve anonymous group data, and no personal information will be presented. If you are interested in the results, they will be available on our EU website: <https://www.remapcap.eu/>

**Who is funding it?**

The Coordinating Principal Investigator for this study is Professor Marc Bonten, at the University Medical Center (UMC) Utrecht, Netherlands. This research has received funding from the Rapid European COVID-19 Emergency Research response (RECOVER) consortium by the European Union’s Horizon 2020 research and innovation programme (#101003589) and from the UK National Institute for Health and Care Research (NIHR). The cost of some treatments may be covered by companies that make these products. These companies are not involved in the design, analysis, or reporting of results from the trial.

The UK Principal Investigator is Professor Anthony Gordon at Imperial College London, and the UK Trial Coordinating Centre is ICNARC, Napier House, 24 High Holborn, London WC1V 6AZ.

 **Who has reviewed and approved it?**

All research involving patients in the NHS is looked at by an independent group of people called a Research Ethics Committee. This study has been reviewed and approved by the **London - Surrey Borders HRA Ethics Committee.**

**Informational video**

Please feel free to watch a short video that summarises the study by scanning the QR code below with your phone’s camera:

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 **List of common side effects of study medication**

The below side effects are considered common for these treatments.

**Antibiotics (including macrolide antibiotics)** may cause the following side effects: Liver inflammation (Hepatitis), diarrhoea, dizziness, headache, stomach pain, tingling, nausea, vomiting, heartburn, bad taste, inflammation of mouth and tongue, worsening vision, deafness, anorexia (food disorder), itching, joint pain, fatigue, vein inflammation, anaemia (low iron), abnormal heart rhythms (arrhythmias), excessive sweating, shortness of breath, drowsiness, anxiety, confusion, and nervousness.

**Hydrocortisone and dexamethasone**  can cause the following side effects: Fluid retention, abnormal appetite, high blood sugar levels, pain in muscles or joints, nausea, stomach pain, headache, dizziness, tingling in hands or feet, sleeping disorders, increased risk of infection, high blood pressure, and general state of discomfort (malaise).

**Oseltamivir** can cause the following side effects: Headache, nausea, vomiting, stomach pain, acid reflux, runny nose, dizziness, trouble sleeping, increased risk of infection, cough, sore throat, and general state of discomfort (malaise).

**Baloxavir** rarely causes side effects. No side effects are listed in the information about the medication, that occur in more than 1% of patients.

**Baricitinib** can cause the following side effects: Lung (respiratory tract) infections, herpes infections, urine infections, skin infections, infection of the intestines, abnormal laboratory results (such as high platelet count, high cholesterol, high liver enzymes, and high enzymes associated with muscle problems), headache, nausea, stomach pain and skin problems such as acne.

**Tocilizumab** can cause the following side effects: Lung (respiratory tract), skin, or urine tract infections, herpes infections, stomach problems (such as pain, inflammation, or constipation), mouth ulcers, abnormal laboratory results (such as low white blood cells, high cholesterol, high liver enzymes, and high bilirubin), headache, dizziness, eye inflammation, high blood pressure, weight gain, coughing, shortness of breath, swelling of hands and legs due to fluid build retention (peripheral oedema), and itchiness.

**Convalescent plasma** may cause the following side effects: increased risk of blood clots (thrombosis) and reaction to the transfusion.

*(please delete treatment(s) that the site is not participating in)*

*Besides the side effects mentioned above, all medications can cause rashes or allergic reactions and there are other side effects which are rare (these occur in less than 1% of people). Your doctor knows these side effects and will look out for them.*



**CONSENT FORM FOR PATIENTS ABLE TO GIVE CONSENT**

**(FOR PATIENTS WITH CAPACITY or now RECOVERED CAPACITY)**

**REMAP-CAP**

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient Study ID** |  | **Site #** |  |
| **Name of Principal Investigator**(use CAPITALS) |  |

 **Please initial each box if you agree with the following:**

I, *(forename and surname)*………………………………………………………………………………………………, freely agree to take part in the study.

|  |  |
| --- | --- |
|  | 1. I confirm that I have read (or had read to me) and understood this patient information sheet for the above study and have been able to ask questions which have been answered fully. |
|  | 2. I agree/continue to take part in the following domains: **antibiotics, macrolides, corticosteroids, influenza (flu) antivirals, immune modulators, or immunoglobulin therapy**  (*delete domain(s) that the site is not participating in)(strike through domain(s) if the patient does not agree)* |
|  | 3. I understand that I can choose to take part, and I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. |
|  | 4. I understand that my identity will never be given to any third parties, and any information collected will remain confidential. |
|  | 5. I agree that my medical records and other personal data generated during the study may be looked at by representatives of the sponsor (UMC Utrecht), by people working on behalf of the sponsor, and by representatives of regulatory authorities, ICNARC, and NHS Digital, where it is relevant to my taking part in this research. |
|  | 6. I agree that I will allow the researchers to decide how to use the results of this study. |
|  | 7. I understand that I will be contacted by ICNARC or my local hospital in six months to answer questions about my quality of life and wellbeing.  |
|  | 8. I understand that minimal randomisation data collected about me will be transferred outside of the EEA where the privacy rules of the European Union do not apply. I understand that an equivalent level of protection will be ensured for my data.*(Note: if this point is refused, the patient cannot be included in the trial)* |
|  | 9. I give consent for blood samples/nose swabs collected from me to be used to support other research or in the development of a new test, medication, or treatment by an academic institution or commercial company in the future, including those outside of the United Kingdom (which the sponsor - UMC Utrecht - has ensured to keep secure).  |

Patient’s name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Consent** date (dd/mmm/yyyy):       /       /       Time: : (24hr)

**To be completed by the impartial witness\*** *in the event the patient is competent but unable to read, or unable to sign or date the informed consent form.*

**I confirm that the patient information and informed consent have been accurately explained to the patient, the informed consent has been apparently understood by the patient, and the patient has voluntarily agreed to consent to participate in the study.**

Impartial witness’ name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

*\*An impartial witness is independent of the study, who cannot be unfairly influenced by people involved with the study (e.g., an independent nurse or a patient visitor)*

Date (dd/mmm/yyyy):       /       /       Time: : (24hr)

**To be completed by the delegated site staff obtaining consent**

I hereby declare that I have provided complete and accurate information about the study, and I have answered all questions.

If new information becomes known during the study that could affect the consent for participation, I will inform the patient in good time.

Investigator name (or delegate): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date (dd/mmm/yyyy):       /       /

*1 original copy for ISF; 1 copy for participant; 1 copy for hospital notes*

*To ensure confidence in the process and minimise risk of loss, all consent forms must be printed, presented, and stored in double sided format*