**INVESTIGATOR SITE HEADED PAPER**

**Welfare Attorney/Welfare Guardian/Nearest Relative Information Sheet - Overview**

Your relative / friend are invited to take part in the REMAP-CAP research study. This is because your relative / friend is suffering from community acquired pneumonia (CAP). Pneumonia (lung infection) is an important, common health problem.

We are continuing to test different treatments that may be beneficial for patients to ensure we provide the best possible treatment for your relative / friend. In this information sheet we have listed each treatment available at your hospital, including any potential benefits and risks. If you are happy for your relative / friend participate, they will be allocated by chance (called randomised) to at least one of these treatment options, but you or we will not know which treatment choice your relative / friend will receive before this.

Before you decide whether you wish for your relative / friend to take part, it is important for you to understand why the research is being done and what it will involve. This sheet tells you the purpose of this study, what will happen to your relative / friend if they take part and provides more detailed information about how the study will be carried out. Ask us if there is anything that is not clear or if you would like more information and discuss it with others if you wish.

If you do not wish for your relative / friend to be part of this study, no further information will be collected about them for the trial and the doctors will continue to provide them with whatever medical treatment is needed. Thank you for reading this.

**Important things to know**

* Your relative / friend have been admitted to hospital with CAP and it is important to treat them as soon as possible
* CAP is a common health problem and we need to know which treatments are best
* Your relative / friend may be eligible to receive a number of different treatments
* These treatments will be randomly chosen for your relative / friend by a computer system (by chance)
* All treatments and a list of their possible benefits and risks are included in this information sheet
* All your relative / friend’s data will be kept confidential
* We will follow up with your relative / friend in 6 months and ask them to complete a questionnaire
* Your relative / friend can withdraw from this study at any time and they will continue to receive the local standard treatments and care

**Information about the research**

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

The treatment for pneumonia patients is generally based on national and international guidelines that guide healthcare professionals to choose the best treatments from the evidence available. The evidence on which these guidelines are based, often comes from research conducted with patients admitted to a different hospital department than the ICU. Insufficient research has been done among patients with severe pneumonia admitted to the ICU, and it is not clear whether these guidelines are suitable for these seriously ill patients.

The aim of this study is to investigate which of these treatment options are best for patients admitted to ICU with severe pneumonia

**What medical treatments are being investigated?**

In this study, several different treatments are being compared at the same time. These treatments, which are available at your hospital, for CAP can be put into the following different groups:

1) antiviral medication; 2) antibiotics; 3) duration of macrolide treatment; 4) Supportive treatment - Whether to use hydrocortisone; 5) Vitamin C Therapy and 6) Cysteamine therapy

*[delete as appropriate].*

**Why have I been chosen?**

You have been asked whether you think your friend / relative would wish to take part in this study as they have been admitted to ICU for CAP. We know that treating patients early in this situation provides the best opportunity for medications to work well and so we need to include patients as soon as possible after they become unwell. We are planning to study about 1000 patients in total, admitted to different hospitals within the UK. We are also working closely with research partners internationally.

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

It is up to you to decide whether your friend / relative would wish to take part. If you do think your friend / relative would wish to take part, you will be given this information sheet to keep and be asked to sign a consent form. Your friend / relative is still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part at all, will not affect the standard of care your friend / relative receives.

This is a randomised study. Randomisation is a process that can be compared to tossing a coin. Sometimes we need to make comparisons to see which way of treating patients is the best. People are put into groups and then compared. The groups are selected by a computer which has no information about the individual – i.e. so patients are put into the groups by chance. Each group has a different treatment and these are compared.

Additionally, this study is an ‘adaptive’ study. This means that the chances of being assigned to any of the treatment options may change on the basis of the study results, in favour of the most promising treatment. Neither you nor your friend / relative’s doctors will be informed of these changes in randomisation. This study assesses multiple different types of treatment. Your friend / relative may be eligible for all of them or only some of them, depending on their individual clinical condition. It is important for the treatment of their pneumonia that the treatments are started as quickly as possible. This is why these treatments may have already been assigned (‘randomized’) to your friend / relative when they are admitted to ICU. The doctor or researcher will explain the study and ask for your consent for your friend / relative’s participation. If you do not consent to participate in the study, no further data will be collected from your friend / relative. The treatment that was previously started will be continued or will be changed if your doctor thinks this is necessary.

If you do consent to your friend / relative’s participation in the study, they will continue to be treated with the treatments already started. Various routine data collected from them throughout their hospital stay as part of routine care will be used for the study. If the doctors feel that your friend / relative’s condition changes they can change their treatments as necessary.

**What do I have to do?**

You do not need to do anything for the study. A researcher will collect data from your friend / relative for the study, and your friend / relative will not notice anything. The data collected for the study are already collected as part of their daily and ongoing medical care. With your permission, we will also use routinely collected data held by either the Case Mix Programme, the national clinical audit of UK critical care units, run by the Intensive Care National Audit & Research Centre (ICNARC) or by NHS Digital. These data will include information regarding your friend / relative’s health that will be important to answer the objectives of the study and will include data from this and future hospital stays and survival data. We would also like to contact your friend / relative in 6 months time with a short telephone call to ask about their quality of life and wellbeing.

If you feel that your friend / relative would not wish to be part of this study, no further information will be collected about them for the trial and the doctors will continue to provide them with whatever medical treatment is needed.

**What are the possible advantages and disadvantages of participating in this study?**

The treatments being investigated in this study are the same as the treatments used in daily practice. The only difference is that the study will randomly determine which treatment your friend / relative receive instead of their doctor. This study will tell us if some treatments are better than others but we cannot guarantee that taking part in this study will benefit your friend / relative directly but it will help improve treatment for people with pneumonia in the future.

All medical treatments can cause side effects. The risks from side effects are similar if you choose for your friend / relative to not to be in the study. Your friend / relative’s doctor will know what treatment they are receiving at all times, and so the doctors will be looking out for any side effects.

**What if something goes wrong?**

University Medical Center Utrecht (UMCU) (the trial sponsor) holds insurance policies which apply to this study. If in the unlikely event your friend / relative experience serious and enduring harm or injury as a result of taking part in this study, they may be eligible to claim compensation without having to prove that UMCU is at fault. This does not affect their legal rights to seek compensation. If your friend / relative is harmed due to someone’s negligence, then they may have grounds for a legal action.

If you / your friend / relative wish to complain, or have any concerns about any aspect of the way your friend / relative has been treated during the course of this study then you should immediately inform the local Investigator (Dr…………………………………………., contact details at end). The normal National Health Service complaints mechanisms are also available to you / your friend / relative.

**Will information from this study be kept confidential?**

Yes. This is a large global trial and we will follow the law by making sure your friend / relative’s information is kept private and secure. UMC Utrecht is the sponsor for this study based in the Netherlands. We will be using information from your friend / relative’s medical records in order to undertake this study and UMC Utrecht will act as the data controller for this study. This means that they are responsible for looking after your friend / relative’s information and using it properly. UMC Utrecht will be storing de-identified study data on servers based in Sydney Australia. This information will be kept for 15 years after the study has finished.

Your friend / relative’s rights to access, change or move their information are limited, as we need to manage the information in specific ways in order for the research to be reliable and accurate. If your friend / relative withdraws from the study, we will keep the information about them that we have already obtained. To safeguard their rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your friend / relative’s information by contacting privacy@umcutrecht.nl.

**[NHS site name]** will collect information from your friend / relative’s medical records for this research study in accordance with the sponsor’s instructions.

**[NHS site name]** will keep your friend / relative’s name, NHS number and contact details confidential and will not pass this information to UMC Utrecht. **[NHS site name]** will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for their care, and to oversee the quality of the study. Certain individuals from UMC Utrecht and regulatory organisations may look at their medical and research records to check the accuracy of the research study. UMC Utrecht will only receive information without any identifying information. The people who analyse the information will not be able to identify your friend / relative and will not be able to find out your friend / relative’s name, NHS number or contact details.

Minimal randomisation and clinical data will be collected on servers in Sydney Australia which will collect some personal information about your friend / relative for this global study. This information will include their initials, date of birth and gender and basic eligibility health information. The information will be held securely with strict arrangements about who can access the information. With your permission, in order that we can contact your friend / relative in 6 months and identify them in the Case Mix Programme database (as outlined above) this hospital will provide your friend / relative’s name, telephone number and NHS number to ICNARC (based in the UK), alongside some additional clinical data. Once your friend / relative has been identified, the trial team will share your friend / relative’s postcode, date of birth and NHS number (held by the Case Mix Programme), along with their name with NHS Digital. This will enable NHS Digital to provide us with information as described above.

**[NHS site name]** will keep identifiable information about your friend / relative from this study for 15 years after the study has finished. When you agree that your friend / relative would wish to take part in a research study, the information about your friend / relative’s health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your friend / relative’s information will only be used by organisations and researchers to conduct research in accordance with the [UK Policy Framework for Health and Social Care Research](https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/)**.**

This information will not identify your friend / relative and will not be combined with other information in a way that could identify them. The information will only be used for the purpose of health and care research, and cannot be used to contact your friend / relative or to affect their care. It will not be used to make decisions about future services available to your friend / relative, such as insurance. It is necessary for us to process your friend / relative data as described to allow us to perform a task in the public interest (lawful basis).

**What will happen to the results of the research study?**

The study stops for your friend / relative once they have completed their 6 month follow up telephone conversation with a member of the clinical research team. Your friend / relative will not be personally informed about the results of the study. The results of this study will be presented at medical meetings and published in scientific journals. Only anonymous group information and no personal information will be presented. If you are interested in the results you will be able to look them up after the trial has finished. The website link where you can see the overall results will be: [www.remapcap.org](http://www.remapcap.com).

**Who is organising and funding the research?**

The Coordinating Principal Investigator for this study is Professor Marc Bonten, at the University Medical Center Utrecht, Netherlands. This research has received funding from the EU FP7-HEALTH-2013 INNOVATION-1 Grant as part of the global PREPARE consortium. The cost of some treatments may be covered by pharmaceutical companies that make these products.  These pharmaceutical companies have no involvement 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 the study?**

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.**

**Who can I contact for independent research information?**

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]

**Further information**

Thank you for considering your friend / relative’s participation in this study. If you have any questions about this research, the local study staff will be more than happy to answer them. Their contact details are:

**Study Investigators Contact details**

|  |  |
| --- | --- |
| **Study Investigator** |  |
| **Study Nurse** |  |
| **Day time Telephone** |  |
| **Emergency Telephone** |  |

**Treatments available at this ICU**

**1. Use of antiviral medication.** When a patient has pneumonia caused by an influenza virus, some doctors will prescribe a drug called Oseltamivir, an antiviral medication. Some doctors do not routinely use Oseltamivir, and those who do may prescribe it for different lengths of time. At this site, this study evaluates:

No Oseltamivir

Oseltamivir for five days

Oseltamivir for ten days

The doctors in this ICU have selected these options because they do not know which of them is best, but believe that all of these options are safe and effective. Therefore, these options are different types of “standard care”. The participant will only receive these treatments if they have pneumonia that is believed or known to be caused by Influenza. *[delete if not taking part in antiviral domain]*

**2. Choice of antibiotic.** All patients that have pneumonia are given antibiotics to help fight infection, but some doctors give different antibiotics. This project is comparing [insert number] combinations of antibiotics in this hospital: [*to be adjusted for each hospital]*

Amoxicillin-clavulanate + clarithromycin

Ceftriaxone + clarithromycin

Piperacillin-tazobactam + clarithromycin

Ceftaroline + clarithromycin

Moxifloxacin or levofloxacin

The doctors in this ICU have chosen to have these options available in the study as all of these options are known to be safe and effective to treat pneumonia. If your friend / relative is not in the study, it is very likely that the doctors would treat them with one of these options. However, it is not known which option is best.

*[delete if not taking part in antibiotic domain]*

**3. Duration of macrolide treatment.** Macrolide antibiotics are used to treat some types of pneumonia but also have some anti-inflammatory actions. Most doctors give macrolide antibiotics to most patients with pneumonia but stop after a few days. It has been suggested that longer treatments may provide beneficial anti-inflammatory effects. In this research project, stopping the macrolide antibiotic after three days will be compared with continuing it for up to 14 days. *[delete if not taking part in macrolide treatment domain]*

4. **Supportive treatment - Whether to use hydrocortisone**. Hydrocortisone is an anti-inflammatory medication. Some doctors believe it helps reduce inflammation in the lungs and elsewhere in the body, and that this helps the body to recover. Other doctors disagree and don’t use the medicine, and others use the medicine only when a patient is very unwell (is in “septic shock”). At this site, this study evaluates:

No corticosteroids

A fixed duration of treatment with hydrocortisone

Hydrocortisone given only when the patient is in “septic shock”

The doctors in this ICU don’t know which treatment is best but believe all options are safe and reasonable. Therefore, the choice of whether to use hydrocortisone or not is comparing different types of “standard care”. *[delete if not taking part in hydrocortisone domain]*

**5. Vitamin C therapy**. It has been suggested that high doses of vitamin C may be useful to treat infection and the inflammation often seen in sepsis. However, there is no clear evidence of benefit for this treatment yet.

The following interventions will be available:

• No vitamin c (no placebo)

• Intravenous Vitamin C for 4 days

*[delete if not taking part in Vitamin C domain]*

**6. Cysteamine Domain**

Cysteamine has antibacterial and antiviral properties, as well as anti-inflammatory effects and may potentially increase the effectiveness of antibiotics you may be given. Cysteamine would be administered alongside the standard or care treatments for the treatment of severe, community acquired pneumonia, influenza and COVID-19 associated pneumonia.

The following interventions will be available:

• No cysteamine

• Cysteamine

*[delete if not taking part in the Cysteamine domain]*

**Possible side effects**

Different types of antibiotics and antiviralsare used as part of the study. These medications are used as part of normal care, and the side effects are minimal, but these drugs can still give side effects. The antibiotics and antivirals used as part of this study may have the following side effects:
Diarrhoea, dizziness, headache, stomach ache, tingling sensations, nausea, vomiting, heartburn, unpleasant taste, inflammation of the mouth and the tongue, deteriorating vision, deafness, loss of appetite, low blood sugar, itching, skin rash, joint pain, fatigue, vein inflammation, general anaemia, cardiac arrhythmia, excessive sweating, shortness of breath, sleepiness, anxiety and confusion, and nervousness.

These side-effects are similar for most different antibiotics and antivirals. *[delete if not participating in the antibiotic / antiviral domain]*

Hydrocortisone may have the following side effects:
High blood pressure, fluid retention, nausea, increased risk of infection, high blood pressure, general discomfort (malaise) and hypersensitivity. *[delete if not participating in hydrocortisone domain]*

Vitamin C may potentially cause kidney stones. *[delete if not participating in the Vitamin C domain]*

Cysteamine is used in the treatment of cystinosis. Side effects include rashes, itchiness, facial flushing, wheezing, shortness of breath, low blood pressure, temporary changes in liver blood tests and low white blood cells. [delete if not participating in the Cysteamine domain].

Other rare side effects may occur (in less than 1% of people) but the doctors and nurses looking after your relative / friend will watch carefully for these possible effects and treat them as necessary and even stop the treatment if needed.

**CONSENT FORM FOR PATIENTS UNABLE TO GIVE CONSENT**

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient Study ID** |  | **Site #** |  |
| **Name of Research Doctor** |  |

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

I, *(forename and surname)*…………………………………………………………………………………………………… freely

agree *for my relative / friend* to take part in the study.

* I confirm that I have read and understood the participant information sheet dated 16th August 2021 v2.7 for the above study and have been able to ask questions which have been answered fully.
* I agree for my relative / friend to take part in the antiviral domain.  *[delete if not taking part in antiviral treatment domain]*
* I agree for my relative / friend to take part in the antibiotic domain. *[delete if not taking part in antibiotic treatment domain]*
* I agree for my relative / friend to take part in the macrolide domain. *[delete if not taking part in macrolide treatment domain]*
* I agree for my relative / friend to take part in the corticosteroid domain. *[delete if not taking part in corticosteroid treatment domain]*
* I agree for my relative / friend to take part in the Vitamin C *domain* [*delete if not taking part in Vitamin C domain]*
* I agree for my relative / friend to take part in the Cysteamine *domain* [*delete if not taking part in Cysteamine domain]*
* I understand that my relative / friend’s participation is voluntary and I they are free to withdraw at any time, without

giving any reason and without my medical care or legal rights being affected.

* I understand my relative / friend’s identity will never be disclosed to any third parties and any information collected will remain confidential.
* I agree that my relative / friend’s medical records and other personal data generated during the study may be examined 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.
* I agree that I will not seek to restrict the use to which the results of the study may be put.
* I understand that my relative / friend’s will be contacted by ICNARC in six months to ask about their quality of life and wellbeing. *[delete if not taking part in follow-up aspect]*
* I understand that minimal randomisation data collected about my relative / friend’s will be transferred outside of the EEA.
* I agree that my relative / friend’s consent will override my consent when they are able to give informed consent.

|  |  |
| --- | --- |
| **Attorney, Guardian, Relative**  | **Person responsible for collecting the informed consent** |
| *Date:**Signature:**Printed Name:* | *Date:**Signature:**Printed Name:* |
| *Witness Consent (in the event the patient cannot sign)**Date:**Signature:**Printed Name:* |  |