

**Hospital Name:**   
(use CAPITALS)

**Patient Name:**   
(use CAPITALS)

**Study ID:**   
(enter after randomisation)

**1. Information about the study has been provided to me:** I confirm that I have read (or had read to me) and understood the Participant Information Leaflet (V8.0 26-Jan-2021) and I have had the opportunity to consider the information and ask questions. These have been answered satisfactorily.

**2. Voluntary participation:** I understand that my / my child's participation is voluntary and that I am free to withdraw [my child] at any time, without giving any reason, and without my/his/her medical care or legal rights being affected.

**3. Access to study data about my child:** I give permission for relevant sections of my / my child's medical notes and information collected during the study to be looked at, in confidence, by authorised individuals from this hospital, the University of Oxford, and regulatory authorities to check that the study is being carried out correctly.

**4. Access to my/my child's medical information:** I agree that medical information collected by the doctors and hospitals which provide me/my child with care and which may be located in local or national health and research organizations (including hospital admission, civil registration, audit and research data) may be provided to the study coordinating centre both during and for up to 10 years after the scheduled follow-up period. I understand that information that identifies me/my child will be passed securely to such bodies to make this possible and that I can opt out of this at any time by writing to the coordinating centre team.

**5. Data stored on computer:** I understand that information about my/my child's progress in the study will be recorded on a computer database, and that this data will be stored on computers supervised by the University of Oxford. I understand that this information will be kept securely and confidentially.

**6.** I am aware that a blood sample will be sent to a central NHS laboratory for measurement of coronavirus and antibodies against it if I/my child enter the monoclonal antibody comparison.

**7. Agreement to take part:** I have read the information (or had it read to me), had an opportunity to ask questions and agree [for my child] to take part in the above study.

..... PRINTED name of parent/guardian/participant (if aged ≥16)	..... Signature	...../...../..... Today's date
..... PRINTED name of person taking consent	..... Signature	...../...../..... Today's date

*\*1 copy for participant; 1 copy for researcher site file; 1 (original) to be kept in medical notes*

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**If parent/guardian is not able to be present physically or sign for themselves but has capacity to give consent**

I witnessed accurate reading of the consent form to the potential participant's parent/guardian, who could ask any questions and got satisfactory replies.

I confirm that they gave their consent freely.

.....

PRINTED name of witness

.....

Signature

...../...../.....

Today's date

.....

PRINTED name of person taking consent

.....

Signature

...../...../.....

Today's date

*\*1 copy for parent/guardian; 1 copy for researcher site file; 1 (original) to be kept in participant medical notes*

**Hospital Name:**

(use CAPITALS)

**Child/Young Person**

**Name**(use CAPITALS):

**Study ID:**

(enter after randomisation)

**Information about the RECOVERY Trial for children 10-15 years old**

Your doctors have found, or suspect, you have an infection called COVID-19, or have recently had COVID-19. This condition is caused by a type of virus called a coronavirus. Most children and young people who get coronavirus get better without coming to hospital. Of those who are admitted to hospital, some will need more treatment such as oxygen or machines to help breathing. Some children and young people have become unwell a few weeks after having COVID-19. The RECOVERY trial has so far found that a medicine called steroids can be used to treat people with coronavirus who need oxygen. We do not know which other medicines are best to use to treat coronavirus or the complications of the infection.

The reason we are doing this study is to find out if the medicines currently being tested help people get better quicker from coronavirus infection or the later illness linked to COVID-19.

All of the medicines you might receive in the study have been used to treat children with other medical conditions (except for one which hasn't been given to children before and is only being used in children aged at least 12 years old). The medicines are listed in the more detailed information given to your parents or guardian. If you and your parents/guardian decide that you can take part then:

- the study doctors and nurses will examine you and take some blood tests to check it is safe for you to take part in the study.
- young women will also have a urine pregnancy test if they might receive certain medicines. This needs to be done even if you are certain you are not pregnant.
- a computer will decide which extra treatment you will receive as part of the study - the medicines are only given in hospital: when you go home the study treatment will be stopped.
- if you and your parents/guardian decide you can take part then they will sign a consent form and if you want to you can sign below to show you also have understood this information and agree to take part.

If you have any other questions please ask your parents, your doctors or nurses or the research doctors or nurses.

Signature .....

Today's date...../...../.....

*\*1 copy for child; 1 copy for researcher site file; 1 (original) to be kept in participant medical notes*

# **Information about the RECOVERY Trial for younger children (to read with parents/guardian)**

You have come into hospital because you are poorly with coronavirus or you may have had coronavirus a few weeks ago and now become poorly from your body's response to the virus.

The doctors and nurses in the hospital will be doing all they can to help you get better.

Your parents (or guardians) have agreed for you to take part in a study to find out whether there are extra medicines that can help people get better faster.

## **What will happen?**

- the nurses and doctors will listen to your chest and check your blood tests to make sure it is safe for you to take part
- you will have the new medicine as one of your treatments in hospital. You won't have to take the medicine after you go home.
- when enough children and grown-ups have taken part, we will work out whether the new medicines work
- if you have any other questions, please ask your parents, your doctors or nurses.

## **Invitation to participate for parents/guardians of children 15 years and under and for young people age 16 and 17 years old**

We are inviting people of any age who have been admitted to hospital with (or suspected to have) COVID-19 to consent to join this research study comparing possible treatments. This form gives information about the study including the aims, risks and benefits of taking part.

**Please note:** Some of the treatments described below may not be available at your hospital or suitable for you or your child (or you/your child may have received them already). Your doctor will be able to explain which treatments would be considered for you as part of this trial.

### **WHAT YOU SHOULD KNOW ABOUT THIS RESEARCH STUDY:**

#### **1) Why is this research being done?**

Your doctors have found, or suspect, that you/your child has a disease called COVID-19, or has had this infection in the past few weeks and is now producing an exaggerated response to this infection. This condition is caused by a type of virus called SARS-CoV-2, or coronavirus for short. About 19 out of 20 patients who get coronavirus get better without coming to hospital. Of those who are admitted to hospital, most also get better, but some may need oxygen or mechanical ventilation before they do so. However, a few percent do not get better.

Children and young people may also become unwell several weeks after COVID-19, even if they had no symptoms at the time of the initial infection. The condition is called Paediatric Multisystem Inflammatory Syndrome temporally associated with COVID-19 (or PIMS-TS for short). This is a rare condition and most children/young people with the condition will not be seriously unwell, however some will need treatment in intensive care to support their breathing and circulation. All children/young people with the condition have high levels of inflammation. In a small number of cases, the blood vessels around the heart can become inflamed and larger than normal.

The RECOVERY trial has recently shown that dexamethasone, a steroid medicine, can be used to treat adults with COVID-19 who need oxygen. There are several other medicines which may turn out to be helpful (or possibly harmful) when added to the usual standard of care. We are learning more about the condition called PIMS-TS all the time, as this condition has only been recently identified. We don't know yet if specific treatments that might be useful in active COVID-19 infection might also be helpful in children and young people with PIMS-TS. This study aims to find out whether any of these additional treatments are of any help for COVID-19 in children or the illness linked to previous COVID-19.

#### **2) What is the purpose of this study?**

This study aims to compare several different treatments that may be useful for patients with COVID-19, or PIMS-TS which is linked to COVID-19. These treatments have been recommended for testing by the expert panel that advises the Chief Medical Officer in England. Some are taken by mouth and some are given into the veins via a cannula. Although these treatments show promise, nobody knows if any of them will turn out to be more effective in helping patients recover than the usual standard of care at your hospital (which all patients will receive).

The treatments, which may be given to children and young people in addition to the usual care at your hospital, are different depending on whether the child/young person has respiratory infection due to current COVID-19 infection or whether they have the PIMS-TS inflammatory condition a few weeks after being exposed to COVID-19:

1. For PIMS-TS (the inflammatory condition), treatments include corticosteroids and intravenous immunoglobulin (which is commonly used to treat a similar but different inflammatory condition called Kawasaki disease).

2. For children and young people who have COVID-19 respiratory illness, treatments may also include hydrocortisone (a steroid treatment for babies), baricitinib (a medicine used to treat some types of arthritis in children and adults),

or (for children aged 12 or over) a mixture of two antibodies which have been designed to neutralise the coronavirus (called monoclonal antibodies, or Mab for short).

Corticosteroids have been shown to be useful in people with COVID-19 acute infection needing oxygen, but have not yet been shown to be useful in PIMS-TS, which occurs a few weeks after COVID-19 infection itself. A national NHS England survey of clinicians has shown that while both intravenous immunoglobulin and corticosteroids are agreed treatments for the PIMS-TS inflammation after COVID-19, we do not yet know which of these (if any) should be used as the first treatment. For patients whose PIMS-TS condition is more severe, tocilizumab (which is used in adult and childhood inflammatory disorders) and anakinra (which is widely used in several conditions in children/young people with rare conditions associated with severe inflammation) are also options. At present, we don't know whether any of these are effective in treating COVID-19. However, the side-effects are well-known from other uses and your doctor will be able to monitor you/your child appropriately. Only medicines used before to treat children of your/your child's age group will be given to them as part of the trial (except for the monoclonal antibody which hasn't been given to children before and is only being used in young people aged at least 12 years old). The doctors treating you/your child are able to exclude treatments from the randomisation process, if these treatments are not suitable for you/your child, however they are not able to pick exactly which of the suitable treatments you/your child receives.

### **3) Who is doing the study?**

The study is being conducted by researchers at the University of Oxford, which acts as the sponsor for the research, working with doctors at many hospitals across the UK.

### **4) Who is being included in the study?**

Patients of any age (including babies) may be included in this study if they have COVID-19 confirmed by a laboratory test for coronavirus (or considered likely by their doctors), or are suspected of having the condition called PIMS-TS, which is linked to COVID-19, and are in hospital. Patients will not be included if the attending doctor thinks there is a particular reason why none of the study treatments are suitable.

### **5) What happens next if I agree that I/my child can be included in this study?**

If you decide for you/your child to take part, you will be asked to sign the consent form. Next, brief details identifying you/your child and answering a few questions about you/your child's health and medical conditions will be entered into a computer. If you are willing for you/your child to have the monoclonal antibody treatment, a blood sample will be sent to a central laboratory for measurement of coronavirus and antibodies against it. The results will not be available to you/your child's medical team and the sample will be destroyed once testing is complete. Young females of child-bearing potential will have a urine pregnancy test before being able to be offered the baricitinib or anakinra medicines. The computer will then allocate you/your child at random (like rolling a dice) to one of the possible treatment options. In all cases this will include the usual standard of care for your hospital. It may also include an additional treatment, which might be given by mouth, by injection under the skin or into a vein via a cannula. Neither you nor the doctors can choose which of these options you/your child will be allocated to. If you/your child's PIMS-TS condition is severe or should deteriorate, then your doctors may choose to enter you/your child into a second phase in which the computer will allocate you/your child at random again to one of the further possible treatment options (in addition to any previous study treatment and always including usual standard of care for your hospital).

Additional information about you/your child's health will be recorded and entered into the study computer but no additional physical visits will be required after you/your child leaves the hospital. If you/your child has taken part in the second randomisation you/your child may be reviewed in hospital or receive a phone call approximately 6 weeks after leaving hospital to check on your/your child's recovery. In some instances, information about your/your child's health (both prior to, during, and after the study) may be obtained from medical records or databases (including NHS Digital, Public Health England, other equivalent bodies, and genetic or other research databases if your child has provided samples to them) so that the study team can get more detailed or longer term information about the effects of the study treatments on your/your child's health for up to 10 years after the end of your/your child's participation. We may write to you to tell you about the trial periodically, but you will be able to opt-out of these communications if you prefer.

**Important note:** if you/your child receives intravenous immunoglobulin as part of therapy, you/they should avoid live vaccines up to **3 months** following treatment. Examples of live vaccines include: MMR, rotavirus, chicken pox, BCG and the nasal flu vaccine (but not the injected form of flu vaccine). COVID-19 vaccinations are not live but should be deferred for 90 days after discharge if you/your child received the monoclonal antibodies. The risk of repeat infection

*during this period is very small as we know that the immunity gained from COVID-19 infection is similar to that provided by the vaccine and lasts at least three months after infection.*

#### **6) What are the possible benefits of being in the study?**

We do not know if any of the treatments being tested will have additional benefits. The study treatment may or may not help your child personally, but this study should help future patients.

#### **7) What are the possible risks of being in the study?**

Apart from the known side effects of these treatments (which may include tummy upset and blood test abnormalities), there is the unlikely possibility of a severe reaction to any study drug. The monoclonal antibody treatment (which is in early and rapid development, and currently unlicensed) has been given to over 4000 people with COVID-19 to date, a small number (less than 1 in 100) of whom developed reactions during the infusion or shortly thereafter. The potential side effects of the Mab include allergic reactions (rash, fever, chills) and increased difficulty breathing and are easily treated (eg, by slowing or stopping the infusion). Baricitinib and anakinra may cause tummy upset and blood test abnormalities, rarely including low blood counts, for which children and young people will be monitored. Although tocilizumab and anakinra have been very rarely associated with liver damage in prolonged use this is not expected to be a problem with the short-term administration in this study. The side effects of anakinra are also known to include allergic reaction and for prolonged use an increase in susceptibility to other infections (in this study the use is short term). All treatments offered to children of different ages have been used in children and young people of the same ages to treat other medical conditions (except for the monoclonal antibody, although other similar treatments are used in children). Once you/your child has been included in the study, you and the doctors will know which treatment the computer has allocated for you/your child. The doctors will be aware of whether there are any particular side effects that they should look out for.

#### **8) Young people who may be pregnant**

Women who are pregnant may be included, however, the effect of some of the treatments on unborn babies is uncertain. Anyone pregnant will not receive baricitinab or anakinra as they may be harmful in pregnancy or when breast-feeding, which is why adolescent girls will all have a pregnancy test before receiving these treatments, even if they are certain that they are not pregnant. All the other treatments (except the Mab) have previously been used in pregnancy for other medical conditions without safety concerns being raised. The monoclonal antibody has not been given to pregnant women before, but is being tested as pregnant women are at risk from COVID-19. If females do receive treatment and are not already pregnant, as a precaution, we advise they should not get pregnant within 3 months of the completion of the trial treatment(s). Please ask your hospital doctor if you would like more information.

#### **9) Can I stop the study treatment or my child's participation early?**

If you or your doctor want to stop the study treatment before the course has been completed, then you are free to do so. If you decide that you do not wish any more information to be collected about you/your child, you are free to say so (although de-identified information that has been collected up to that point will continue to be analysed by the research team).

#### **10) If I have any questions or problems, who can I call?**

If you have any questions, please speak to your hospital medical team. Further information about the study will also be available on the study website ([www.recoverytrial.net](http://www.recoverytrial.net)).

#### **11) What information do you hold about me and how do you keep it private?**

All information about you/your child's health will be kept private. The only people allowed to look at the information will be the doctors who are running the study, the staff at the study coordinating centre, and the regulatory authorities who check that the study is being carried out correctly. A privacy notice is on the study website ([www.recoverytrial.net](http://www.recoverytrial.net)).

#### **12) Do you/your child have to take part and are there any financial costs or payments?**

Joining the study is voluntary. The decision whether to take part will not affect you/your child's care. All trial treatments will be free. Neither you nor the medical staff will be paid for your/your child's participation in this study.

#### **13) What else can you tell me?**

The study is funded by UK Research and Innovation and the National Institute for Health Research, not the makers of any of the study treatments (who may provide the treatment free of charge to the trial). If we find out any new information that might affect your decision to stay in the study, we will give it to you. The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment that is provided.