mulTi-Arm therapeutiC sTudy in pre-Icu patients admitted with Covid-19 – Experimental drugs and mechanisms (TACTIC-E)

PARTICIPANT INFORMATION SHEET & INFORMED CONSENT FORM

You are being invited to take part in a COVID-19 research trial. Please take the time to read the following information carefully and ask us if you have any questions.

MORE INFORMATION IS AVAILABLE AT www.camcovidtrials.net

1. What is the purpose of the trial?

COVID-19 is a disease affecting the lungs and is caused by a new coronavirus known as SARS-CoV2. The purpose of this trial is to identify the best way to treat patients infected with COVID-19 by comparing different treatments which act on the immune system. The reason for this is because in severe COVID-19 infection, there is an "over-reaction" of the immune system which involves the whole body. This has led to interest in drugs that control or "modulate" the immune system as potential treatments.

2. What treatments are investigated?

Patients who sign up for this trial will receive one of three different treatment options whilst in hospital, in addition to the usual clinical care for COVID patients:

1) EDP1815 (an unlicensed drug which is being developed for the treatment of inflammatory diseases)
2) Ambrisentan and Dapagliflozin. Ambrisentan is a licensed drug which targets the walls of blood vessels in the lungs and blunts inflammatory activity in the lungs. It is commonly used to treat a condition known as pulmonary arterial hypertension. Dapagliflozin is a licensed drug which helps the kidneys excrete glucose and it is commonly used in type 2 diabetes mellitus.
3) UNI911 is a new (unlicensed) formulation of Niclosamide to be administered through inhalation (using a machine [nebuliser] that helps you to breath in a medicine through a mask or a mouthpiece) and nasal spray. Niclosamide has previously been used for 50 years as an oral drug to treat tapeworm. Niclosamide has effect on several viruses, including a good activity against SARS-CoV-2.

All trial drugs work to "calm down" the immune system.

3. Which treatment will I receive?

The treatment you will receive will be allocated to you at random (like rolling a dice). This means you will receive either

1. EDP1815 daily (as a capsule taken twice a day) until discharge from hospital and for a maximum of 14 days;
2. Ambrisentan and Dapagliflozin, two different drugs, each taken as a single capsule once a day, or
3. UNI911: This drug will be taken as an inhalation product, i.e. as a nebuliser solution and a nasal spray solution each given twice daily for up to 10 days or until discharged. This may be increased to a maximum of 14 days at the discretion of the doctor, in addition to standard of care. Pre-treatment with a licensed beta2 agonist (salbutamol) will also be used. Patients will stop treatment at hospital discharge, or
4. The standard of care you would normally receive.

As the study progresses, additional drug treatments may be added or removed, depending on the latest scientific evidence. We may also take samples of your blood for routine clinical tests, and the option of additional samples to look at your response to the infection.

4. What are the side effects of the drugs?

Ambrisentan:

Very common (more than 10 in 100 of patients): headache, peripheral oedema, fluid retention,

Common (less than 10 in 100 of patients): anaemia, dizziness, cardiac failure, palpitations, low blood pressure, flushing, nosebleeds, difficulty breathing, upper respiratory congestion, nausea, vomiting, diarrhoea, abdominal pain, constipation, increased liver enzymes (transaminases), chest discomfort or pain, lack of energy, fatigue.

Dapagliflozin:

Very common (more than 10 in 100 of patients): hypoglycaemia (low blood sugar when used with insulin or sulphonylurea drugs).

Common (less than 10 in 100 of patients): genital infections, urinary tract infections, dizziness, rash, back pain, painful or difficult urination, increased urine output, blood test results which show an increase in haematocrit (increase in the volume of red blood cells in your whole blood), decrease in creatinine renal clearance, which indicates kidney function, or dyslipidaemia (changes in the fat concentrations).

EDP 1815:

No specific side effects have been described with EDP 1815.

UNI911:

The symptoms below sometimes occur when patients take this medication by mouth. However, you will only use this medication through breathing/inhalation. Frequencies of the side effects are not known: side effects

have included rashy, itchy skin, breathlessness, dizziness, blue-ish skin, small broken veins, nausea, stomach ache, abdominal pain, loose stools, gagging, fatigue, excessive sweating.

5. Why have I been invited?

You have been invited to participate in this trial because you are or suspected to be COVID-19 positive and are considered to be at risk of developing severe symptoms.

6. Do I have to take part?

Joining the study is voluntary. Your care will not be affected by your decision whether you take part.

7. What are the possible benefits?

We are not yet sure if the treatments will have any benefit, but this study will help to identify treatments for future patients. There may be side effects of these treatments.

8. What are the possible risks of being in the study?

The treatments may cause side effects. However, Ambrisentan and Dapagliflozin are used in other health conditions and their side effects are known. Your doctors will monitor you closely for any side effects from the treatments you receive as part of this trial.
No specific side effects have been described for EDP1815.

The inhalation procedure for UNI911 may cause coughing and unpleasantness in the upper airways and mouth – taking short breaks during the inhalation helps alleviate these effects. The inhalation of medication is expected to take 10-20 minutes. When this medication is given via nose, you may experience a mild sore throat.

Blood tests may cause some pain/bruising at the site from which the blood sample is taken. You will need to use adequate contraception for the duration of the 90-day trial.

9. Pregnancy and Contraception information

You should not participate in this trial if you are planning to become pregnant or father a child during the trial. Women who are able to have a baby must use reliable forms of contraception for the entire duration of the trial (90 days) after upon completion of the last treatment. Men are required to use adequate contraception for the entire duration of the trial (90 days) upon completion of the last treatment.

If you or your partner becomes pregnant during the trial (within 90 days) after completion of the last treatment, you should inform your trial doctor immediately.

10. What happens when the trial stops?

Once the trial has ended you will be referred back to regular treatments. Pending the results of the trial, treatment guidelines may change. If you or your doctor wants to stop the study treatment, you can stop it at any time.

11. Can I stop the study treatment or my participation early?

If you 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, feel free to say so (but de-identified information that has been collected up to that point will continue to be analysed by the research team).

12. Expenses & Payment?

You will be reimbursed travel expenses for any research visits which require you to attend a hospital visit after you have been discharged.

13. Optional Endothelial cell collection

In some centres in the UK, we are also conducting a smaller study for patients participating in the main study. We will provide you with an additional information sheet and consent form describing an optional procedure called Endothelial Cell Collection. You can still take part in the TACTIC-E trial if you choose not to take part in the endothelial cell collection.

14. What if there is a problem?

If you have any concerns about any aspect of this trial, you should speak to your trial doctor who will do their best to answer your questions. If you wish to complain or have any concerns about any aspect trial, you can do this through the NHS complaints procedure. In the first instance it may be helpful to contact the Patient Advice and Liaison Service (Tel: +44 (0)1223 256170, email: pals@addenbrookes.nhs.uk) at your hospital.

15. Will my personal information be kept confidential?

All information about you and your 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 and a more detailed patient information sheet are on the study website.

16. What will happen to the results of the trial?

The results of the trial will be anonymous and you will not be able to be identified from any of the data produced. Coded datasets from the trial may also be made available to other researchers in line with national and international data transparency initiatives. These researchers may be outside the European Union and EEA zone where privacy laws may not be as stringent – however, none of your personal details will be sent outside the EU. When the results of this trial are available, they may be published in peer reviewed medical journals and used for medical presentations and conferences. If you would like to obtain a copy of the published results, please contact your trial doctor directly who will be able to arrange this for you.

17. Who is funding and sponsoring the trial?

The trial is being funded by Evelo Biosciences, Astrazeneca and UNION therapeutics A/S, and is sponsored by Cambridge University Hospitals NHS Foundation Trust.

18. Who has reviewed this trial?

This trial has been reviewed and given favourable opinion by an independent Research Ethics Committee, (the West Midlands Coventry & Warwickshire REC) to protect your interests. The Medicines and Healthcare Products Regulatory Agency (MHRA) who are responsible for regulating medicines in the UK have also reviewed this trial.

Further information and contact details

If you have any questions or require any further information about the trial, please feel free to contact:

Telephone:

Principal Investigator (PI): Dr Edward Banham-hall
Tel: +44 (0) 1223 348320/349009

Chief Investigator (CI): Dr Joseph Cheriyan
Tel: +44 (0) 1223 256653

Research Nurse: Annette Hubsch/Jo Helmy
Tel: +44 (0) 1223 586852

In the event of an emergency please contact:

Tel: +44(0)1223 926008 or
Tel: +44(0)1223 245 151 then 157864 (bleep number)

(Occasionally this may be answered by an alternative trial doctor)

Should you have any concerns about your patient participating in the study, please feel free to contact a member of the study team.

INFORMED CONSENT FORM

Trial Title: mulTi-Arm Therapeutic study in pre-ICu patients admitted with Covid-19 – Experimental drugs and mechanisms (TACTIC-E)

Principal Investigator: _____ **Participant Number:** _____

1	I have read and understood the Short Participant Information Sheet version 3.0 dated 3 March 2021 for the above trial and I confirm that the trial procedures and information have been explained to me. I have had the opportunity to ask questions and I am satisfied with the answers and explanations provided.
2	I understand that my participation in this trial is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care or legal rights being affected.
3	I understand that my personal data might be transferred between the trial team at different trial sites in relation to my participation in this trial. I understand that any personal data will be sent using (secure/encrypted mail servers).
4	I understand that my GP will be informed of my participation in this trial and be sent details of the TACTIC-E trial.
5	I understand that I may not receive the results from COVID-19 test/s I take as part of this trial.
6	I understand that the doctors in charge of this trial may close the trial, or stop my participation in it at any time without my consent.
7	I agree to provide blood samples for research related to this trial, which may be stored for up to 5 years.
8	I agree that DNA (genetic material) will be isolated from my donated blood sample and analysed through the use of advanced laboratory techniques.
9	I understand that coded trial datasets may be shared with researchers who may be based within or outside the European Union and European Economic Area.

OPTIONAL

		YES	NO
10	I am happy to be contacted in the future about further trials or extensions to this trial.		
11	I am happy for my information to be exchanged with other study teams where I have also been involved in a COVID19 biomarker study		
13	I agree for any remaining blood samples, which were not used in this trial analysis, to be stored for use in future for ethically approved research		

FOR WOMEN OF CHILDBEARING POTENTIAL ONLY

		YES	NO
12	If I become pregnant during, or in the 90 days after receiving the trial drugs, I agree to information being collected about me, my pregnancy and my baby.		
13	I understand that sections of my medical notes or information related directly to my pregnancy may be looked at by responsible individuals from the sponsor, regulatory authorities and research personnel where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.		
14	I agree to give my pregnancy information voluntarily and understand that I am free to withdraw at any time without giving a reason and without my medical care or legal rights being affected. I understand that all data collected up to the withdrawal of consent will be kept confidential.		

I agree to participate in this trial:

_____	_____	_____
Name of patient	Signature	Date
_____	_____	_____
Name of person taking consent	Signature	Date

Time of Consent (24hr clock) _____:_____

1 copy for the patient, 1 copy for the trial team, 1 copy to be retained in the hospital notes.

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Principal Investigator: _____ **Participant Number:** _____

If participant is not able to read the text and/or sign for themselves but has capacity to give consent

I witnessed accurate reading of the consent form to the potential participant, who could ask any questions and got satisfactory replies. I confirm that they gave their consent freely.

.....	.....	...../...../.....
PRINTED name of witness	Signature	Signature Date

.....	.....	...../...../.....
PRINTED name of person taking consent	Signature	Signature Date