Participant Information Sheet
Professional Legal Representative – Post randomisation

ALPHA-2 AGONISTS FOR SEDATION TO PRODUCE BETTER OUTCOMES FROM CRITICAL ILLNESS ('A2B TRIAL')

This patient was eligible to take part in this research study because they are/were being treated with calming drugs (sedation) and pain-killers to keep them comfortable while they are/were on the breathing machine (ventilator) in the intensive care unit. Unfortunately, they were not well enough to be able to decide for themselves whether to take part in this research and they were entered into the research study by a process approved by the research ethics committee. We would now like to ask you as a Professional Legal Representative if you will give consent for them to remain in the study. This is permissible under the Adults with Incapacity (Scotland) Act 2000 and the Mental Capacity Act 2005.

To help you decide whether or not this patient should remain on the study, please take time to read the following information about why the research is being done and what it will involve. Talk to others about the study if you wish and ask if there is anything that is not clear or if you would like more information before you make a decision. We would ask that you put aside your own views about the research and consider what you think the past and present feelings and wishes of this patient would have been, had they been able to consent for themselves.

If a relative is not present in the intensive care unit then we would approach other individuals who can act as a Personal Legal Representative. In Scotland this would include a welfare attorney or welfare guardian and in the rest of the UK it would include any person who knows the individual and is willing to act as a Personal Legal Representative. If a Personal Legal Representative is not available we would then approach a Professional Legal Representative who may be an independent doctor or an individual nominated by the local healthcare trust.

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NIHR | National Institute for Health Research

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If they do continue on the study, when they have regained consciousness and are able to understand the purpose of this study, we will ask their permission to continue and if they decide to withdraw from the study, this will overrule your decision.

If you have any questions at any time, please feel free to contact a member of the research team (details at the end of the Information Sheet).

Thank you for your time

What is the purpose of the study?

The purpose of this study is to try to find the best way to keep patients comfortable while they are on a ventilator. We aim to recruit around 1437 patients to the trial from 40-50 Intensive Care Units (ICU) in the UK.

Most patients in the Intensive Care Unit (ICU) who are on a ventilator need sedation and pain killers to keep them comfortable. However, we know that keeping patients too sleepy with these drugs can make their ICU stay longer, and may make other problems like confusion more likely.

So, we want patients to be as comfortable and as awake as possible, but it is difficult to get this balance right and at present we don't know which choice of drugs is best and most effective.

Most ventilated patients are started on a sedation drug called propofol, which is good at reducing anxiety and making people sleepy. However, it is not a pain killer, so additional pain medicines are needed.

Two other drugs that are sometimes used later in the ICU stay are clonidine and dexmedetomidine (dex). These belong to a group of drugs called alpha-2 agonists, which work in a different way to propofol, to provide both sedation and pain relief. Using these drugs may help nurses keep patients more awake and comfortable on the ventilator.

We want to find out if starting clonidine or dex early in ICU and using them instead of just propofol can help keep patients more comfortable and reduce their time on the breathing machine. We also want to know if using clonidine or dex can decrease problems like delirium (confusion) and anxiety.

Results from a large international study (the SPICE III Trial), which compared dexmedetomidine with usual care (propofol), suggest that older and younger patients may respond differently to the two drugs. This could include how safe and effective the drugs are for older and younger patients. The doctor in charge of this patient has considered this uncertainty when deciding whether they were eligible for this study, and felt they should be considered for participation. We are monitoring our data very closely during the trial, in case we start to see important differences between the age groups. This is being done by an independent safety monitoring committee who would discontinue the trial if they had any concerns.

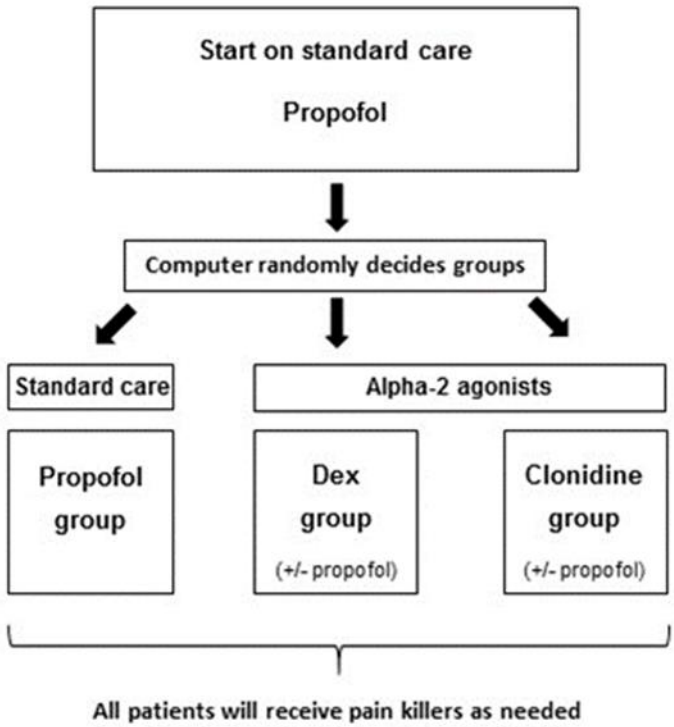
Do I have to agree for this patient to take part?

No. It is up to you to decide on this patient's behalf whether or not to agree for them to take part. If you agree you will be given this information sheet to keep and be asked to sign a consent form. If you agree you are still free to withdraw at any time without giving a reason.

What will happen if I agree for this patient to take part?

If you agree to this patient taking part in the study we will use a computer to randomly decide which of three different sedation approaches to use for them.

When they start on the breathing machine, all patients will be on propofol and a pain killer (current standard care). After starting on the study one group will continue with this standard care; one group will be treated using propofol and Dex, and one group will be treated with propofol and clonidine. All patients will receive extra pain-killers as needed. In the groups that receive dex or clonidine the clinical staff will reduce and sometimes stop the propofol over several hours so the sedation is mainly provided using the dex or clonidine.



The patient will be in one of the three groups until they no longer require any sedation in the ICU. This is usually around the same time that they come off the breathing machine.

We ask permission to take a 20ml blood sample (about 4 teaspoons full) on the first and third or fourthday of the study, but these additional blood tests are optional and patients can still take part in the study without them. We will test the blood samples to find out if patients on Alpha-2 agonists (Dex or Clonidine) have less inflammation than those receiving standard care (propofol). The blood samples will also be used for genetic DNA analysis to better understand the way different people respond to alpha-2 agonists. This may include reading the patient's DNA sequence and comparing it to other people's DNA, to look for genes that cause different responses to the drugs being studied. We will also use the patient's genetic data to try and better understand the biological processes underlying their illness, by looking at the sequence of genes that may affect them.
No DNA results will be returned to patients, but their DNA data may be shared anonymously with other researchers.

All other aspects of care during and after ICU will be decided by the doctors and nurses looking after the patient. They are not affected by being in the study.

We will follow up the patient three times after they join the study, at 1 month, 3 months and 6 months. The follow-ups will involve completing questionnaires and will ask what they remember about the ICU, how they are currently feeling, and their healthcare use. They will take around 20-30 minutes to complete. The questionnaires will either be posted to the patient and they be can completed and returned to us by post. Alternatively a researcher may phone the patient and the questionnaires can be completed during the call. There is no requirement for the patient to come back to hospital because of the study.

The 1 month follow-up will be conducted by a researcher from the hospital and the 6 month follow-up by a researcher from the Edinburgh Clinical Trials Unit (ECTU). The 3 month follow-up will either be conducted by a researcher from the hospital or ECTU. Researchers in ECTU will have access to the patient's contact details so they can carry out the follow-up. They may also check with the hospital that they have the patient's current address and phone number in case this has changed recently before getting in touch.

If this patient takes part in the study from the 1st of October 2023, we will only be follow them up once, at 30 days. This is because the recruitment period for the trial ends on the 31st of October and to finish the trial on time, we have decided to only conduct 30 day follow ups from the beginning of October

We may also use blood samples and data collected to answer other important questions if ethical approval is given for these additional studies.

What are the possible benefits of taking part?

Taking part in this study may help to improve outcomes for patients requiring treatment with a ventilator in the ICU in the future. There is no direct benefit to taking part in the trial.

What are the possible disadvantages of taking part?

The drugs used in this study are commonly used sedation drugs that have known side effects and the doctors and nurses who will be caring for the patient in the ICU are trained to recognise the risks associated with sedation and will decrease or stop the drugs if necessary.

What if there are any problems?

If you have a concern about any aspect of this study please contact <insert name and contact details here> who will do their best to answer your questions

The normal National Health Service complaints mechanisms will still be available to you and won't be affected by agreeing to take part in the study.

What will happen if I don't want to carry on with the study

You are free to withdraw your consent to the patient's participation **at any time** without giving a reason and any study treatment would be stopped. This would not affect the standard of care they receive in any other way or their legal rights. If you choose to withdraw the patient from the trial they would continue to receive Propofol as part of their usual care.

Once the patient is approached about remaining in the study, they can also choose to withdraw from the study **at any time**.

What happens when the study is finished?

The whole study is expected to take four years. We plan to publish the results shortly after this, through medical publications, websites, and press releases, but individual patients will not be identifiable in any published results.

At this point we will be happy to forward a summarised version of the main findings of the study at the patient's request.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard patients' privacy at every stage. All information and samples will be stored by the University of Edinburgh and Edinburgh Clinical Trials Unit. They would only be transferred to other researchers after all necessary approvals were in place.

In order to monitor and audit the study we will ask your consent for responsible representatives from the study sponsors to access the patient's medical records and data collected during the study, where it is relevant to taking part in this research. We will also ask for the patient for consent for this once they are well enough.

How will we use information about this patient?

We will need to use information from this patient's medical records and nationally held databases for this research project. This information will include

- Name
- Contact details – address and telephone number
- Date of Birth
- Community Health Index (CHI) number (patients in Scotland only). The Community Health Index (CHI) is a population register, which is used in Scotland for health care purposes. The CHI number uniquely identifies a person on the index.
- Hospital number (for all other UK patients).

People will use this information to do the research or to check this patient's records to make sure that the research is being done properly.

People who do not need to know who this patient is will not be able to see their name or contact details. This patient's data will have a code number instead.

We will keep all information about this patient safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that this patient took part in the study.

What are your choices about how this patient's information is used?

You can stop this patient being part of the study at any time, without giving a reason, but we will keep information about this patient that we already have.

If you choose for this patient to stop taking part in the study, we would like to continue collecting information about their health from central NHS records/ the patient's hospital. If you do not want this to happen, tell us and we will stop.

We need to manage this patient's records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about this patient.

If you agree for this patient to take part in this study, you will have the option for them to take part in future research using this patient's data saved from this study.

Where can you find out more about how this patient's information is used?

You can find out more about how we use this patient's information

- at www.hra.nhs.uk/information-about-patients/
- by contacting the Data Protection Officer at either
    - University of Edinburgh. Email: dpo@ed.ac.uk or call 0131 651 4114
    - NHS Lothian: Lothian.DPO@nhs.net or call 0131 465 5444

Who is organising and funding the research?

This study has been sponsored by the University of Edinburgh and NHS Lothian. It is funded by the National Institute of Healthcare Research Health Technology Assessment (HTA) Programme.

Who has reviewed the study?

Like all research in the NHS, this study has been reviewed by an independent Research Ethics Committee. A favourable ethical opinion has been obtained from Scotland A Research Ethics Committee. The study has also been approved by the Medicines & Healthcare products Regulatory Agency (MHRA) and local NHS R&D Departments. Previous ICU patients and their relatives also helped us design this trial.

Researcher Contact Details

If you have any further questions about the study please contact <insert name> on <insert phone
number> or email on: <insert email address>

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact <insert contact details>

Complaints

If you wish to make a complaint about the study please contact:

<insert contact details> to be adapted depending on research site.

Find below the example for NHS Lothian

Patient Experience Team
2 – 4 Waterloo Place, Edinburgh, EH1 3EG
feedback@nhslothian.scot.nhs.uk

Tel: 0131 536 3370

Participant ID:		Centre ID	

CONSENT FORM
Professional Legal Representative – Post randomisation

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Please **initial** box

1. I confirm that I have read and understand the Professional LR Post-randomisation information sheet (18 MAY 2023, V5.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
2. I understand that this patient's participation is voluntary and that I am free to withdraw my consent at any time without giving any reason and without this patient's medical care and/or legal rights being affected. ☐
3. I give permission for the research team to access this patient's medical records for the purposes of this research study ☐
4. I understand that relevant sections of this patient's medical notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh and/or NHS Lothian), from the NHS organisation or other regulatory authorities where it is relevant to their taking part in this research. I give permission for these individuals to have access to this patient's data and/or medical records. ☐
5. I give permission for this patient's personal information (including name, address, date of birth, telephone number and consent form) to be passed to the University of Edinburgh and Edinburgh Clinical Trials Unit for administration of the study and follow-up purposes. ☐
6. I give permission for this patient's Community Health Index (CHI) number/hospital number to be collected and passed to the University of Edinburgh and Edinburgh Clinical Trials Unit. ☐
7. I agree that the information held and maintained by NHS Digital, NHS National Services Scotland and other central UK NHS bodies may be used to provide information about this patient's health status. ☐
8. I agree to this patient taking part in the substudy which would involve giving two 20ml blood samples which will be used to study inflammation in the blood and for genetic DNA analysis. Yes ☐ No ☐
9. I give permission for DNA analysis, including whole genome sequencing, to be conducted on this patient's samples Yes ☐ No ☐
10. I agree that information collected about this patient can be used to support other research in the future, and may be shared anonymously with other researchers. Yes ☐ No ☐
11. I agree that this patient's blood and DNA samples can be used to support other research in the future, and may be shared anonymously with other researchers. Yes ☐ No ☐
12. I agree to this patient continuing to take part in the above study ☐

Participant ID:		Centre ID	

I understand that this patient's data will not be shared beyond those noted on the consent form and that access will be managed via a secure system

Please initial box

☐ I confirm that I am Professional Legal Representative for _____

Name of Person Giving Consent	Date	Time	Signature

Name of person receiving consent	Date	Time	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record