

Participant Information Sheet

Welfare Attorney, Welfare Guardian or Nearest Relative (Personal Legal Representative) – Pre randomisation

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

Your relative is eligible to take part in this research study because they are being treated with calming drugs (sedation) and pain-killers to keep them comfortable while they are on the breathing machine (ventilator) in the intensive care unit. Unfortunately, they are not well enough at the moment to be able to decide for themselves whether to take part in this research, so we are therefore asking you as their welfare attorney or guardian or nearest relative if you will give consent on their behalf to join 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 your relative should take part, 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 your relative 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.

FUNDED BY

NIHR | National Institute
for Health Research

This study is funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (16/93/01). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

If they do take part, when your relative has regained consciousness and is 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 1800 patients to the trial from 40 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 recently compared dexmedetomidine with usual care (propofol), suggest that older and younger patients may respond differently to the two drugs. Although the significance of this finding and the possible reasons for it are still uncertain, we will monitor our data very closely during the trial, in case we start to see important differences between the age groups.

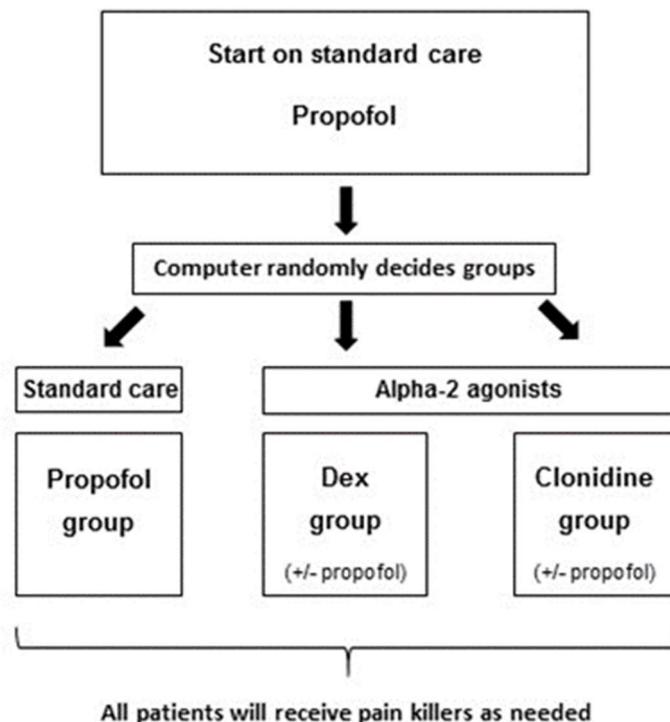
Do I have to agree for my relative to take part?

No. It is up to you to decide on your relative'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 my relative to take part?

If you agree to your relative 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.



Your relative 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 fourth day of the study, but these additional blood tests are optional and your relative 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 your relative'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 your relative's genetic data to try and better understand the biological processes underlying your illness, by looking at the sequence of genes that may affect them. No DNA results will be returned to your relative, but your relative's DNA data may be shared anonymously with other researchers.

We would also like to ask your opinion on how comfortable you think your relative is and if you feel you are able to communicate with them. You will be asked these questions while visiting your relative.

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

We will follow up your relative 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 participant and they can be completed and returned to us by post. Alternatively a researcher may phone the participant and the questionnaires can be completed during the call. There is no requirement for your relative 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 3 and 6 month follow-up by a researcher from the Edinburgh Clinical Trials Unit (ECTU). Researchers in ECTU will have access to your relative's contact details so they can carry out the follow-up. They may also check with the hospital that they have your relative's current address and phone number in case this has changed recently before getting in touch.

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 your relative 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 your relative'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 your relative from the trial they would continue to receive propofol as part of their usual care.

Once your relative 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 your relative'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 your relative's medical records and data collected during the study, where it is relevant to taking part in this research. We will also ask for your relative's consent for this once they are well enough.

We may link records about your relative with nationally held databases to find out about their health status over a longer period without having to contact them directly, but this would only be done after all necessary approvals were in place. In order to identify your relative on these databases we will collect their Community Health Index (CHI) number (patients in Scotland only) or their hospital number (for all other UK patients). 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.

For additional details on what data will be held about your relative and who will hold and store this information please refer to the Data Protection Information Sheet.

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 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@nhsllothian.scot.nhs.uk

Tel: 0131 536 3370

Participant ID:		Centre ID	
------------------------	--	------------------	--

CONSENT FORM
Welfare Attorney, Welfare Guardian or Nearest Relative
(Personal Legal Representative – Pre randomisation)

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

Please **initial** box

1. I confirm that I have read and understand the information sheet (DD MMM YYYY and Version Number) and the Data Protection Information Sheet (DD MMM YYYY and Version Number) 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 my relative's participation is voluntary and that I am free to withdraw my consent at any time without giving any reason and without my relative's medical care and/or legal rights being affected.
3. I give permission for the research team to access my relative's medical records for the purposes of this research study
4. I understand that relevant sections of my relative'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 my relative's data and/or medical records.
5. I give permission for my relative'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 my relative'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 my relative's health status.
8. I agree to my relative 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 my relative's samples Yes No
10. I agree that information collected about my relative can be used to support other research in the future, and may be shared anonymously with other researchers. Yes No
11. I agree that my relative'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 provide my opinion on my relative's level of comfort and my ability to communicate with them and I give my permission for this data to be used.
13. I agree to my relative taking part in the above study

Participant ID:			Centre ID
------------------------	--	--	------------------

I understand that my relative'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 Personal Legal Representative for _____
 and that no other Personal Legal Representative exists

Relationship to participant _____

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