Trust headed paper

COmBining memantine and cholinesterase inhibitors in Lewy body dementia Treatment trial (COBALT)

INVITATION

We are inviting you to take part in a research trial called COBALT. This information sheet tells you more about why it is being done and what it might mean for you. Please read the following information carefully to help you decide if you want to take part. You don't have to decide straight away and you may want to talk to your friends and family to help you decide if you want to be involved in the trial. Ask us if you have any questions or want to know more.

KEY POINTS

- The trial will look at the use of a drug called Memantine as a treatment for people with Dementia with Lewy Bodies (DLB) and Parkinson's Disease Dementia (PDD).
- We are hoping to recruit 300 patients in total in the UK.
- If your friend/relative decides they would like to take part, they will be randomly put into one of two trial medication groups; either the **placebo group** (a 'dummy' drug) or the **treatment group** (Memantine). They will have an equal chance of being in each group.
- Your friend/relative's trial doctor and the local trial team will not know which group they are part of or which trial medication they are taking during the trial.
- You will have planned visits and phone calls with the local trial team, and will be asked to complete questionnaires about your friend/relative's symptoms, and also how you are feeling throughout the trial.
- Your friend/relative will be asked to complete a diary to help track their medication use and if they feel unwell. You may need to help them complete this.
- The local trial team will follow all local and national guidelines relating to Coronavirus and your safety.

Please read the following information for further details about the COBALT trial if you are interested in taking part and see page 11 for contact details.

COBALT

TRIAL PARTNER INFORMATION SHEET

Why is the COBALT trial needed?

Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD) are related complex illnesses with a wide range of distressing symptoms. Acetylcholinesterase Inhibitors (AChEI) are commonly used medicines (brand names donepezil, rivastigmine and galantamine) that can help people with DLB and PDD by improving day to day functioning and thinking abilities.

Another drug which might help is **Memantine**. Memantine is a prescription drug used to treat moderate to severe confusion in Alzheimer's disease and may help to improve memory, awareness and the ability to perform daily functions. It is not clear if taking Memantine at the same time as an acetylcholinesterase inhibitor will help people with DLB/PDD. The safety and side effects of memantine are well known and the more common ones are described in this leaflet.

The COBALT trial aims to find out if adding Memantine to AChEI improves overall health and functioning for people with DLB or PDD.

We are looking for 150 patients with DLB and 150 patients with PDD, from across the UK to take part.

Why have I been invited to take part in the COBALT trial?

You have been invited because you support a friend or relative whose symptoms suggest they may have PDD or DLB, and they have been taking AChEI for at least 12 weeks. They are aged 50 or over and their clinical team and the local trial team think that they could be eligible to take part.

We are asking you to take part in the trial alongside your friend or relative to provide us with valuable information about them and about yourself.

Do I have to take part in the COBALT trial?

No, it is up to you to decide if you want to take part in the trial. If you agree to take part, you can change your mind and stop taking part in the trial at any time, without having to give a reason.

Given the current coronavirus pandemic, is it safe for me to take part?

We can reassure you that the trial will follow all recommended COVID-19 local and national guidelines. Most of the trial visits can be done from your friend/relative's own home if they are unable to or feel uncomfortable coming into the hospital. All required COVID-19 safeguards will be used. Your local trial team will be in touch with you before arranging any face-to-face visits which will then follow the most up to date guidance on social distancing. If you have any questions, at any time, about the COBALT trial and Coronavirus please speak to the local trial team. Their contact details are listed on page 11 of this information sheet.

What does taking part involve?

If you and your friend/relative would like to take part, you will both be invited to a consent and screening visit where a trial doctor will go through this information sheet, answer any questions you may have, and ask you to complete a consent form to confirm that you would like to take part in the COBALT trial. There will be some things that will need to be checked at the visit to make sure that your friend/relative can take part. More information about this can be found in the next section.

Consent and Screening Visit

This visit will take around 40 – 60 minutes and you can ask any questions you may have.

If you and your friend/relative would like to take part in the trial, you will be asked to come into the hospital or clinic together for an appointment. This visit may be able to be done at your or your friend/relative's home,– either in person or by video/phone call. The trial team will discuss the options with you when arranging the visit.

At the consent and screening visit a trial doctor will talk you through the trial and answer any questions you might have. If you would like to take part, you will be asked to confirm this by signing a consent form. After this, a trial doctor will do some checks to confirm that your relative/friend can take part in the trial. This will include looking through their medical history as well as asking some questions about their memory and symptoms and any medication that they take.

To decide whether your relative/friend can take part, the doctor will need to look at blood test results to review their liver function and kidney function. If they have had blood taken for these tests in the past 6 months, the doctor can review these results. If they have not had these tests done in the past 6 months, they will need to have a blood sample taken, so that these tests can be carried out to confirm that they can take part. Blood samples that are sent to the local hospital laboratory for analysis will be destroyed once a result has been confirmed in line with routine hospital practice. Blood samples that are sent to the local hospital laboratory for analysis will be destroyed once a result has been confirmed in line with routine hospital practice. The doctor will discuss this with you and your relative/friend.

If the doctor is happy that your relative/friend meets the criteria for COBALT, the trial doctor will confirm that they are 'eligible'. Being eligible means your relative/friend can take part in the trial, if they wish. After they have been confirmed as eligible to take part, a member of the local trial team will randomise your relative/friend to one of the two trial groups described on the next page.

On the basis of information provided by your friend/relative and also from their medical records, the local trial team will decide whether they are eligible for the COBALT dementia with Lewy bodies trial (COBALT-DLB) or the COBALT Parkinson's disease dementia trial (COBALT-PDD). In some cases, this diagnosis may be slightly different from the one given to them by their usual care team. For example, someone might have been told they have Lewy body dementia rather than Parkinson's disease dementia specifically. However, it is important to stress that we are only using these terms for the purpose of including your friend/relative in the appropriate trial, and the choice of term won't influence their involvement or the care that they receive.

If your relative/friend is not eligible to take part in the trial, you will not be able to take part and they will continue under the care of their usual care team outside of the trial.

If your friend/relative is eligible to take part, you will be given a copy of the consent form to keep and you and your friend/relative will share a unique ID number which will be used instead of your names on trial documents. Only the trial team and your friend/relatives usual care team will know this number links to you and your friend/relative.

With their permission, we will inform your relative/friend's GP that they are taking part in the COBALT trial. It will also be noted in their hospital medical records so that staff in the hospital know that they are taking part in the trial.

Randomisation

The trial randomisation is performed by a computer. The randomisation decides by chance if your friend/relative will receive the active or placebo trial medication, a bit like flipping a coin. A placebo is a dummy drug that looks the same as the real one but is a harmless substance that has no effects. They will have an equal chance of being in each group. They will be prescribed the trial medication for 52 weeks. The amount (dose) of trial medication will be increased gradually in the first 4 weeks of the trial until they reach their personal maximum dose, and this will be no more than 20mg.

Group 1: Placebo	**Group 2: Memantine**
If participant is put in group 1, they will be given the placebo trial medication. This is a 'dummy' drug. It looks exactly the same as the real drug but it is made with non-active ingredients.	If participant is put in group 2, they will be given the active trial medication, memantine. Only participants in this group will receive memantine.

- The group that your friend/relative is put into will be randomly picked by a computer. We call this randomisation. Your friend/relative's doctor and usual care team will not have any say in which group they are put into.

- To make it a fair comparison, you and your friend/relative won't know which group they are in, neither will their doctor, usual care team or COBALT trial team, unless there is a clinical reason or emergency that means this information is needed for their safety.

Trial Visits

You and your friend/relative will be interviewed by members of your local trial team using standardised questionnaires to measure various things, including their memory, symptoms, how you and your relative/friend are feeling and how they have used the healthcare system. These will be done at 3 timepoints during your participation in the trial: At the start (baseline), week 26 and week 52. These visits will take place at the hospital but may take place at your friend/relative's home if necessary.

Baseline Assessments

You and you friend/relative will be asked to attend a baseline visit. 'Baseline' means these are the first assessments and are done before your relative/friend starts taking their trial medication. The baseline visit will include the following:

- A brief physical examination
- Questions for your friend/relative (the participant) taking around 60 minutes
- Questionnaires relating to the participant completed with you, taking around 60 minutes
- Questionnaires completed by you (the trial partner), taking around 30 minutes

Breaks can be taken during the visit and if you or your friend/relative becomes tired, it will be possible to complete the assessments on another day.

Follow up assessments

You and your friend/relative will be asked to attend a follow up visit at week 26 (the middle) and week 52 (towards the end) of the trial.

- Your friend/relative will be asked some questions about their symptoms, along with a brief physical examination, taking around 120 minutes in total
- Your friend/relative will be asked to complete some questionnaires about how they are feeling, taking around 30 minutes – these can be done remotely by video or telephone call with help from you, their trial partner.
- You will be asked some questions relating to your friend/relative and about yourself taking around 25-75 minutes; - these can be done remotely by video or telephone call if needed.

Trial Calls

Your friend/relative will be contacted by phone/video call from the trial team at weeks 3, 8, 14 and 38 of the trial. This should take around 10-20 minutes

During each phone call your friend/relative will be asked questions which will include:

- if they have missed any doses of the trial medication.
- If they have been unwell at all or have experienced any possible side effects.
- If they have started any new medications or if they have had any changes made to their existing medications.
- If they have visited their GP or any other medical appointment.

They will be able to write these things in their participant diary to help you and them remember what has happened between trial calls. More details can be found on the next page about the participant diary.

End of trial call

A phone call will be made to your friend/relative at week 56 to record any side effects or other events they may have experienced since the week 52 visit. Following this call, their usual care team will be informed that they have finished the trial.

Optional long-term follow-up (24 months)

Your friend/relative will be asked if they would be willing for the local trial team to follow up on their progress 12 months after they have stopped the trial medication. This will either be by a review of their medical records or by speaking to you/them directly; whichever is preferred. This is to help us to understand the long-term outcomes for patients with DLB/PDD following treatment with memantine and is completely optional.
They will also be asked if you would be willing to have the local trial team have access to their medical records for up to 10 years after you have finished the trial to follow up how they are doing and what their current treatment is even further in the future.

Participant diary

Your friend/relative will be given a printed diary to complete. The dose that they should take will be noted on the diary and will be updated if the dose changes. We will ask them to document that they have taken their trial medication each day and if they miss a dose, why this was missed. We will also ask them to document any medications they might start taking or if there are any changes made to their existing medications. We would also like them to note any symptoms or medical events they have experienced (anything from headaches to breaking a bone) and if they have visited their GP or has any other medical appointment. The trial team will ask for this information at follow up visits and during trial calls, so the diary will help your friend/relative keep track. You may need to help your friend/relative to complete the diary.

Participant safety card

Your friend/relative will also be given a small card to carry which will include information on the trial and numbers that they can contact if they feel unwell. If your friend/relative attends **ANY** hospital or clinic for treatment outside of their scheduled appointments, they **MUST** give the doctor or other health care professional this card so that they know your friend/relative is taking part in the COBALT trial and so they can contact the local trial team if necessary.

Trial medication (Placebo or memantine)

When we talk about trial medication, this includes the placebo as well as the memantine. Your friend/relative will be prescribed doses of trial medication by the local trial team over a maximum time of 52 weeks. The trial medication will be either collected by you/them, or the local trial team may be able to arrange to have this delivered to them. A signature may be required for the delivery. The prescription of this trial medication is free of charge, but any other prescriptions for medications that your friend/relative is currently prescribed or may be prescribed during the trial, will be arranged and charged as they would be normally.

Trial medication should be kept in a safe place and out of the reach of children.

Your friend/relative will receive **four** lots of trial medication over the 52 weeks they are participating in the trial.

To enable their body to adjust to the trial medication your friend/relative will be prescribed a low dose of medication at first, which will gradually be increased over the first 4 weeks of the trial. They will be given instructions on how to increase the dose. Once they have reached their personal maximum

dose, which will be no more than 20mg, they will stay on this from week 5 to week 52, unless there is a medical reason this needs to change.

If your friend/relative feels unwell while taking the medication, they can contact the local trial team to discuss this at any point during the trial using the details on page 11 of this information sheet.

Collecting empty/left over packs of trial medication

Your friend/relative will be asked to return any empty or leftover packs of trial medication four times during the 52 weeks of the trial. This may be done either by dropping them off at their local hospital clinic or by arranging collection with your local trial team. The local trial team will discuss this with you and them.

Side Effects

As with any medicine, the medication used in this trial may cause side effects. Memantine is widely prescribed drug and is generally tolerated by most people. Some of the more commonly reported side effects include drowsiness, dizziness, balance problems, shortness of breath, constipation and headache. Memantine can have minor to moderate influence on the ability to drive and use machines; therefore if your friend/relative drives or operates machinery they should take special care if they continue to do this.

If your friend/relative experiences any of these side effects, they should let their local trial team know straight away. The local trial doctor can talk to you more about what these mean if you are unsure about any of them. The side effects experienced may only be temporary, but it is important that these are reported to the local trial team so that they can be monitored. Any side effects your friend/relative experiences should be recorded in the participant diary.

Bioresource volunteers

Bioresource Centres contribute to a national project to research common conditions, as well as rare diseases that are affecting people throughout England. Bioresource is seeking to understand the links between genes, the environment, health and disease including conditions such DLB and PDD so that new treatments can be developed. We would like to ask your friend/relative as part of participating in the COBALT trial, if they would be willing for someone from the Bioresource team to approach them to take part in the national Bioresource programme. As part of this some additional blood samples will be stored and used now and in the future to support health research including, for example, looking at what genes that might cause disease or make it worse with the aim of developing new treatments.

Giving permission to be approached by the Bioresource team is optional and your friend/relative can participate in the COBALT trial without having to give permission to be approached by the Bioresource team.

Personal information and postcode collection

The local research team will collect your friend/relatives demographic information including their date of birth, Sex at birth, ethnicity, years in education and education level reached. This will help us to find out if we are getting a mix of different people represented in the trial.

We would like to collect your relative/friend's postcode as part of the information that we record about them. This again will help us to find out if we are getting a mix of different people from different areas, and if where your friend/relative lives has any relation to their symptoms or response to the trial medication. Only the local team and the COBALT central database manager will be able to see their postcode. The postcode will only be used to identify the location where your friend/relative lives and will not be used to identify them by the central trial team.

Further Supporting Information

Will I receive any expenses or payments for participating?

You will not be paid for your participation in the COBALT trial. Your relative/friend will receive the trial medication free of charge and reasonable travel costs to attend face to face trial visits.

What happens when the COBALT trial stops?

At the end of the trial your relative/friend will continue with their standard clinical care. This may include taking memantine if their doctor thinks this is in their best interest and it can be arranged by their doctor. Your friend/relative may also choose to consent to allow the trial team to access their medical information for up to 10 years, to continue to follow up their treatment and clinical progress. Your friend/relative would not be required to attend any other trial visits if they consent to this, and their information would remain confidential and pseudonymised, which means that an ID number is used instead of their name. This is optional and whatever they choose will not affect the standard clinical care that they receive.

We hope that the results of this trial will help us say if memantine is helpful for patients with DLB and PDD. The results of the trial will be made available on the COBALT website (add website address) once the trial is finished.

What are the benefits of taking part?

We cannot promise the trial will help your relative/friend directly, but the information we get from this trial may help to improve the treatment for people with DLB and PDD. People who participate in research may gain significant satisfaction from contributing and the regular contact from the local trial team. If you want to find out more about taking part in research trials you can visit the NHS website here: www.nhs.uk/conditions/clinical-trials.

What are the possible disadvantages or risks of taking part?

You will be asked questions about your feelings, your life and about your friend/relative's symptoms and behaviour. The members of the local trial team are very experienced and carefully trained. They will make every effort to make sure you and your relative/friend feel supported and comfortable during the visits. They will check with you that you are happy to carry on but please remember that you can ask them to stop and take a break at any time.

We want your friend/relative to be safe in this trial at all times, but all medical treatments carry some risk. Memantine is used to treat patients with Alzheimer's Disease throughout the UK, and there are some known side effects, as listed on page 7 of this information sheet.

If your friend/relative does experience side effects of the trial medication, their local trial team will be able to discuss this with them and may be able to treat them to try to alleviate their symptoms. If their trial doctor or another medical professional treating them needs to find out which trial medication they are taking (memantine or placebo), this information is available in case of an emergency.

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

You can stop taking part (withdraw) at any time, for any reason and without giving a reason.

We ask if you are happy for us to record why you decided to withdraw from the trial.
If you withdraw from the trial, we will keep the information about you that we have already obtained and will use it to inform the results of the trial. Your friend/relative can withdraw from the trial medication and carry on completing the trial visits and calls or withdraw from the trial completely. Your friend/relative will be fully cared for and supported in line with their hospital's standard practice if they choose to withdraw.

What if there is a problem?

If you have a concern about any aspect of this trial, you can speak to a member of the trial team (this could be at the hospital or clinic, or one of the local trial team) who will do their best to answer your questions. Further contact details are included at the end of this information sheet. If you are still unhappy and want to raise your concerns with someone who is not directly involved in your friend/relatives care, you can contact <site to localise with local details such as PALS phone number and email address>

In the unlikely event that you or your friend/relative are harmed during the trial and this is due to someone's negligence (they were careless) you may have grounds for legal action and compensation, but you may need to meet your own legal costs. NHS Indemnity does not offer no-fault compensation (for harm that is not anyone's fault).

The Newcastle Clinical Trials Unit, part of Newcastle University, is managing the trial on behalf of the trial NHS sponsor. Newcastle University also has insurance arrangements in place to cover Newcastle University staff involved in designing and managing the COBALT trial.

What will happen to the results of the COBALT trial?

- The results will be published in medical journals and presented in meetings to other doctors, nurses, researchers, and patients.
- A report will be written for the trial funder.
- All trial data that is published will be anonymous. Your identity will always be protected.
- The results will be available at the end of the trial through publications, in the wider press, on the trial website, and directly to patient DLB/PDD groups e.g. via Dementia UK.

- Pseudonymised data will be made available to other researchers both within and outside the UK to help inform other research trials. While countries outside of the UK may not have data protection or privacy laws that offer participants the same level of protection as the laws within the UK, we will not share any data alongside yours or your friend/relatives name.
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Will my taking part in the COBALT trial be kept confidential?

Yes. All of the information collected will be entered on computers that are kept secure and password protected.

- You will be given a unique identification number instead of writing your name on trial documents which means that the documents and data will be pseudonymised. This number will be linked to your friend/relatives unique Identification number. The local trial team at the hospital/clinic will be able to link this number back to them using their date of birth, name and NHS/CHI number.
- Information with your ID number will only be shared with members of the central trial team, both in and outside of the UK. Your name will not be included with any information shared about you.
- Your contact details will never be shared with anyone else outside of the local trial team.
- You will not be named in any results, reports or anything on our website. Very occasionally, information might be given during the trial that we would have a legal obligation to pass on to others (for instance information which suggested your friend/relative or others were at risk of harm). In this case, we would have to act on this information by telling your friend/relatives doctor or others involved in their care. You and your friend/relative would be informed if this happens.
- The local trial team will have access to your contact information during the trial to organise trial visits.
- At the end of the trial, all trial information will be kept in a secure storage area (this is called archiving) for at least 10 years. This makes sure any queries about the running of the trial have been answered. All information will be held securely to make sure we protect your confidentiality, after which it will be safely destroyed.
- We will ask your permission for a copy of the completed consent form to be sent securely to the Newcastle Clinical Trials Unit (NCTU). This is so that the NCTU team can carry out planned checks of completed forms.

Who is organising and funding the COBALT trial?

The central trial doctor (also known as the 'Chief Investigator') is Professor John-Paul Taylor, who is a Consultant in Old Age Psychiatry and Professor of Translational Dementia Research. He is based in Newcastle upon Tyne. The central trial team also includes senior doctors and nurses, university experts in research trials and members of the public.

Trial sponsor: Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust. The COBALT trial is managed by the Newcastle Clinical Trials Unit on behalf of the sponsor.

Trial funder: The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (reference NIHR 129175). This body is funded by the UK government to carry out research for the benefit of the NHS and its patients.

Up to 25 UK trusts will be taking part in COBALT. Each trust will have a trial doctor, called a Principal Investigator (PI). The PI for your trust is Dr/Professor _____

Who has reviewed the COBALT trial?

The funder reviewed the trial plan as part of the application for funding. All research in the NHS is also looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by the East of England - Essex Research Ethics Committee.

A group made up of DLB and PDD patients, their relatives and caregivers, has also been involved in deciding how to carry out the COBALT trial. We also asked this group to consider what assessments we should include, and they have looked at the information sheets to make sure they are presented in a clear way, are easy to understand, and include all of the information required for you to decide whether you want to take part in the trial.

Who is providing the trial medication?

A company called ModePharma has provided the active trial medication (memantine) and made the placebo to match for this trial.

What if relevant new information becomes available?

If, during the course of the trial, new information becomes available that is relevant to you, we will tell you about it and discuss whether you should or would like to withdraw from the trial. If it is better for you to withdraw, you can do this without giving a reason. This will not affect the care that your friend/relative receives.

How will we use information about you?

We will need to use information provided by you for this research project.

This information will include your;

- Initials
- Name
- Contact details

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

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

While information you provide during the trial will be sent to Australia this will not include your initials, name or contact details. They must follow our rules about keeping your information safe.

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 you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from medical records. If you do not want this to happen, tell us and we will stop.
- We need to manage your research 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 you.

Where can you find out more about how your information is used?

You can find out more about how we use your information;

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.cntw.nhs.uk/about/research/
- by asking one of the research team
- by sending an email to the sponsors data protection officer at DPO@cntw.nhs.uk.

Thank you for taking the time to read this information sheet, and for your interest in the COBALT trial. Please see the local team contact details below.

[LOCAL CONTACT DETAILS