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) symptoms.
- We are hoping to recruit 300 patients in total in the UK
- If you meet the criteria and decide to take part, you will be randomly put into one of two trial medication groups: either the **placebo group** (a 'dummy' drug) or the **treatment group** (Memantine). You will have an equal chance of being in each group.
- Your trial doctor and the local trial team will not know which group you are part of or which trial medication you are taking during the trial.
- You will have planned visits and phone calls with the local trial team who will ask you questions about your symptoms, behaviours and how you feel while you are taking part in the trial.
- You will have a 'trial partner', who will be asked also to answer questions about you and about themselves.
- You will be asked to complete a participant diary to help track your medication use and if you feel unwell. Your trial partner can help you complete this.
- Your doctor and the 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 trial if you are interested in taking part and see page 13 for contact details

COBALT

PATIENT INFORMATION SHEET

Why is the COBALT Trial needed?

Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD) are 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 in this trial.

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

You have symptoms that suggest you may have PDD or DLB and have been taking AChEI for at least 12 weeks. You are aged 55 or over and your clinical and the local trial team think that you could be eligible to take part.

Do I have to take part in the COBALT trial?

No, it is entirely up to you to decide if you want to take part in the trial. If you choose not to, you will continue to get the normal (standard) treatment arranged by your doctor.

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. Your future care will not be affected in any way.

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 own home if you 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 follow the most up to date guidance on social distancing. If you have any questions, at

any time, about this trial and coronavirus please speak to your local trial team. Their contact details are listed on page 12 of this information sheet.

What does taking part involve?

If you would like to take part, you will be invited to a consent and screening visit where someone from the 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 you can take part. More information about this can be found in the next section.

You will need to ask someone to act as your 'trial partner' for the trial. This is someone who knows you well and can answer questions about your symptoms and progress. It should be a person who sees you regularly (at least once a week) and who is willing to take part with you in the trial and attend appointments with you. They can be a family member or friend or trusted carer, for example. We will also ask your trial partner questions about themselves and how they are feeling.

Consent and Screening Visit

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

If you would like to take part in the COBALT trial, you, and the person who you have asked to be your trial partner will be asked to come into the hospital or clinic for an appointment. This visit might be able to take place at your home, either in person or by video/phone call. The local trial team will discuss the options that are available to 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 you can take part in the trial. This will include looking through your medical history as well as asking you some questions about your memory and symptoms and any medication that you take.

To decide whether you can take part, the doctor will need to look at blood test results to review your liver function and kidney function. If you have had blood taken for these tests in the past 6 months, the doctor can review these results. If you have not had these tests done in the past 6 months, you will need to have a blood sample taken, so that these tests can be carried out to confirm that you 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. The doctor will discuss this with you.

If the doctor is happy that you meet the criteria for COBALT, they will confirm that you are 'eligible'. Being eligible means that you can take part in the trial if you wish. After you have been confirmed as eligible to take part, a member of the local trial team will randomise you to one of the two trial groups described below. The person you have asked to be your trial partner will also need to give their consent to take part.

On the basis of information provided by you and also from your medical records, the local trial team will decide whether you 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 you by your 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 purposes of including you in the appropriate trial, and the choice of term won't influence your involvement or the clinical care that you receive.

If you are not eligible to participate in COBALT, you will not be able to take part and will continue under the care of your usual care team.

If you are eligible to take part, you will be given a copy of the consent form to keep and a unique ID number which will be used instead of your name on trial documents. Only the local trial team and your usual care team will know this number links to you.

With your permission, we will inform your GP that you are taking part in the COBALT trial. It will also be noted in your hospital medical records so that staff in the hospital know you are taking part in the trial.

Randomisation

The trial randomisation is performed by a computer. The randomisation decides by chance if you 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. You will have an equal chance of being in each group. You will be prescribed 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 you are put in group 1, you 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 you are put in group 2, you will be given the active trial medication, memantine. Only patients in this group will receive memantine.

- The group that you are put into will be randomly picked by a computer. We call this randomisation. Your doctor and local care team will not have any say in which group you are put into.

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

Trial Visits

You and your trial partner will be interviewed by members of your local trial team using standardised questionnaires to measure various things, including your memory, symptoms, how you are feeling, and how you 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 in some cases may take place in your home if necessary.

If something is found during a medical examination or a trial visit that the trial team feel might need further investigation, they may pass this on to your usual care team to follow up with you.

Baseline Assessments

You will be asked to attend a baseline visit. 'Baseline' means these are your first assessments and are taken before you start taking your trial medication. It may be possible for this to take place in your home and/or to combine this with the screening visit. The baseline visit will include the following:

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

Breaks can be taken during the visit and if you become tired, it will be possible to complete the assessments on another day.

Follow up assessments

You will be asked to attend a follow up visit at week 26 (the middle) and week 52 (towards the end) of the trial. It may be possible for these to take place in your home.

- You will be asked questions about your symptoms, along with a brief physical examination, taking around 120 minutes in total.

- You will be asked to complete some questionnaires relating to you with support from your trial partner, taking around 30 minutes – these can be done remotely by video or telephone call.
- Your trial partner will be asked some questions relating to you and about themselves taking around 25-75 minutes; these can be done remotely by video or telephone call if needed.

Trial Calls

You will be contacted by phone/video call from the trial team at weeks 3, 8, 14 and 38 of the trial. These calls should take around 10-20 minutes. During each call you will be asked questions which will include:

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

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

End of trial phone call

You will be called at week 56, which is 4 weeks after you have stopped the trial medication, to record any side effects or other changes you may have experienced since the week 52 visit. Following this call, your usual care team will be informed that you have finished the trial.

Optional long-term follow-up (24 months)

You will be asked if you would be willing for the local trial team to follow up on your progress 12 months after you have stopped the trial medication. This will either be by a review of your medical records or by speaking to you directly; whichever you prefer. This is to help us understand the long-term outcomes for patients with DLB/PDD following treatment with memantine and is completely optional.

You will also be asked if you would be willing to have the local trial team have access to your medical records for up to 10 years after you have finished the trial to see how you are doing and what your current treatment is even further in the future.

Participant Diary

You will be given a paper diary to complete. The local trial team will write in here the dose of trial medication and you will update the diary to confirm that you have taken it each day and if you miss a dose, why this was missed. We will also ask you to document any medications

you might start taking or if there are any changes made to your existing medications. We would also like you to note any symptoms or medical events you have had (anything from headaches to breaking a bone) and if you have visited your GP or has any other medical appointment. The trial team will ask you for this information at follow up visits and during trial calls, so the diary will help you keep track. Your trial partner can help you to complete the diary. If there are any changes to the dose of trial medication that you receive, the local trial team will update the diary or may ask you to do this with help from your trial partner.

Participant safety card

You will also be given a small card that you must always carry for safety purposes. The card includes information on the trial and numbers that you can contact if you feel unwell. If you attend **ANY** hospital or clinic for treatment outside of your scheduled appointments you **MUST** give the doctor or other health care professional treating you this card so that they know you are taking part in the COBALT trial and so that they are able to 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. You will be prescribed doses of trial medication by the local trial team over a maximum time of 52 weeks. This will be either be collected by you or your local trial team may be able to arrange to have this delivered to you. You may be required to sign for any delivery. The trial medication prescription is free of charge for you, but any other prescriptions for medications that you are currently prescribed or may be prescribed during the trial, will be arranged, and charged to you as they would be normally.

You should keep your trial medication in a safe place and out of the reach of children.

You will receive **four** lots of trial medication over the 52 weeks you are participating in the trial.

To enable your body to adjust to the trial medication you will be prescribed a low dose of medication at first, which will gradually be increased over the first 4 weeks of the trial. You will be given instructions on how to increase your dose in the patient diary. Once you have reached your personal maximum dose, which will be no more than 20mg, you will stay on this from week 5 to week 52, unless there is a medical reason that this needs to change.

If you feel unwell while taking the medication, you can contact the trial team to discuss this at any point during the trial using the details on page 13 of this information sheet.

Collecting empty/left over packs of trial medication

You 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 your local hospital clinic or by arranging collection with your local trial team. The local trial team will discuss this with you.

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 you drive or operate machinery please take special care if you continue to do this.

If you experience any of these side effects, it is important that you let your 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 to report these to your local trial team so that they can be monitored. You can record any side effects that you experience in your 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 you, as part of participating in the COBALT trial, if you would be willing for someone from the Bioresource team (if this is available at your hospital) to approach you 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 <u>you can participate in the COBALT trial without having to give permission to be approached by the Bioresource team</u>.

Personal information and postcode collection

Your local research team will collect your demographic information. This will include your 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 postcode as part of the information we record about you. This again will help us to find out if we are getting a mix of different people from different areas, and if where you live has any relation to your symptoms or response to the trial medication.

Only the local team and the COBALT central database manager will be able to see your postcode. The postcode will only be used to identify the location where you live and will not be used to identify you by the central trial team.

Further Supporting Information

Will I receive any Expenses or payments?

You will not be paid for your participation in the COBALT trial, but reasonable travel expenses will be reimbursed. You will receive the trial medication free of charge.

What happens when the COBALT trial stops?

At the end of the trial, you will continue with your standard clinical care. This may include taking memantine, if you and your doctor think that this is in your best interest and can be arranged by your doctor. You may also choose to consent to allow the trial team to access your medical information for up to 10 years after you have finished taking part in the COBALT trial. We would like to continue to follow you up to find out what medications you are taking and how you are doing after you have finished the trial. You would not be required to attend any other trial visits and would not be contacted personally if you consent to this. Your information would remain confidential and pseudonymised, which means that an ID number is used instead of your name.

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 https://research.ncl.ac.uk/cobalttrial/ once the trial is finished.

What are the benefits of taking part?

We cannot promise the trial will help you directly, but the information we get from the COBALT trial may help to improve 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 in the COBALT trial?

We want you 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 you do experience side effects to the trial medication, the local trial team will be able to discuss this with you and may be able to treat you to try to alleviate your symptoms. If your trial doctor needs to find out which trial medication you are taking (memantine or placebo), this information is available in case of an emergency.

You will be asked questions about your feelings, your life, and your symptoms. The members of the local trial team carrying out the trial visits with you are very experienced and carefully trained. They will make every effort to make sure you 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.

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

You can withdraw from the trial medication and carry on completing the visits and calls or withdraw from the trial completely. You can withdraw at any time for any reason, without giving a reason. You will be fully cared for and supported in line with your hospital's standard practice if you chose to withdraw.

If you decide to withdraw from the trial completely, we will ask you to complete a form and confirm whether you would be happy for the local trial team to:

- continue collecting information about you until the end of the trial from your medical records, without the need for you to be contacted.
- 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.

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 your 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 care, you can contact <site to localise with local details such as PALS phone number and email address>

In the unlikely event that you 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.

Will my GP be informed?

Your GP will be told that you are taking part in this trial. They will be given a copy of this information leaflet. It will also be noted in your hospital medical records so that staff in the hospital know you are taking part in the 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 National Institute for Health Research (NIHR) who fund the COBALT trial.
- 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. 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 your name.

Will my taking part in this trial be kept confidential?

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

- You will be given a unique trial identification number instead of writing your name on trial documents which means that the documents and data will be pseudonymised. The local trial team at your hospital/clinic will be able to link this number back to you using your date of birth, name, and NHS/CHI number.
- Information that we have recorded about you, including information about any side effects or hospital visits you have while you are taking part in the COBALT Trial, will be shared with members of the central trial team, both in and outside of the UK with your ID number only (pseudonymised). Your name will not be shared with this information.
- Your name and address will be used by your local trial team if you choose to have your trial medication delivered to 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 you or others were at risk of harm). In this case, we would have to act on this information by telling your doctor or others involved in your care. You would be informed if this happens.
- The local trial team will have access to your contact information during the trial to organise trial visits as well as for ongoing safety. 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. This is optional and you can write on the consent form if you agree to this or not.
- We will ask your permission for sections of your medical record to be sent securely to the NCTU, if this is necessary. This is so that the NCTU team can review the trial data remotely, as part of the monitoring of the trial. The data transferred will be pseudonymised, redacted and relevant to the trial. This is optional and you can consent to this or not.

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.

The COBALT trial sponsor is Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust.

The trial funder is the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (trial reference NIHR129175). 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 NHS Trusts will be taking part in COBALT. Each Trust will have a local trial doctor, called a Principal Investigator (PI). The PI for your trust is Dr/Professor _____

Who has reviewed the 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 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 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 you receive.

How will we use information about you?

We will need to use information from you, from your medical records and your GP for this research project.

This information will include your;

- Initials
- NHS/CHI number
- Name
- DOB
- 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.

Some of your information will be sent to Australia but your name, NHS/CHI number, contact details and initials will not be sent. 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 trial team contact details on the next page.

[LOCAL CONTACT DETAILS]

Notes

Please use this page to make any notes you would like to ask the trial team/trial doctor.