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optimistic

PATIENT INFORMATION SHEET: OPTIMISTIC Trial

***O**bservational **P**rolonged **T**rial **i**n **M**yotonic Dystrophy type 1 to **I**mprove Quality of Life **S**tandards, a **T**arget **I**dentification **C**ollaboration*

We would like to invite you to participate in a research project called OPTIMISTIC which is collaboration between [local PI] and doctors and researchers in the UK, the Netherlands, Germany and France. Before you decide whether or not to participate, we need to be sure that you understand why we are doing the study, and what it would involve if you agreed to take part. Please take time to read this information carefully. On the last page of this leaflet you will find a space for 'My Questions' please use this space to write down any questions you may wish to ask your doctor, your research nurse or GP. We will do our best to explain and provide any further information you may ask for now or later. You do not have to make an immediate decision to participate if you are not ready.

Why have I been invited to participate in the OPTIMISTIC Trial?

You have been contacted because you have a rare neuromuscular disease, myotonic dystrophy type 1.

What is the purpose of this study?

Myotonic dystrophy type 1 is a progressive disease with typical symptoms which include progressive muscle weakness, daytime sleepiness and fatigue. There are no known medicines to treat the major symptoms of myotonic dystrophy type 1 with the exception of the drug Modafinil, which is sometimes used to help control excessive daytime sleepiness.

Our research group is a Europe-wide collaboration of myotonic dystrophy type 1 specialists including doctors, therapists and researchers. The OPTIMISTIC study is a randomised controlled trial that will use a unique personalised therapy attempting to reduce fatigue (this therapy will be called the "intervention"). We will compare the outcome of the group that received the intervention with those who did not. This is called the comparison or control group. The group you will be allocated to will be decided in a random way (a bit like tossing a coin, but done by a computer.) You will have a 50:50 chance of being part of the group receiving the therapy or the comparison group. Both groups will be carefully monitored throughout the study.

As with any chronic medical condition your partner, family, or other people close to you often provide essential care and support. In addition to your participation we would like, with your agreement, to invite someone who helps you deal with your myotonic dystrophy symptoms to participate in the study. We will give your partner/carer an information leaflet about the trial and if they wish to participate they will be asked to accompany you to the screening visit to sign a consent form. We will ask them to complete a few brief questionnaires when you attend for your study visit. The therapist will assist them on how they can support you and encourage you to achieve your personal goals. The therapy will also allow us to provide support and advice for your partner/carer. If you or your partner/carer does not wish to participate in this part of the study, you can still take part in the main study and in no way will this affect your future care or treatment.

The intervention will use cognitive behavioural therapy (CBT) to try to reduce levels of fatigue and improve your quality of life. This will be done using a range of different techniques, depending on your specific situation. The main focus will be to gradually increase your day to day activities. During the therapy sessions other issues may be addressed such as sleeping problems, problems you experience when starting activities, interaction with others, attitudes towards your fatigue and your disabilities or coping with pain. The intervention will be developed to meet your personal goals and abilities so will be different for everyone involved. CBT will only be provided for the duration of the study. A summary of CBT is given below.

If this study shows that the therapy benefits people with myotonic dystrophy, we hope to change clinical guidelines and practice so that care and management may be improved for people with myotonic dystrophy type 1, their carers and families.

Do I have to take part?

No. It is entirely up to you whether or not to take part. Participation in this study is entirely voluntary and you are free to withdraw from the study at any time without having to give a reason. This will not affect your future medical care or your relationship with medical or nursing staff looking after you. If you, your study doctor, or one of your clinicians decides you should withdraw from the study, we would like your permission to keep and analyse the data already collected.

What is Cognitive Behavioural Therapy?

Cognitive Behavioural Therapy (CBT) is a type of psychological therapy. According to CBT how a person thinks and what they do in response to problems is important. By changing your behaviour and way of thinking you can try to learn to manage or solve your problems. CBT is a coaching process that can help an individual to change unhelpful thoughts and behaviour. In order to change, a person must be actively involved in the therapy and practise with new ways of coping in daily life. Specific goals are set and the person and the therapist work together in reaching these goals. CBT has been successful in helping people with long term conditions particularly in relation to fatigue.
The trial will test if CBT can:

- Reduce fatigue experienced by myotonic dystrophy patients.

- Help people with myotonic dystrophy learn to compensate for problems in taking initiative or starting an activity, e.g. by learning to schedule activities.
- Improve relationships with significant others.

If you are randomised into the intervention groups and both you and your carer/partner agree, your carer/partner will be invited to attend parts of your CBT sessions.

What will happen to me if I take part?

There are a few things we need to check to see if you are eligible, but if you are and you want to take part then you will be put into one of two groups; either the intervention group or the comparison group. Which group you are in will be decided randomly by computer.

You will be asked to come to the myotonic dystrophy clinic in the Royal Victoria Infirmary Hospital for 5 to 12 visits over 17 months depending on which group you are assigned to. All travel expenses will be reimbursed. A study summary is given below.

Screening Visit (Visit 1) - 3 hours – Both Groups

At the first visit you and your carer/partner will have the opportunity to discuss the study in more detail and ask the study team any questions you or your carer may have. If you agree to take part you will be asked to sign a consent form explaining your participation. You will be given a copy of this along with this Participant Information Sheet for your records. A few simple tests will be performed at this time to assess your suitability to participate in the study.

At this visit we will:

- As you general questions about your health, activities and specifically about your condition
- Check your Age, height, weight and calculate your Body Mass Index (BMI)
- Ask you to complete 4 brief, simple questionnaires
- Ask you to complete the six minute walk test
    - This involves walking up and down a corridor for 6 minutes; we measure how far you can walk and how many times you need to rest and ask you to rate your perception of excretion during the walk.
- Check your genetic diagnosis
    - If you have not had a genetic diagnosis you will be referred to your clinic for a blood test.

If you are not eligible to take part in the study, we will explain why and you will not be required to attend for any further trial visits.

Baseline Visit (Visit 2)- 4 hours - Both Groups

At your next visit, the baseline visit we tell you if you are in the group receiving the therapy or in the comparison group. This will be randomly decided by a computer. At this visit all participants will be asked to:

- Fill in questionnaires about your physical status, quality of life and activity levels
- Do a 6 minute walk test (described above)
- Give a urine sample

Physical activity will be assessed using a piece of equipment called an actometer. This is a watch-like device that will be worn on your ankle. The device measures how active you are on a normal day. You will be asked to wear this device for fourteen consecutive days after the visit. It is waterproof and can be worn to shower and bath. It will be attached to your preferred ankle by a member of the study team and you will be shown how to remove it if necessary. You will be asked to return the actometer at the end of the test period in a stamped addressed envelope which will be provided by the study team. The data in the device will be analysed by special computer programmes when it is returned to the study team.

- Give a blood sample (30 mls, or about 2 tablespoons)

Some of the blood will be used to prepare a DNA sample. Myotonic dystrophy type 1 is caused by changes in the genetic material, DNA. The myotonic dystrophy gene is about the same length in most people. But, in people with myotonic dystrophy type 1, the gene is much longer. The gene can also become longer as a person with myotonic dystrophy gets older. As a general rule longer myotonic dystrophy genes are associated with earlier and more severe symptoms.

In this study we want to see if the way you respond to the therapy is affected by the length of your myotonic dystrophy gene. DNA will be prepared from the blood sample taken at this visit to determine the length of your myotonic dystrophy gene at the start of the study. We will also prepare a DNA sample from blood taken at your last visit. With your approval, we would also like to look at some of the DNA that was collected when you were first diagnosed.

It is likely that variation in other genes will also affect how severe your myotonic dystrophy symptoms are and how you respond to the intervention. We will also investigate this additional genetic variation by sequencing all of the DNA in your blood cells.

We will also use your blood and urine samples to measure specific chemicals known to be involved in muscle function and metabolism. As these will be taken before, during and at the end of the study we will be able to see any changes in the levels of these chemicals during the study.

If you are allocated to the intervention group an appointment will be arranged for your first CBT session.

What is the Intervention?

As part of the intervention you will have 10 months of contact with behavioural and exercise therapists, delivered over 10-14 sessions. The sessions will mostly be face to face but these can be carried out over the telephone or using the internet (SKYPE, Face Time) depending on your preference and internet access. These visits may also be arranged so the therapist can visit you and your carer at home. With your permission the interview sessions will be recorded (audio only). All the sessions will be tailored specifically to your needs. If your partner or carer has agreed to take part in the study they can also be involved in these sessions. The intervention will be different for every person involved but it may include some of the following activities:

- Improving your sleep patterns
- Learning how to start more activities
- Increasing your daily physical activity and other desired activities
- Discussing how you can change the way your symptoms affect you, e.g. pain and fatigue.
- Improving your relationships with others.

Each CBT session will last around 50 minutes and you will be asked to perform different activities at home. The trial team will remain in regular contact with you throughout the period of the intervention. You will be able to ask questions at any stage.

The information that we collect from the actometer (*ankle watch*) will help us create a plan to increase the amount of activity you undertake. This may involve a very small increase in activity, for example walking around the house more. If you are already quite active your plan might include cycling every day or going swimming more regularly. You will be given the opportunity to choose this for yourself in the therapy sessions.

Visit 3, 4 and 5 – Both Groups 4 hour visits.

At each visit we will ask you about your general health and the medication you are taking. The trial visits will happen independently of your routine clinic appointments.

- **Visit 3** is approximately 5 months after the baseline visit (visit 2), about half way through the study.
- **Visit 4 (4 hours):** is approximately 10 months after the baseline visit.
- **Visit 5** is approximately 16 months after the baseline visit and is the last study visit.

The following core activities will be performed at every visit.

- Asked to fill in the same questionnaires as at the baseline visit
- Complete the 6 minute walk test
- We will fit the actometer which will be worn for 14 days. You will be asked to return it using the envelope supplied by the study team.

In addition, at **visits 4 and 5** we will ask you to give blood and urine samples.

The last page of this leaflet has a diagram that explains how the visits work.

How does the study fit into my routine care?

We will not alter your medication or change any other treatment you receive in any way. You should continue to attend all medical appointments as normal. However, if you are taking an antidepressant or Ritalin and your GP or clinician increases the dose the study team will have to be informed as this may lead to you being withdrawn from the study. Your GP will be informed of your participation and will be asked to contact the trial team to discuss any changes to your medication.

What will happen to any blood and urine samples I give?

We will ask you to provide a urine sample. When we take blood we will take about 2 tablespoons, both samples will be stored and analysed at the end of the trial at the researcher's specialist laboratories. Some of samples will be sent to members of the study team in the Netherlands to look for unique molecules while some will be sent to members of the study team in Glasgow for DNA analysis. Your samples will be stored at the Newcastle MRC Centre Biobank for Neuromuscular Diseases using a barcode so you can not be identified.

If you agree, some of the blood sample you provide will be stored at the Newcastle Biobank for Research of Neuromuscular Disorders to be used in future research. The Newcastle Biobank stores blood under strict custodial guidelines (08/H0906/28+5) If we share your blood samples with other researchers, some of whom may be outside the European Union as your samples are labelled using a barcode you cannot be identified. All blood samples will be stored for up to 20 years. Any research using your blood samples will be subject to proper scientific and ethical review.

You will not receive the results of your study blood and urine tests.

Expenses and payments

You will not be paid to take part in this study but we will be able to reimburse for your travel expenses for coming to study visits.

What are the possible disadvantages and risks in taking part?

The additional visits to the muscular dystrophy centre or research facility may be inconvenient and having blood samples taken may be uncomfortable for some people.

You will be asked to complete questionnaires relating to different aspects of your symptoms for example; pain, fatigue and general well-being. The research nurse or therapist will be able to assist you to complete the questionnaires.

You will be asked to wear an actometer for a period of two weeks after each scheduled study visit. The actometer is a watch like device that will be fitted around your ankle by the trial staff. Initially this may feel a little unfamiliar but this will soon pass. This devise is often worn by sports men to monitor their training progress. You will be able to carry out all your usual daily

activities as normal. You will also receive instructions on how to remove it and post it back to the study team.

What are the side effects of any treatment received when taking part?

For those in the intervention group there may be a temporary increase in fatigue because of the exercise part of the therapy. This will be monitored by the research team.

What are the possible benefits of taking part in the study?

You will be monitored closely during the study by the study team. The tests we do will give us (and you) information about your general well-being. If any of these investigations reveal any new abnormality we will let you, your GP and clinicians know. The study may not immediately benefit you, but if the intervention is effective then this may improve the quality of care and management for people with myotonic dystrophy type 1 in the future. Further information and study progress will be available on the study's webpage; www.optimistic-dm.eu

What will happen to the results at the end of the study?

The results will be published in scientific journals, presented at conferences and may be used in guidelines to help doctors provide care to patients with myotonic dystrophy type 1. Study results will also be made available to you, patient organisations to publish in their newsletters and on their websites. You will not be identified in any publication of results.
In addition, we will also ask your permission for the research team to contact you in relation to future research you may be interested in. By giving permission to contact you, you are not giving consent to participate merely to be informed of other research projects.

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

Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw from the study at any time without having to give a reason and without this affecting your future medical care or your relationship with medical or nursing staff looking after you. If you, Dr [PI] or one of your clinicians decides you should withdraw from the study, we would like your permission to retain and analyse the data already collected, this will include any blood and urine samples you have given. We would also invite you and your carer to attend a withdrawal visit, this is optional. If you do attend a withdrawal visit, we would like to perform the measurements and activities scheduled at Visit 5. These will be prioritised incorporating you and your carers preferences.

Will my participation in the study be kept confidential?

Yes. All the information that is collected about you during the course of this study will be kept strictly confidential.

With your permission, the sessions you have with the therapist as part of the intervention may be taped (audio only, not video). The recording will be typed up verbatim and your name will

not be used on the tape or transcript. The tapes and transcripts will be kept in a locked cabinet and tapes will be destroyed 1 year after the study is completed.

At the end of the study the confidential records will be kept for 5 years and then destroyed.

The confidential handling, processing, storage and disposal of data are in accordance with the Data Protection Act 1998.

Will you inform my General Practitioner (GP)?

With your permission we will inform your GP of your participation, any relevant clinical results, and of any new medical problem we find as a result of your participation in the study.

What happens if something goes wrong?

If you have a complaint about your participation in the study you should first talk to a researcher involved in your care. You can ask to speak to a senior member of the research team or the Complaints Officer for Newcastle upon Tyne Hospitals NHS Foundation Trust at the Patient Relations Department on 0191 223 1382. In the event that something goes wrong and you are harmed during the study there are no special compensation arrangements**.** If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against the Newcastle upon Tyne Hospital NHS Foundation Trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate.)

If you feel that you have been treated unfairly throughout the research, or would like to comment on the conduct of any aspect of this research, please contact the Patient Advice and Liaison Service (PALS) 0800 0320202

Who is managing and funding this research?

The study has been organised by Dr Grainne Gorman and her colleague Professor Hanns Lochmuller at University of Newcastle and Newcastle upon Tyne Hospital NHS Foundation Trust. The study is funded by European Union Seventh Framework Programme.

Who has reviewed the study?

The North East England (Sunderland) Ethics Committee which has responsibility for scrutinising proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of medical ethics.

Contact Details

For additional information contact:

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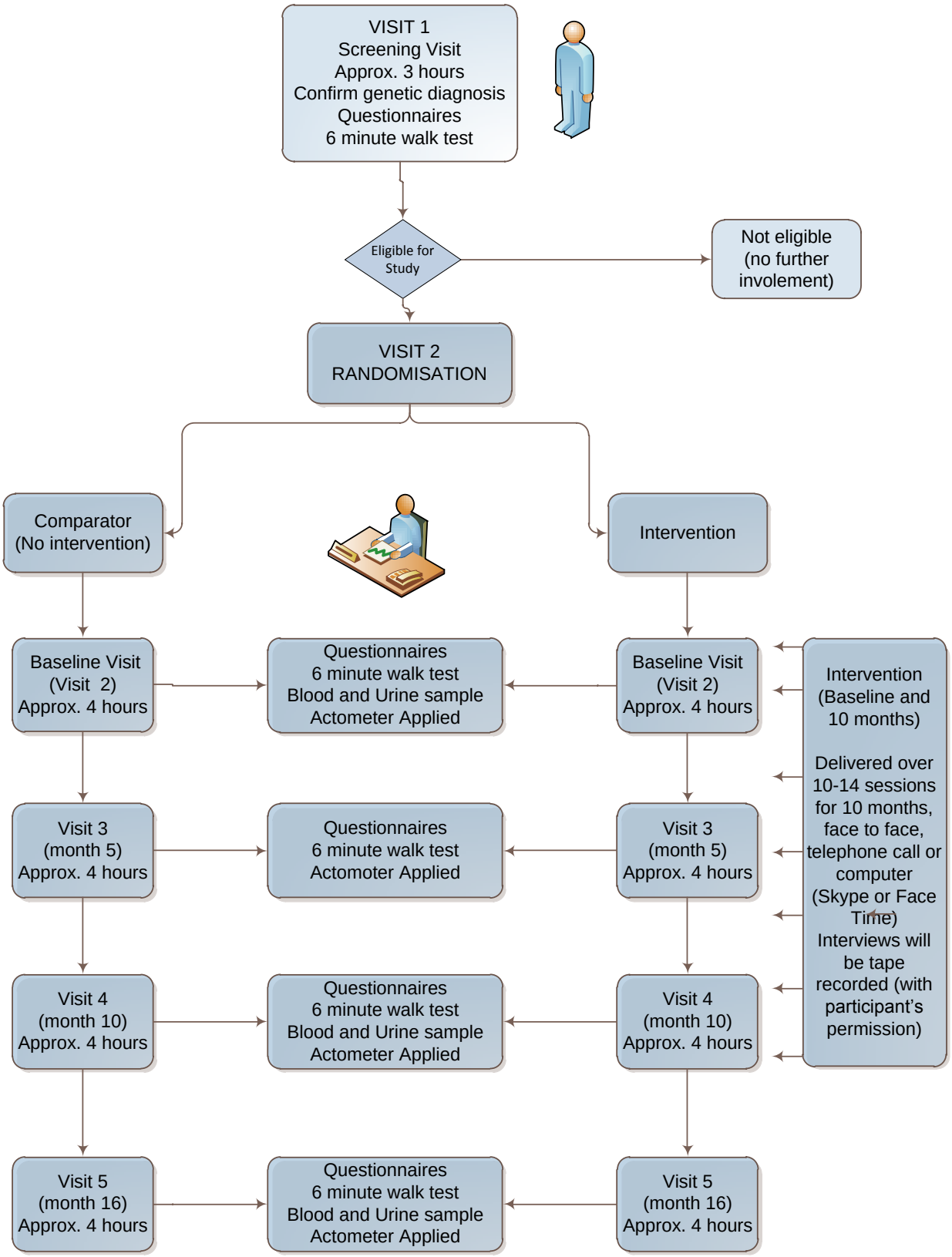
There is also more information on the OPTIMISTIC website: http://optimistic-dm.eu.

If during the study you become unwell or are concerned, contact NHS Direct if you are unwell and need urgent advice or assistance do not delay in seeking further advice or treatment as usual through the NHS services.

Thank you for reading this information sheet and considering taking part in this study.

OPTIMISTIC STUDY - VISIT SCHEDULE



My Questions