

**Duchenne Muscular Dystrophy: Double-Blind Randomized Trial to Find  
Optimum Steroid Regimen (FOR-DMD)**

**Participant Information Sheet for Parents**

**Study Chair:**

Robert C. Griggs, MD  
University of Rochester  
Department of Neurology  
265 Crittenden Blvd, CU 420669  
Rochester, NY 14642-0669

**Study Co-Chair:**

Kate Bushby, MD  
Institute of Genetic Medicine  
International Centre for Life  
Central Parkway  
Newcastle upon Tyne  
NE1 2BZ  
United Kingdom

**Site Investigator:**

<sup>1</sup>[NAME]  
[ADDRESS]  
[TELEPHONE #]  
[FAX #]  
[EMAIL ADDRESS]

**Introduction**

You are being asked to give consent for your child to take part in the FOR DMD study. Before you decide about taking part it is important for you and your child to understand why the research is being done and what it will involve. Please take time to read the following information carefully and ask the person who presents it any further questions you may have before making your decision about whether your child should take part. If you wish, you can talk with your family doctor or Specialist in DMD as well as your family and friends before you decide if you wish your child to participate. Your child also will receive an information sheet, written in child-friendly language, explaining the study. In that child's information sheet, we ask him to talk to you about the study and suggested he decides together with you whether he wants to take part.

This study will be registered on the internet with ClinicalTrials.gov. You can access this website to gain more information ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)).

Once we have answered all your questions, and if you decide that your child should take part in this study, we will ask you to sign a consent form, indicating that you agree for your child to participate. You will be given a signed copy of the consent form to keep. This form has important information and telephone numbers and you should keep this copy to refer to throughout the duration of the study.

---

### **What is the FOR DMD study?**

The FOR DMD (Finding Optimum Regimen Duchenne Muscular Dystrophy) research group, comprising doctors, other health professionals and scientists, is seeking to develop the best available dose of steroids to treat Duchenne muscular dystrophy. [INSERT NAME OF INSTITUTION] is conducting this study in co-operation with the United States National Institutes of Health (NIH).

As you will know, boys with Duchenne muscular dystrophy experience progressive muscle weakness as they grow up. Corticosteroids are currently the only medicine that has been shown to increase muscle strength in boys with DMD. Benefits include an increase in the length of time that boys could continue to walk, reduction in the development of curvature of the spine, a longer time of adequate breathing, and possible protection against the development of heart problems.

Doctors have tried different ways of prescribing corticosteroids in order to decrease undesirable side effects of the drug. However, no carefully controlled, long-term study has ever looked at the effects of different corticosteroids to see which one improves strength the most and which one causes the fewest side effects, over a period of time. Different doctors in different countries prescribe the drugs in different ways, and some do not prescribe corticosteroids at all.

The FOR DMD study aims to compare three ways of giving corticosteroids to boys with DMD to determine which increases muscle strength the most, and which causes the fewest side effects. Using the results of this study, we aim to provide patients and families with clearer information about the best way to take these drugs.

### **What are the medications that the FOR DMD study will use?**

The corticosteroids that will be used in this study are Prednisolone and Deflazacort. Both have been shown to benefit muscle strength in boys with DMD in previous studies.

This study will look at three ways of taking these corticosteroids by the mouth:

1. Prednisolone 0.75mg/kg/day
2. Prednisolone 0.75mg/kg/day switching between 10 days on and 10 days off treatment
3. Deflazacort 0.9mg/kg/day

All three dosages are commonly used in boys with Duchenne muscular dystrophy and have shown to be beneficial.

For this study, the steroids will be in the form of tablets. Participants will take between two and six tablets every morning, depending on their weight. Your child will be asked to take the study tablets orally with water or any other drink every morning, on a full stomach (after breakfast).

Your child will take the study medication he is randomly assigned to until the end of the study (for between 36 and 60 months).

The dosage of the study drug (number of tablets) your child will take may be adjusted according to his body weight at each visit. If your child experiences side effects due to the study drug, the study doctor may decide to interrupt or reduce the study drug that your child is receiving. In this case the study doctor will give you detailed instructions on the new amount of study drug to be taken by your child.

### **Why have you asked my child to take part?**

Your child is being asked to participate in this study because he has Duchenne muscular dystrophy (DMD), he is the correct age and he is attending one of the DMD clinics at a hospital that is taking part in this study. We aim to recruit 300 boys with DMD to take part, across 40 sites in five countries.

### **Does my child have to take part?**

Participating in this study is voluntary and therefore it is up to you and your child to decide if you want your child to take part in this study or not. If you decide that your child should take part in this study, you will be asked to sign a consent form, indicating that you agree for your child to participate. In addition, your child will be also asked to sign an assent form.

If you decide that you do not wish your child to take part in this study, your child's future treatment will not be affected and you can discuss medical care options with the study doctor. Your child is also free to leave the study at any time without giving a reason. This will not affect the standard of care that your child receives.

### **What is a multi-centre, double blind, randomised trial?**

FOR DMD is a multi-centre, double-blind study.

It is a '**multi-centre**' study as it is being run in a number of different hospitals.

In research it is known that people sometimes report that they are feeling better if they know that they are being given a certain treatment that they believe will work for them. Research has also shown that results can be influenced if the doctor or researcher believes that a medication they give a study participant is better than another. This causes a problem for study results as it is impossible to say whether a treatment really did work or not. The best way to solve this problem and to maintain the highest standards of research is to ensure that neither the people taking the study medication nor their doctors know which treatment they are on. This type of research is called a '**double blind**' study, ie both participants and researchers are 'blind' to the medication taken.

When we do not know the best treatment, we need to compare different approaches. For the comparison to be fair, we need to make sure that there is no difference between the people in the groups that are being compared. We do this by putting people into groups at **random** – like tossing a coin or throwing a dice - rather than by choice. In the case of FOR DMD, a central computer is used to decide which group participants are put into.

Your child will have a one in three chance of taking any of the study dosages. In this study there is no placebo group, which means that all participants will receive active drugs (Prednisolone or Deflazacort). However, to be sure that boys who fall in a similar weight range but are on different study medications or dosages all take a similar number of tablets, some of the tablets will be placebo tablets. A placebo is a dummy drug that looks like the study drug but contains no active medication. The tablets will look exactly the same and no one will know which treatment group they are in. Therefore, all of the tablets your child takes may contain active study drug, or some may contain study drug and some may be placebo.

## **What will happen if I agree my child will take part and what tests will he receive?**

### **Screening:**

If your child appears to be eligible and if you agree that he should participate in the study, we will ask you and your child to attend for a screening visit.

During the screening visit, the study will be explained to you and your child in detail and you will be asked to give written consent or permission for your child to participate. If your child is old enough, and with your permission, he will also be asked to give his permission by signing an assent form.

The screening visit will take between four and five hours and will allow the study doctors to review the health status of your child carefully, to ensure that he meets all the necessary requirements to participate in this study. This may take more than one visit, so the overall screening process will take between one and three months.

At the screening visit, your child will be asked to swallow some dummy tablets (no active drug) to make sure that he is able to swallow the study medication without problems. If you wish, you can have some more dummy tablets so that he can try this at home, too, to make sure that you are happy that he is able to.

The following tests will be carried out:

- Physical examination and vital signs (height, weight, waist circumference, blood pressure, pulse)
- Medical history including assessment of exposure to specific illnesses (chicken pox, tuberculosis)
- Medication history
- Current medications, vitamins and supplements
- Blood sample for routine laboratory tests, vitamin D and bone markers. An anaesthetic cream might be applied around your child's forearms to make the area numb and reduce discomfort
- Urine sample collection for analysis
- Motor skills test (jumping, hopping, time to stand from lying etc)
- Six-minute walk test (6MWT). The study staff will ask your child to walk back and forth between markers on the floor in order to see how far he can go in six minutes
- Examination of ankle joint range of motion by a Physiotherapist
- Physiotherapy assessment and advice
- Lung capacity test. The study staff will ask your child to blow as hard as he can into a tube
- Eye test for cataracts (a clouding of part of the eye called the lens)
- Full-body DEXA scan (x-ray) for bone and muscle mass. Your child will be asked to lie still for up to 10 minutes while the DEXA machine scans his body. In addition to the information about lean and fat tissue, we will obtain information about your child's bone density. This information can tell us if he is at high risk of bone fractures.
- X-ray of wrist to give information on growth and physical development
- Heart function tests – electrocardiogram and echocardiogram. For the electrocardiogram, 12 electrodes will be placed on the skin of your child's chest. For the echocardiogram, the technician will use a microphone device that makes and receives sound waves. This test will be performed to check the size and shape of your child's heart.

Most of these procedures are part of the current care recommendations in DMD and therefore you and your child should be familiar with them. If you do not know some of these tests or you have any questions about specific study procedures, please ask the study doctor.

When screening procedures are completed and your child has been confirmed as eligible for the study, your child will randomly (by chance) be assigned to one of the three study drug treatments described above. Your child's study drug will be ordered and you will be asked to come back for a baseline visit. No one (not the study doctor, you or your child) will know which of the three drug dosages your child is receiving (the study is 'double-blind'). However, if the study doctor needs to know your child's treatment group in an emergency, he or she can find out.

### **Baseline Visit:**

At the baseline visit, your child will be enrolled in the study. This visit will take between three and four hours.

The following tests will be carried out:

- Physical examination and vital signs (height, weight, waist circumference, blood pressure, pulse)
- Current medications
- Urine sample for analysis
- Motor skills test (jumping, hopping, time to stand from lying etc)
- Six-minute walk test
- Ankle joint examination by a Physiotherapist
- Physiotherapy assessment and advice
- Lung capacity test
- Examination of face and upper body for swelling (side effect of corticosteroids)
- Review of diet and behaviour
- Quality of Life questionnaire completion (PedsQL questionnaires). You and your child (if he is able) will be asked to complete a questionnaire asking about your child's quality of life. This questionnaire will take up to 10 minutes for each of you to complete.
- Behavioural questionnaire completion. We will ask you to complete four questionnaires about your child's behaviour (PARS-III, Iowa Conners, Strengths and Difficulties questionnaires and Revised Rutter Scale).

At the end of the baseline visit, the study doctor will provide you with the study drug and will explain to you how and when your child should start taking the study drug. Your child will take the study medication he is randomly assigned to until the end of the study (up to 60 months).

### **Study Visits:**

Once the baseline visit is completed and your child begins taking the study drug, he will be asked to return for a visit three months later. Visits will then be scheduled every six months for a minimum of 36 months (six more visits) up to a maximum of 60 months (10 more visits), depending on how early your child begins the study. The number of six-month visits varies because every child in the study will be asked to continue taking the study drug until all participants (approximately 300 boys) complete the 36 months of treatment period. Thus, children who start earlier will have more visits than those who start later in the study.

The evaluations in this study will be carried out as part of your child's standard care for Duchenne muscular dystrophy but will also be part of the study protocol and follow-up. Both medical care and research will be carried out at the same visit. This

means that if your child is taking part in the study, he will not need to attend further clinical appointments for his DMD follow-up.

At each visit, the dosage of the study drug (number of tablets) your child will take may be adjusted according to his body weight. If your child experiences side effects due to the study drug, the study doctor may decide to interrupt or reduce the study drug that your child is receiving. In this case the study doctor will give you detailed instructions on the new amount of study drug to be taken by your child.

At the end of each visit, the study doctor will order the adjusted dosage of the study drug and the new supply will be shipped directly to your home a few days after each study visit. You will be provided with study drug to be continued until the new supply arrives to your home. You will be asked to confirm with the study staff as soon as the new study drug supply has arrived at your home. The study staff will instruct you to start the study drug from the new supply only when no tablets will be left in the wallets your child is using from the old supply.

You will be also asked to return all used and unused study drug wallets to study staff at each visit during the study.

#### Three-month Follow-up Visit:

This visit will take between two and three hours. All tests that were carried out at the baseline visit will be repeated. In addition, you will be asked to fill out a Treatment Satisfaction Questionnaire, indicating how satisfied you are with your child's treatment. Your child's study medication will be reviewed and his dosage may be adjusted based on his weight or if he has experienced any side effects. Any changes will be explained to you. The doctor will arrange for more study medication to be sent to you.

#### Six-month Follow-up Visits at six, 12, 18, 24, 30, 36, 42, 48 and 60 months:

These visits will take between two and three hours. These visits will be exactly the same as the three-month follow-up visit.

#### Additional evaluations:

Additional tests will be performed at some visits. These visits might therefore take longer and/or be in a different place and/or on a different day to your study visit.

Each year, starting at the 12-month visit, the following tests will also be carried out:

- Eye test
- Blood sample for routine laboratory tests, Vitamin D levels and bone markers
- Urine sample collection for analysis
- Full-body DEXA scan (x-ray) for bone and muscle mass
- Quality of Life questionnaire completion

The heart function tests carried out at the baseline visit will be repeated every two years until your child is ten years old, and then yearly after that (beginning at the two-year (24 month) visit) as per standard care.

#### Three-year (36-month) Follow-up Visit:

At the three-year follow-up visit, in addition to the procedures described above for the six-month visit, your child will have x-rays of his spine and wrist to monitor his bone health and his growth. You will be asked which treatment and regime you think your child has been on during the study.

These procedures take approximately 30 minutes in total to perform and may take place in a different location and/or on a different day to your study visits.

#### Between visits phone calls:

For the first six months following baseline visit, the study doctor or the study coordinator will call your home once a month between visits to see if your child is feeling well and is taking the study medication, and to see whether you or he has any concerns. Thereafter, the study doctor will call you every three months.

A final telephone call will be made by the study doctor or the study coordinator 30 days after your child's final visit, to follow up on any adverse effects your child may have experienced (see Table 2).

#### Video monitoring:

During some study visits, the doctor will ask to film your child with a video camera during his function tests, six-minute walk test, muscle strength tests and North Star Ambulatory assessment. This recording will be used to ensure that assessments are being performed reliably. The recordings will be treated confidentially, like all other data collected in the study, and will only be viewed by members of staff working on this study. Your and your child's permission for video monitoring will be sought each time. You do not have to agree, and your child can still participate in the study if you do not give permission for the video monitoring.

#### Biobanking:

An optional part of the FOR DMD study involves the collection of blood samples for 'biobanking'. The EuroBioBank ([www.eurobiobank.org](http://www.eurobiobank.org)) is a European network of 'banks' that store biological material (eg blood) from patients with rare diseases for research.

Giving samples for 'biobanking' requires your specific consent, and additional collection of blood from your child at screening visit and annually thereafter. Blood samples for biobanking will be collected with the other blood samples for the study, so no additional blood draw is required. Blood samples will be collected for serum and plasma and to extract DNA and RNA. These samples will be stored in the MRC Neuromuscular Centre BioBank in Newcastle upon Tyne, UK for use in approved research projects in the future. Researchers wishing to use samples from the EuroBioBank must obtain approval from the MRC BioBank Committee. Further information will be provided in a separate information sheet for 'biobanking'.

Giving the blood samples for 'biobanking' is optional, and your child is allowed to participate in the study if you do not agree to give blood samples for 'biobanking'.

#### **Will I need to have any tests during the study?**

Only the boys taking part in the study will have the clinical tests described above but we will ask you to complete questionnaires on quality of life, treatment satisfaction and your child's behaviour and mood.

#### **How long will the study last?**

The overall time that your child will stay in this study will depend on when he is enrolled within the study timeline. He will be in the study a minimum of 36 months (three years) if he is recruited toward the end of the study and a maximum of 60 months (five years) if he is recruited very early in the course of the study. Children who are enrolled and complete the three years of treatment first will continue the study drug until all participants finish the 36-month treatment period.

The end of the study will be 30 days after your child's final visit, when a telephone call will be made by the study doctor or the study co-ordinator to follow up on any adverse effects your child may have experienced.

### **Other medications**

During screening, you should inform the study staff of all prescription and non-prescription drugs, supplements, vitamins and health foods that your child is taking. Live vaccines should not be administered in patients taking corticosteroids and non-steroidal anti-inflammatories should be avoided. There are no other specific restrictions on the medications your child can take during this study; however, other medication may interact with corticosteroids. Therefore, it is important that you discuss with the study doctor any medication your child has been prescribed and inform the study doctor as soon as possible if your child starts a new medication (prescribed or over-the-counter) or there are any changes to the doses of his current medications.

If your child is on dietary supplements, the dose of the supplement should stay the same throughout the study.

### **What are the risks of taking part in the study?**

We want your child to be safe in the study at all times, but all medical treatments carry some risk. The major risks of participating in this study involve the possible side effects of corticosteroids. Most of these side effects are very well known and will be monitored carefully throughout the study. Your child may experience some or all of the side effects listed below. Some of these side effects may be reversible but each person's reaction is different. The study doctor will discuss this with you. For example, corticosteroids can cause your child to gain weight and his face to appear puffy. They can also cause bones to break more easily and slow growth (height restriction). Your child's behaviour may change and he may become more emotional and irritable and any existing behavioural problems may change (they may get worse or they may improve). Other possible side effects include increased blood pressure, upset stomach, development of eye cataracts and a weakened immune system (more likely to catch an infectious disease). There may be changes in the skin such as excessive hair growth, acne and easy bruising.

It is impossible to say how someone will feel taking the study medication because people react differently. If your child becomes unwell or has an adverse reaction to the study drug, the study doctor will be able to make changes to it and will advise you on management and treatment. An "I am on steroids" card will also be given to you to show to doctors in case of emergencies. Although the card will not say which corticosteroids your child is receiving, the maximum dose of steroids that the child might take according to his weight band will be recorded on the card, so that it will be informative in the case of medical emergencies.

Stopping corticosteroid treatment suddenly can be dangerous and might cause symptoms such as abdominal pains, diarrhea, vomiting, muscle weakness and fatigue, extremely low blood pressure, kidney dysfunction, or changes in mood and personality due to adrenal failure. If your child does not take the study drug for any reason, you should contact the study doctor as soon as possible for advice. If it becomes necessary for your child to stop taking the study medication, the study doctor will provide advice on how to do so safely.

During the collection of blood samples, your child may experience pain and/or bruising at the place on the arm where blood is taken. An anaesthetic cream will be applied to your child's arm to make the area numb and reduce discomfort. Rarely, a



clot may form and infections occur where the blood is taken, or your child may faint. Study staff will be able to help if this happens.

During the x-ray of his wrist and back, and the DEXA (bone and muscle) scan, your child will be exposed to a small amount of radiation, which in the context of natural exposure is of no significant additional risk. There may be some minor discomfort from lying in the same position for up to 10 minutes while having the DEXA scan.

The tablets used in this study are FOR USE BY RESEARCH PARTICIPANTS ONLY. Please take care to keep them out of the reach of children or people who have trouble reading or understanding written directions. Use of the study medicine by persons who have not been carefully screened could be dangerous. It is important that you inform the study doctor if your child has any medical symptoms or problems during his participation in the study, even if they are mild or you do not think that they are related to the study drug.

Please call the study doctor if your child has any symptoms or you have concerns or questions.

**Are there benefits to taking part in the study?**

There may be no direct benefit from taking part in this study. However, the potential benefits to your child from being in this study include evaluations and close monitoring by a muscle disease specialist.

The knowledge gained from this study may help in the future treatment of Duchenne muscular dystrophy, but this may not be of direct benefit to you/your child.

**What other options are there?**

You and your child do not have to participate in this study. Your child can be prescribed prednisolone or deflazacort without participating in this study. If your child does not participate in this study it will not make any difference to his current or future medical care.

You can also discuss with the study doctor other treatment or clinical trials which might be or become available. If you would like to enrol your child in another study during the course of your child's participation in the FOR DMD trial, please tell the study doctor of your plans. Your study doctor will be able to advise you on what to do if you wish your child to participate in another trial.

**What if new information becomes available?**

Sometimes during the course of a study new information becomes available. We will inform you of any new findings developed during the course of the study that may affect your or your child's willingness to participate in this study.

**What happens when the research stops?**

Both of the drugs that we are investigating are available on prescription and will continue to be available after the research is over. Your doctor will discuss with you the medication to be prescribed to your child at the end of the study treatment period or when the research stops for any other reason.

At the end of the study, we may perform additional long-term follow up studies and you and your child might be asked if you would be willing to participate. These additional follow up studies would require additional consent from you.

### **What happens to the results of the study?**

When we have answers to the questions in the study, we will use this information to give all patients the best possible treatment. The results of this study will be provided to you in language that you will be able to understand. The results will also be published in medical journals, which are read by doctors, and presented at conferences to be shared with other healthcare professionals, families with DMD boys and people and organisations that work with boys with DMD. They will also be sent to the organisation that funded the research, in a full report.

### **Does my child have to stay in the study?**

No. Your child is free not to take part, or to leave the study at any time without giving a reason and this will not affect the care he receives now or in the future.

He can stop taking the study medication but continue the follow-up and come to each visit until the end of the study to provide follow-up data (withdrawing partially). Or he can decide to stop both the study medication and follow-up visits (withdrawing completely). If you do not wish to continue follow-up visits, you and your child will be asked to return for a final visit. At this visit, the study doctor will ask your child to perform some tests as planned for the three-year follow-up visit.

If you decide that you wish your child to withdraw completely from the study, we would like to retain any data collected up to the point of withdrawal, for our research. You can also decide to stop the study for your child if he is going to take part in another clinical trial. Just tell someone on the study staff that you wish to withdraw your child from the study, and they will tell you what to do.

If your child withdraws from the study, for any reason, he will no longer receive the FOR DMD study drug; however, he could continue corticosteroids (Prednisolone or Deflazacort) under prescription by your clinician.

Please note: in all cases, the study drug should not be stopped suddenly. If the study drug has to be stopped, for any reason, the study doctor will give you instructions about how to discontinue it.

### **Are there other circumstances for withdrawal?**

The study doctor may decide that it is in the best interest of your child to stop taking part in the study. He or she will explain the reasons for this and arrange for your child's routine care to continue.

Your child may be withdrawn from the study if he is unable to follow the study doctor's directions or if his medical condition changes so that staying in the study may be of risk to his health. The appropriate regulatory agencies could discontinue the study if the safety of participants is found to be at risk. If the study is stopped, we will let you know about this and your child will have a final examination to ensure that this health has not been affected. You will also be told how to stop the study medication safely.

### **What are the costs to participate, and what about expenses and payments?**

The study medicine will be provided at no cost to you and your child while he takes part in this study. Most of the study tests are part of current standards of care for your child, so he would need them whether or not he was taking part in the study and they are covered by the National Health Service (NHS). The other study procedures will also be provided free of charge.

Neither you nor your child will receive payment or reimbursement of expenses for taking part in this study.

### **Will anyone else know my child and I are in this study?**

We will keep your and your child's details and study information confidentially. Only key people who have a need or right to know will know that you are in the study. The study is being overseen by the Newcastle Clinical Trials Unit (NCTU), which is part of Newcastle University. An authorised person from the NCTU will look at some parts of your child's medical records and the data collected during the study. The study data and your child's medical records may also be looked at by representatives of regulatory authorities and by authorised people from the hospitals taking part in the study, to check that the study is being carried out correctly. All will have a duty of confidentiality to you and your child as research participants – this means that they will not tell anyone outside of the study about you or your child. We will all do our best to meet this duty.

With your permission, we will let your child's GP, and other healthcare professionals involved in his care, know that he is taking part in the study.

### **Who is organising and funding the research?**

This study is funded by the National Institutes of Health (NIH) National Institute for Neurological Disorders and Stroke (NINDS), in the United States of America (USA). The University of Rochester (USA) and Newcastle University (UK) are co-ordinating the study in collaboration with a number of hospitals across the UK, Europe, USA and Canada.

### **What happen if my child gets hurt taking part in this study?**

There are no special compensation arrangements in the event that something goes wrong and your child is harmed during the research study. Newcastle University has insurance cover for negligent harm. NHS bodies have insurance for clinical negligence for people under their care. If your child is harmed and this is due to someone's negligence, you may have grounds for legal action for compensation against Newcastle University or the NHS (their employer). The normal NHS complaints mechanisms will still be available to you.

Please contact a member of study staff at the site if your child has any injury during this study that is related to the research.

### **What if there is a problem?**

Any complaint about how you have been treated during the study or any possible harm you might suffer will be addressed. If you have a concern about any aspect of this study, you should ask to speak to the study doctor who will do his or her best to answer your questions.

If you are still unhappy and wish to complain formally, you can do so through the hospital's procedure Patients Complaints Service (PALS) 0800 0320202

### **Who has reviewed the study?**

All research studies are reviewed by an independent Research Ethics Committee to protect you and your child's safety, rights, wellbeing and dignity. This study has been reviewed and approved by South Central – Southampton Research Ethics Committee B.

### **What if I have any more questions?**

If you have any questions about this study, please ask the study doctor or call: [NAME AND PHONE NUMBER OF CONTACT PERSON FOR STUDY INFORMATION].