Guy's and St Thomas' NHS
NHS Foundation Trust

EvelinaLondon

PARENT/GUARDIAN INFORMATION LEAFLET

ADAPT (Atopic Dermatitis Anti-IgE (omalizumab/Xolair) Paediatric Trial)

Your child is being invited to take part in a research study. Before you decide whether you wish your child to take part, it is important for you to understand why the research is being carried out and what it will involve. Please take your time to read through the following information carefully and discuss it with others if you wish. Please ask us if anything is unclear or if you would like more information.

WHAT IS THE PURPOSE OF THE STUDY?

Up to 1 child in 5 has eczema. Many of these children are successfully treated by creams or medicines. However, a small number of these children have such severe eczema that the available medicines are unable to control their eczema. Other children have side effects from the medication, so that they cannot continue to take it.
The purpose of the study is to see if a new medication, Xolair (also known as omalizumab or anti-IgE), can help children with severe eczema, who have not responded to other available treatments.

WHY HAS MY CHILD BEEN INVITED?

Your child has been invited to take part because he/she has severe eczema which has not responded to routine treatment, because they have had side effects from treatment, or because there are good reasons why they cannot take it. 62 children will be chosen to take part in this study at one site in the UK.

DOES MY CHILD HAVE TO TAKE PART?

Your child does not have to take part in this study. You and your child are free to withdraw your consent and stop participating in this study at any time. If you decide not to take part, or if you decide to withdraw from the study, your child's regular treatment and medical care will not be affected in any way.

WHAT WILL HAPPEN TO MY CHILD IF HE/SHE TAKES PART?

This type of study is known as a randomised study. As we do not always know which way of treating patients is best, we need to make comparisons. All children who decide to take part in this study will be put into one of two groups. Children in each group will then have a different treatment, and the two groups will be compared. The chance of your child being in each of the two groups is 50% (the same as if a coin was tossed).
As we do not know if Xolair is the best way to treat eczema, we will compare it to a placebo or dummy treatment, which does not contain any active treatment. Children will therefore be randomised into one of two different groups:
Group 1 – Participants will receive Xolair 1-2 times a month.
Group 2 – Participants will receive a placebo treatment 1-2 times a month.

Duration of the study
Children will be enrolled between the ages of 4-19 years. After a run-in period, the treatment will take place over 6 months and further monitoring will occur for a further 6 months.

Clinic/ward visits:
There will be a screening visit followed by a baseline and randomisation visit. This will be followed by visits once or twice a month, over a period of 6 months, to receive the treatment. 3 further visits will take place after this, at 24 weeks, then 3 months and 6 months after the last treatment visit.

Duration of visits:
The pre-screening and screening visits will take 2-3 hours. After the first 3 doses of treatment, your child will have to remain for observation for 2 hours. After subsequent doses, they will be observed for 30 minutes. Once treatment has been completed, the visits at 24 weeks, and then 3 and 6 months later will take approximately 2 hours.
You will be given specific appointments for the visits at mutually convenient times. Reasonable public transport costs will be covered by the study.

What exactly will happen?
At the screening visit, your child will be assessed. If he/she is suitable, your child will be randomised (i.e. assigned by a computerised system), into one of the 2 groups described above. All children will have the following procedures performed at their study visits:

- We will obtain a history of their eczema, how it is treated now, and how it has been treated in the past. We will find out about any side effects they may have had from their treatment.
- We will assess your child for signs of asthma, rhinitis (hayfever-type symptoms) and food allergies. This will involve asking you some questions and examining your child. This would be performed as part of a normal allergy assessment. We will also find out what other medication they are taking.
- A basic medical examination including measurement of height and weight and vital signs (temperature, pulse blood pressure for example), together with an assessment of their eczema.
- Skin prick tests to assess for allergies to foods and environmental factors. This involves a small amount of the allergen being placed onto the skin and then pricked through the top layers of skin with a lancet (it does not draw blood). If your child is allergic to any of the allergens being tested a small bump (hive) will develop within 5-15 minutes. This disappears after about 30 minutes.
- Urine test: your child will be asked to pass a sample of urine for testing.

If your child is suitable for the treatment, a baseline and randomisation visit, followed by the treatment visits, will occur.
As part of routine care of children on Xolair, this will include the following:

- Blood tests: this will look at their blood 'IgE' level. This will help us to calculate the dose of Xolair or placebo that they will be on, and to monitor treatment. We will also look for food and other allergies - this would usually be performed as part of an allergy assessment. There will be 2 separate blood tests during the study, which will take place at the same time as routine blood tests where possible. We will take no more than 50mls of blood (about 3 tablespoons) for the study at each visit, depending upon your child's size. These small quantities of blood will quickly be replenished by your child's body. A local anaesthetic ('numbing cream') or 'cold spray' can be applied to minimise discomfort.
- Urine test: your child will be asked to pass a sample of urine for testing.

In addition, because they are on this study, the following will be performed:

- We will also ask you and your child (if they are old enough) to fill out questionnaires about their allergies.
- Blood tests: We will look at blood characteristics which may help us to understand how children respond to the Xolair treatment. These blood tests will be taken at the same time as the routine blood tests described above, so that no extra visits will be required.
- Your child will have photographs taken of their eczema at the baseline visit and at their 24 week visit. These photographs will be taken in the medical photography department by staff who are specially trained to take medical pictures. On each occasion the front, sides and back of the face, body, arms and legs will be photographed. It should take about 30 minutes to take the photographs. So that their eczema can be clearly seen, we will ask your child to undress to their underwear for these photographs. The photographs will provide a clear record of any changes to your child's eczema over the course of the study. Similar photographs are often

used in standard eczema care to help monitor any changes after a new treatment has been started. The photographs will be stored electronically on a secure database that will be accessed by members of the study team and the staff at the medical photography department. Some of the study team may be based outside of the UK/EU jurisdiction (for example in the USA). Copies of the photographs will also be printed out and placed in your child's research folder. When we publish the results of the study in academic journals or at academic meetings we may wish to include some images. Every effort will be taken to ensure that these images do not identify your child, for example we will not include details of their name. You can indicate on the consent form that is attached to this information sheet whether or not you consent to your child's images being used in this way.

- A TEWL (trans-epidermal water loss) test may be carried out to assess your child's eczema. To do this a small probe will touch your child's skin for a few seconds.

The treatment itself will involve the following:

- Xolair or placebo treatment: Your child will receive treatment with either Xolair injections or the placebo injections, depending upon which group they are randomised to. They will receive the injections once or twice a month.
- Your child will be on the Xolair or placebo treatment for a total of 6 months. Treatment will stop after 6 months. Your child will be reassessed at 24 weeks, then 3 months, and 6 months after treatment has stopped.
- During this time if you think your child's eczema may be getting worse, you will be asked to complete an assessment of your child's eczema at home. If your child's eczema is getting worse, you will be asked to contact us. If they have infected or worsening eczema, a course of antibiotics and/or oral steroids, or alternative systemic therapy, may be required.

Some children will also have the following:

- Skin biopsy: if your child has opted to have a skin biopsy, a small sample of skin will be taken before and after the course of treatment. A local anaesthetic will be used to minimise discomfort.

What is Xolair?

Xolair (manufactured by Novartis) is also known as omalizumab. Xolair is currently licensed for patients with severe asthma, but not eczema. It is a type of medicine known as anti-IgE. IgE is a protein produced by the immune system which may be important in children with eczema. Anti-IgE (Xolair) binds to IgE to counteract its effects. Reducing the levels of available IgE in children with eczema may therefore improve their eczema.

How often are the injections?

If your child is randomised to the group to receive Xolair, then your child will be given this as an injection once or twice a month. If your child is randomised to the placebo group, they will receive the placebo injection once or twice a month. Your child's weight and their blood test results will determine the dose of the injections and how often they will have the injections.

WHAT ARE MY CHILD'S ALTERNATIVES?

Your child has been invited to take part in this study as they have not responded to standard treatments for eczema. The alternative would be to try other drugs for eczema, which may be a step up from what they have already used. These drugs may include oral steroids, azathioprine, methotrexate and ciclosporin. They work by suppressing the immune system and may have side effects. They may affect growth, cause weight gain, increase the risk of infection and 'brittle bones', have effects on the liver and kidneys, cause high blood pressure, body salt imbalances, ulcers, gut problems and a condition known as porphyria. Please discuss this with your doctor.

WHAT ARE THE SIDE EFFECTS OF THE TREATMENT?

Safety data suggests that Xolair is well tolerated in children. The most common side effects are pain, swelling, redness and itching at the site of the injection. Headache, fever and stomach pains have been noted by younger children. Some children experience tiredness. Other side effects are rare and may include allergic reactions, including anaphylaxis, and other rare conditions which you may discuss with your study doctor. Treatment may be associated with parasite infections if your child is travelling to a country where these are common.

There may be a small risk of an allergic reaction. Potential symptoms of an allergic reaction may include some or all of the following symptoms: nausea, vomiting, itching, urticaria (nettle rash), angioedema (swelling), wheezing or difficulty in breathing, and/or a drop in blood pressure. Allergic reactions are usually mild but may occasionally be moderate or severe. The most severe type of reaction is called anaphylaxis, which is where the symptoms described become life threatening. The study investigators will do everything possible in order to avoid causing an allergic reaction, but if a reaction were to occur, it would be promptly dealt with by experienced children's doctors and nurses.

WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

Financial and time requirements

Following the screening visit, your child will need to make at least 9 or 15 visits to hospital, depending upon the frequency of their injections. After their first 3 doses of treatment, they will have to remain for observation for 2 hours. After subsequent doses, they will be observed for 30 minutes. On certain visits, they may be required to visit other departments, eg. medical photography, for the procedures outlined above. Additional time will need to be allowed for this. Public transport costs to and from your study visit will be reimbursed. Each visit will take some time but we will endeavour to keep this to a minimum.

Skin prick testing

There is a theoretical risk that your child could have an allergic reaction after skin prick testing. However no severe allergic reactions have ever occurred following skin prick testing in the clinical experience of the study team who perform this test regularly. Skin prick testing will always take place in a clinic by an experienced doctor or nurse who will be able to promptly recognise and treat the signs of any reaction.

Skin biopsy

You may opt for your child to have the skin biopsy. The side effects of a skin biopsy will include: a small scar, discomfort, bleeding and infection. Skin biopsies are often routinely carried out in children, without any untoward effects.

Discomfort associated with study investigations

Skin prick testing

Some children find skin prick testing slightly uncomfortable (to some children it feels like a prickle, others do not feel anything). After skin prick testing has been performed children develop a small hive (a bit like nettle rash) to any of the tests they are allergic too. This can be slightly itchy for a few minutes. Most children tolerate this very well but if necessary a small dose of antihistamine will be given after the testing to minimise the discomfort. It is likely that skin prick testing would have been performed as part of your child's routine allergy clinic assessment.

Blood Tests

The blood test may cause discomfort. However this can be performed using a local anaesthetic ('numbing') cream or 'cold spray' to minimise discomfort. An experienced phlebotomist, nurse or doctor will take the blood. Again it is likely that the blood test would have been performed as part of your child's routine allergy assessment in clinic. Other side effects of the blood test include a small risk of bleeding, bruising, or infection at the site.

Skin biopsy

If your child has a skin biopsy, this will be carried out after a small local anaesthetic injection. Before the injection is given, your child may choose to have a local anaesthetic cream or cold spray applied. An experienced doctor or nurse will perform the skin biopsy. Your child may wish to take a simple painkiller (eg. Calpol) for the biopsy.

WHAT WILL HAPPEN WITH THE SAMPLES WHEN THEY ARE TAKEN?

Once the blood and skin samples have been taken they will be anonymised until they are destroyed. They will only be identifiable via a confidential subject ID number list which will be kept at in a locked office in the Department of Asthma, Allergy and Respiratory Science at King's College London. The samples themselves will be stored in a freezer or liquid nitrogen in the HTA licensed tissue bank in the department of Asthma Allergy and Lung Biology, King's College London (HTA licensing number 12521). The custodians of the samples will be Dr Victor Turcanu and Dr Alick Stephens. The samples will only be analysed by doctors or technicians associated with this research team. The blood and skin samples that are taken will be analysed to try to understand how the specialist blood cells of the immune system are modified by this treatment. They may also be used in other future approved research and may be sent to laboratories within and/or outside of the European Union for further analysis. Genetics samples from your biopsy and blood may be used in future approved research. We hope that this information will contribute further to our understanding of eczema and its treatment.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

Ultimately we hope that the treatments in this study will help your child. However there is no guarantee that your child's eczema will get better if they participate in the study. The information we get from this study may however help us to find better treatments for children with severe eczema, which have fewer side effects.

WHAT IF SOMETHING GOES WRONG?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Please contact: Principal Investigator adapt@gstt.nhs.uk (020 7188 7188 Ext.54293)

If you have a complaint, you should talk to your research doctor who will do their best to answer your questions. If you remain unhappy, you may be able to make a formal complaint through the NHS complaints procedure. Details can be obtained through the Guy's and St Thomas' Patient Advisory Liaison Service (PALS) on 0207 1887188, address: PALS, KIC, Ground floor, North Wing, St Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH .

This trial is co-sponsored by King's College London and Guy's and St Thomas' NHS Foundation Trust. The sponsors will at all times maintain adequate insurance in relation to the study independently. Kings College London, through its own professional indemnity (Clinical Trials) and no fault compensation and the Trust having a duty of care to patients via NHS indemnity cover, in respect of any claims arising as a result of clinical negligence by its employees, brought by or on behalf of a study patient.

WILL MY CHILD'S TAKING PART IN THE STUDY BE KEPT CONFIDENTIAL?

All information which is collected about you and your child during the course of the research will be kept strictly confidential. Any information which leaves the hospital will have your/your child's name and address removed so that you cannot be recognised from it. Research folders will be kept in a secured office at all times. Access to these folders will be restricted to study investigators, study statisticians, the NHS R&D office, monitors, audit and regulatory authorities. Any information that is stored electronically will be kept 'locked' by password access. Your GP will be informed that your child is taking part in the study and of any diagnoses (e.g. asthma) that may be made during the study, unless you inform us that you prefer that this does not happen.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

Once the study is completed the information will be analysed and then submitted for publication to at least 1 peer reviewed scientific journal. No information that will allow the identification of any of the participants will be included in the publication. Once again all the study findings will be made available to participants and their families.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The study is being run by Prof Gideon Lack, Dr Susan Chan, Dr Emma Wedgeworth and their team of researchers.
The ADAPT study is supported by the Efficacy and Mechanism Evaluation (EME) Programme, a Medical Research Council (MRC) and National Institute for Health Research (NIHR) partnership, and the Guy's and St Thomas' Charity.
Participants will not be charged for any investigations or for the medication during the study.

WHO HAS REVIEWED THE STUDY?

London Westminster Research Ethics Committee, the National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation (EME) programme and the Guy's and St Thomas' Charity have reviewed the study.

TERMINATION OF CONSENT FOR ADDITIONAL RESEARCH

If you decide now to agree that your child's blood or skin samples can be used for further research, you can still change your mind at any time in the future. To withdraw consent, contact your doctor and withdraw your consent for the use of your child's blood or skin sample for this research study. After you withdraw your consent, any blood or skin samples for this research study that remain will be destroyed. Your physicians, Dr Chan/Professor Lack may be reached on 020 7188 3300 or 020 7188 1788 x 54293 .

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