The Acne-ID study

Investigating the benefits and harms of reduced daily dose oral isotretinoin in the treatment of acne

Participant Information Sheet (16-24 years)

IRAS ID 1009472

1. You are invited to take part in our research trial

- The Acne-ID trial is looking at the benefits and harms of two different doses of a medication called isotretinoin for the treatment of severe acne.
- This information sheet is to help you understand why the research is being carried out and what it will involve for you if you decide to take part.
- Please take time to read this information and ask us if there is anything that is not clear to you or anything you would like more information on.
- It is entirely your decision whether to take part in this trial. If you agree to take part, you are free to withdraw at any time without giving a reason. If you choose not to take part, your care will continue in the normal way.

2. A summary of the trial

Although many teenagers experience acne, around 1 in 10 of people get severe acne that can also scar the skin. Having acne on your face and body as a young person can affect your confidence, sometimes leading to low mood and anxiety. There is an effective treatment for severe acne called isotretinoin, which is a licenced drug. Although isotretinoin works well at clearing acne, most people who take it experience side effects and some people will experience more than one. Side effects include drying of the lips, skin and lining of the nose (8 in 10 people), aching muscles and tiredness (2 in 10 people) and acne flares when starting treatment (2 in 10 people). Isotretinoin can also harm an unborn child which is why the risk of falling pregnant is assessed, and if required strict measures to prevent pregnancy happening are put in place.

One way to potentially reduce these side effects is to give a lower dose of isotretinoin possibly over a longer period of time. We want to be sure a lower dose possibly taken for longer clears acne as effectively as the standard dose and find out if people are happy to take the tablets for a longer period of time. It is also possible that if the acne is not fully treated at a lower dose, it may come back after stopping treatment sooner than normal, so we also need to check that out.

This trial involves two groups of patients. One group will take the dose of isotretinoin usually prescribed (standard dose) and the other a lower dose. You will not get to choose which group you go into. Due to how isotretinoin works, there is a possibility that the dose may change throughout the treatment course.

3. What is the purpose of the trial?

This study will compare the advantages and disadvantages of two different doses of isotretinoin for people with severe acne – a lower dose, possibly taken for a longer time, or a dose usually prescribed (standard dose) over a shorter duration. We will be comparing how effective the two different doses are at treating acne and we will record side effects and other measures such as how patients feel their acne has changed, how the acne is affecting their life, satisfaction with treatment and any changes in mood.

4. Why have I been invited to take part?

You have been invited to take part in this trial as you and your consultant dermatologist (or a member of their team) have discussed and agreed that you will be starting the medication isotretinoin. We are looking for 800 young people like you who are being treated for severe acne with isotretinoin. All patients are between 12 – 24 years and have been seen in a hospital dermatology department in the UK.

5. Do I have to take part?

No, it is up to you whether or not you take part in the trial. Even if you agree now, you are free to withdraw at a later date. If you do not wish to take part, you will still be eligible to take the standard dose. We will talk to you about the trial and answer any questions you may have. If you agree to take part, we will ask you to sign a consent form.

6. What would taking part involve?

A member of the research team will approach you and provide information about the study and answer any questions you have. If you agree to take part, you will be asked to sign a consent form. With your permission, we will inform your GP about your participation in the study and contact them for quality-of-life data after treatment.

You will be in the study for up to 24 months altogether - up to 12 months or until you stop taking isotretinoin, and 12 months being sent questionnaire to see how you're getting on after you've stopped treatment. Your doctor will see you as often as they see fit, this is likely to be more at the start of treatment and will depend on things like side effects and contraception (if relevant). We will ask a doctor who doesn't know which treatment you're on to assess your acne every time you visit the hospital. We will also be looking at your medical notes to collect information on side effects, mood and how much isotretinoin you have been prescribed.

You won't be paid for taking part in the study, however out of pocket expenses (e.g. prescription costs and travel expenses) will be reimbursed up to the value of £100. If you're eligible for NHS prescription charges, you will be able to claim these back. You will also be able to claim travel expenses to and from the hospital whilst you are on isotretinoin for up to 12 months. You can claim up to £100 total for both prescription and travel costs combined.

First visit:
At your first visit (once you and your doctor have decided to start isotretinoin), you will be given information about the study and asked to sign a consent form. We will ask you to provide some demographic data (e.g. data of birth, ethnicity) and we will ask you to complete some questionnaires about your acne and how it affects your everyday life. If you are not suitable for the study, then you will continue your acne management as planned under the dermatology team.

If you are suitable to take part in the study, with your consent, you will be asked to take a photograph of your acne using your own phone or digital camera. This photograph is for your personal use only to help you best answer questions about changes in your acne and track treatment progress. You will not be asked to share the photograph with the trial staff or upload it anywhere.

You will then be placed in either the low dose isotretinoin group or the standard dose isotretinoin group. This selection is made at randomly via computer. This is called randomisation and makes sure that both groups are similar, which is very important in research. Neither you nor your doctor will be able to choose which group you will be in. Both groups will take isotretinoin daily for up to 12 months, or until your acne clears or you reach

a maximum dose, whichever happens first. You will not be told whether you are in the low dose group or standard dose group, as this might affect how you answer some study questions.

We recommend that you take your isotretinoin capsules at the same time each day with a similar amount of food or drink that contains some fat. This is because the medication is absorbed alongside fat from the diet. For example, this could be with simple meals such as toast with a fat or oil-based spread, or a glass of milk.

Whilst taking isotretinoin:
Whilst taking isotretinoin you will have regular visits with your usual dermatology team. These will vary depending on how you react to treatment but typically will be at 1, 3, 5-6, 8-10 months and when you finish treatment. At each study visit a doctor/nurse who does not know which dose you are on will assess your acne. Your doctor will remind you not to mention which dose you are on as this may affect their assessment.

Whilst taking isotretinoin you will also receive questionnaires via email or post (your choice) some on a monthly basis and others on a 3-monthly basis for up to a year. These can be completed at home. The questionnaires will be relating to your acne (severity and change in acne) and help measure the advantages and disadvantages of isotretinoin treatment (side effects, quality of life, changes in mood, treatment satisfaction). Please do your best to answer all the questionnaires to the fullest, we need as much information as possible to complete the study and find out which dose is best. You will be asked about side effects at your regular dermatology visits and have blood tests 1 month after starting and then every 3 months, which is carried out as part of standard care.

Anyone who may be able to get pregnant whilst taking isotretinoin must enter the Pregnancy Prevention Programme. If relevant to you, your doctor will ask you to sign a form to ensure that you are aware of the risks to an unborn baby. Your doctor will only let you start taking isotretinoin if you are not pregnant, this will be confirmed by a routine pregnancy test in clinic. As it is important not to become pregnant whilst taking isotretinoin, testing throughout the treatment period will vary dependent on risk. Those who are sexually active must use highly effective contraception (the coil (IUD), intra-uterine system (IUS), or contraceptive implant which has been in place for at least 4 weeks) or two forms of contraception together (the hormonal contraceptive pill or contraceptive injection plus a barrier method, such as a condom) and continue to use this method throughout the treatment period and for 1 month after.

After taking isotretinoin:
When you have finished your treatment, you will receive questionnaires via email or post (your choice), some on a monthly and others on a 3-monthly basis, for up to a year. These will help us collect information about side effects, quality of life and whether the acne comes back within a year of stopping treatment. We will also collect information on how much it costs being on the two doses to understand what these different isotretinoin doses might cost patients and the NHS. If your contact details change during this time, please let one of your doctors know.

Text reminders:
With your consent, your name and telephone number will be shared with Esendex, our text messaging provider and their sub processors, and will be used to send you text message reminders about the trial visits and trial questionnaires whilst you are taking part. To find out more about how Esendex stores and protects data, please visit www.esendex.co.uk/information-security-statement.

Optional interviews:
With your consent you may be approached about being interviewed about your experience of isotretinoin. The audio recordings of interviews will be securely transferred and transcribed (changed into written text) in part or full by the University of Nottingham employees or their authorised representatives. If you are interested in taking part in these interviews, we will provide a separate information leaflet and consent form.

Around 30 people who give consent will be invited to take part in a one-off interview to share their experience of acne and isotretinoin. Interviews can be undertaken in person, online (via Microsoft Teams) or via telephone depending on your preference. Interviews will include patients on both low and standard dose, as well as those who decided not to take part in the study. Information from these interviews will be used to help create a decision-making tool to better support patients and dermatologists when isotretinoin is prescribed to acne patients in the future.

Optional study:
Some people may also choose to take part in an additional study to investigate how isotretinoin may work better or have different side effects in certain groups of patients. This will involve providing additional blood samples and skin swabs. This is completely optional. Blood samples and skin swabs will be collected during your first clinic visits and around months 3-4 and months 5-6.

Please note that the participation in both the interviews and sub-study are optional, and we want to assure you that choosing not to participate in either will not impact your involvement in the main Acne-ID trial or your routine care treatment in any manner.

7. What are the possible benefits of taking part?

All participants in the trial will receive isotretinoin because a shared decision has already been made between you and your dermatology team. You will have regular contact with your usual care team and for the trial these are required to happen after the first month every 2 months until isotretinoin is stopped. In addition, there will be remote follow-up by the research team (online questionnaires) for up to a maximum of 24 months. Therefore, within the trial there will be closer remote monitoring of your acne and how you are feeling whilst taking isotretinoin.

Taking part in the trial may not directly benefit you, but the information we collect from this trial aims to help us to treat people with acne in the future. If you are in the low- dose group you may experience fewer or less severe side effects, but this is not yet known and is why the trial is being conducted.

8. What are the possible disadvantages and risks of taking part

Participants in the low dose group may take isotretinoin for longer than if they had received the standard dose. It is expected most participants will stop isotretinoin between 6 and 12 months. Whilst you are taking isotretinoin all the usual care requirements and monitoring will continue.

All patients taking isotretinoin will have an Acknowledgement of Risk Form completed whether they are in the trial or not. The form makes sure all the information about side effects, possible risks and monitoring have been explained. All patients of childbearing potential (could fall pregnant) are at risk of teratogenicity (severe harm to a developing baby) and require contraception, depending on their level of pregnancy risk.

Participants in both the low dose and standard dose groups may experience known side effects to isotretinoin such as:

- Flaring or worsening of acne
- Dry lips/skin/eyes/nose or nosebleeds
- Sensitivity to the sun or sunburn
- Aches and pains in muscles/joints
- Anxiety, depression, irritability, fatigue, poor concentration, suicidal thoughts or other mental health problems
- Problems with getting or keeping an erection (males), vaginal dryness (females), change in periods (females), breast tissue development (males), decreased sex drive (males/females) or other changes in sexual function (males/females)
- Headaches
- Vision concerns/reduced night vision
- Hair thinning
- Nausea/diarrhoea/blood in your stool (poo)

For full information on isotretinoin, please scan this QR code. This is the information leaflet provided at your dermatology appointment.

9. What if there is a problem?

If you have concerns or questions about any aspect of this trial, you should ask to speak to the local research team in the hospital; their contact details are at the end of this information sheet.

If any questions remain, you can contact the trial coordinating centre via email: acne-id@nottingham.ac.uk. If you remain concerned or become unhappy with any aspect of the trial that cannot be resolved by the trial co-ordinating centre wish to complain formally, you can do this through the National Health Service (NHS) Complaints Procedure via your local Patient Advisory and Liaison Service (PALS) <insert Local PALS details / alternative contact for complaints and concerns>.

In the event that something does go wrong and you are harmed during the trial, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for legal action for compensation, but you may have to pay your legal costs. The normal NHS complaints mechanism will still be available to you.

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

While we strongly encourage people to stay in the trial, as your answers contribute to the accuracy and reliability of the study results, we recognize that individuals may, for various reasons, choose to stop taking part. If you decide to withdraw, please be assured that you have the right to do so at any time, and there is no obligation to provide a reason.

If you would like to stop taking part in the trial, please contact your local researchers using the provided contact details at the end of this information sheet. If you withdraw from the trial, the information collected up until that point will be kept and this information may still be used in the study analysis.

11. How will information about me be used?

The research sponsor (University of Nottingham), researchers at the Nottingham Clinical Trials Unit (part of the University of Nottingham) and the local site research team at <insert site name> will need to use information from you, your medical records and potentially your GP for this research project. This information may include your initials, NHS number, name and contact details. The researchers will use this information to do the research or to check your records to make sure that the research is being done properly. For example, they may gather information from your medical notes if you are not able to attend a visit.

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. All information about you will be kept safe and secure. However, the anonymised information collected about you may be used to support other research in the future and may be shared with other researchers.

Once the trial has finished, some of the data will be kept so the results can be checked and you can be told what happened in the trial (unless you tell us you do not want to know). Reports will be written in a way so that no-one can work out that you took part in the trial.

12. What are my choices on how my information will be used

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. After 7 years your data collected during the trial will be disposed of securely.
If you give us your permission, we may keep your contact details so we can get in touch if there is any relevant future research to do with acne treatment that you may be interested taking part in. We need to manage your 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.

With permission, you will also have the option to take part in future research using their data saved from this trial. If you do not wish for your contact details to be kept for a copy of the trial results to be sent to you or to be contacted about future research, these will also be disposed of securely at the end of the trial.

13. 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/ and www.hra.nhs.uk/patientdataandresearch
- at https://www.nottingham.ac.uk/utilities/privacy/privacy-information-for-research-participants.aspx
- http://www.nctu.ac.uk/data-protection/data-protection.aspx
- by sending an email to the Data Protection Officer at dpo@nottingham.ac.uk
- by asking one of the research team
- by sending an email to acne-id@nottingham.ac.uk

14. Who is organising and funding this trial? How has it been reviewed and approved?

The trial is being organised by the University of Nottingham (the Sponsor) and coordinated by the Nottingham Clinical Trials Unit (NCTU). The funding for the trial is provided by the National Institute of Health and Care Research (NIHR), which is funded by the UK Government (Department of Health and Social Care). All research in the NHS is 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 Midlands - Nottingham 2 Research Ethics Committee.

Patients who have lived experience of acne and isotretinoin treatment have helped us plan and design this trial. Their input has helped decide which benefits and harms will be measured in the trial. Patient representatives are also involved in the teams that oversee the running of the trial.

15. What if relevant new information becomes available?

Sometimes we get new information about treatments for acne. If this happens during the trial, your research doctor will tell you about this new information and discuss whether you should continue in the trial. If you decide not to carry on, your research doctor will make arrangements for your care to continue as normal. If you decide to continue in the trial the research team may ask you to sign a new consent form.

16. What will happen to any samples I give?

Samples are not needed for the Acne ID trial however, you will have the option to take part in an additional and separately funded study, to investigate the different influences on the occurrence of acne, for example if this is genetic. If you consent to do so will be asked to provide blood samples and/or skin swab samples.

The separate study using the blood samples and skin swabs will aim to find out more about the mechanisms which affect how well isotretinoin works and the development of side effects. It will also aim to find out how the skin and hair follicle microbiome, which includes the bacteria on the skin, is affected by taking isotretinoin.

The blood samples taken (5-9mls, approximately 1-2 teaspoons full) will be sent by the hospital to the University of York who will store the samples and conduct the research. Samples will be labelled using your participation identification number and date the sample was taken. Therefore, any third parties accessing samples will not have access to identifying information. After the study has been completed, all your samples will be destroyed in line with HTA requirements. As this is a separate study, the results will not be shared with participants.

Blood and urine samples for pregnancy testing, and other monitoring may be taken and reviewed by your usual dermatology team as part of usual care whilst taking isotretinoin. These samples are not for the Acne-ID trial.

17. What happens at the end of the trial?

When the trial ends, your healthcare will continue as normal. At the end of the trial the results will be published in scientific medical journals and presented at conferences. You will not be identified in any publication. We will send you a newsletter with a summary of the trial findings unless you ask us not to.

18. How to contact us

Contact details of your local care team who will be your main point of contact for the duration of the trial:
<insert site team contact details here>
<insert site team contact details here>
<insert site team contact details here>