

Randomised Controlled Trial of a New Relief Inhaler in Mild Asthma: The RELIEF Trial

Participant Information Sheet

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IRAS Project ID: 1006098

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

- The RELIEF trial is looking at whether a combined inhaler is better for treating mild asthma symptoms
- 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 you would like more information
- 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

Approximately 10% of UK adults have asthma. Many have “mild” asthma, requiring a reliever (blue) inhaler for symptoms with or without, low-dose-inhaled steroid treatment. Asthma causes airway inflammation, so treatment with regular inhaled steroids is important. Blue inhalers provide symptom relief but cannot help inflammation. Increasing use of blue inhalers and decreasing use of preventer (usually brown) inhalers is associated with poorer asthma outcomes.

The Global Initiative for Asthma (world-wide asthma recommendations) suggest replacing the first-choice standard blue inhaler for all asthma patients with a combination inhaler containing both reliever and a preventer medicine.

The study aims to determine;

- How effective a combination inhaler might be versus standard care for symptom relief in mild asthma
- Overall costs and savings of the two treatments
- Health care providers and patients views of the new way to treat mild asthma

The RELIEF trial will include 2300 volunteers from GP practices, with mild asthma, across the UK. Participants will be selected at random to be in either one of two groups for the trial. Both groups will continue to use their preventer inhaler, but one group will receive usual care with a blue reliever inhaler (e.g. Ventolin) and the other will receive a combined reliever + preventer inhaler instead (e.g. Symbicort or Fostair). We will also ask you in a monthly text message if you have had any asthma attacks that needed steroid tablets such as prednisolone. We also have some questionnaires about your asthma that we will ask you to complete at different times throughout the trial. The questionnaires will help provide information about how best to understand participants’ experiences and how effective each treatment is. There is also an option for some people to be interviewed about their asthma experiences while in the trial. Your time in the study will be no more than 12 months.

3. What is the purpose of the trial?

Our aim is to find out if using an inhaler which has both the steroid and reliever drugs leads to better asthma control. The main problem in asthma, including 'mild' asthma, is inflammation in the airways of the lungs. Low dose inhaled steroids (usually brown inhalers) reduce this inflammation which is why they are the most important treatment for asthma. Blue, reliever inhalers, are used to help relieve symptoms but they have no effect on the inflammation.

4. Why have I been invited to take part?

You are being invited to take part because you have mild asthma and we would like you to help us find a better way to help treat and control mild asthma. We are inviting 2300 participants with mild asthma, like yourself, to take part.

5. Do I have to take part?

It is completely up to you to decide whether you want to take part and your decision will not affect your care in any way. If you do decide to take part, you will be joining ground-breaking research into understanding how to treat asthma more effectively. You will be given a copy of this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

6. What would taking part involve?

This trial is only open to those who are neither pregnant nor planning to get pregnant, so if you're a woman of child-bearing potential you must agree to use adequate contraception. Acceptable contraceptive methods include: established use of oral, injected or implanted hormonal methods; placement of an intrauterine device (IUD) or intrauterine system (IUS); condom or occlusive cap (diaphragm or cervical/vault caps) with spermicide; true abstinence (when this is in line with the preferred and usual lifestyle of the participant); or vasectomised partner.

If you agree to take part you will be asked to sign a consent form electronically or on paper and to attend appointments with your local trial team, either face-to-face, video conference, or by telephone. The trial is set to last for 44 months in total but you will only be involved in the trial for 12 months.

The treatments we want to compare are "usual care", (the standard blue and usually brown inhalers) versus 'study treatment', (combined inhaler and the, usually, brown inhaler). The combined inhaler is already used for moderate to severe asthma but not for 'mild asthma'. If you are in the 'new treatment' group we will ask you to switch from your usual blue inhaler to the combined inhaler. Whichever group you're in, you'll continue to use your preventer, usually brown, inhaler.

The first appointment

You will be asked to sign a consent form electronically or on paper and complete some questionnaires about you and your asthma. We will then place you in one of two treatment groups. Which treatment group you will be in will be chosen at random by a computer; a process known as randomisation. This means that neither you, nor your doctor, can predict which treatment you will receive. There is an equal chance you will receive either of the two treatments and your doctor will provide information on how to use the inhalers you'll be using on the trial.

The second appointment

One month after you start the trial, we ask that you attend an appointment at your GP practice or talk to the trial team over the telephone just to check you are getting on OK.

Following your progress

We would like to send you a text message from months 2-11 to ask whether you have experienced any worsening of your asthma symptoms that were bad enough to seek help, and then had to take steroid tablets for 3 days or more in the previous 4 weeks. If you respond 'yes' to this text message we will telephone you to ask you about what happened. Your research team will also review your GP medical records to review your asthma treatment. We will also ask you to repeat questionnaires you completed at your first appointment, at home, at 3, 6, and 9 months. Some questionnaires will be completed online via your computer, tablet or phone, others will be completed on

7. What are the possible benefits of taking part?

We do not know if taking part in the trial will directly benefit you but we hope the information we obtain from this trial will help us to understand more about the best way to treat mild asthma. We also hope you gain a better understanding of your asthma and how to control it, and that by being in the trial you may be able to avoid having more severe asthma attacks.

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

As with all medicines, some people experience side effects. For the asthma inhaler being used in this trial these include, palpitations, tremor and oral thrush. A full list of side effects are detailed in each prescribed medications patient information leaflet. However, the medicines used in this trial are already used in the treatment of asthma, and the side effects only affect a small percentage of people. We therefore believe the risks of this trial are very small and the risks of not treating an asthma attack outweigh the risks of the medicines.

9. What if there is a problem?

If you have a concern about any aspect of this trial, you should ask to speak to the researchers, who will do their best to answer your questions. The researchers' contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting your GP practice manager in the first instance.

In the event that something does go wrong, and you are harmed during the research, and this is due to someone's negligence, then you may have grounds for a legal action for compensation against the University of Nottingham, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

10. Pregnancy (where applicable)

If during the trial you become aware that you are pregnant (if applicable) you will need to inform the research team at your clinical practice. The site staff will withdraw you from the trial. This is a clinical trial requirement; however, your GP will continue with your asthma care as per usual clinical practice.

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

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw we will no longer collect any information about you or from you but we will keep the information about you that we have already obtained as we are not allowed to tamper with study records and this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally identifiable information possible.

12. How will information about me be used?

If you join the study, researchers at Nottingham Clinical Trials Unit (part of the University of Nottingham) will need to use information collected from you (and your medical records) for this research project.

This information will 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.

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.

Once the study 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 study.

13. What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your GP records. If you do not want this to happen, tell us and we will stop.

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.

Your contact information will be kept by the University of Nottingham for 12 months after the end of the trial so that we are able to contact you about any the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted).

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 study as stated previously.

After 7 years, your data will be disposed of securely.

We will also ask for your consent to share your name and telephone number with Esendex, our text messaging provider and their subprocessors, which will be used to send you text messages to ask about your asthma and reminders about the study questionnaires whilst you are participating in the trial. Once your participation has ended you will no longer be contacted but Esendex will retain the data for two years or until the end of the trial (whichever occurs first).

14. Where can you find about 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.aspx#Privacynotices>
- by asking one of the research team
- by sending an email to RELIEF@nottingham.ac.uk
- by calling the Nottingham Clinical Trials Unit on 0115 8231610

15. Who is organising and funding this trial? How has it been 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 for Health and Care Research (NIHR). All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by HSC REC B Office for Research Ethics Committees Northern Ireland (ORECNI).

Patients who have previously been treated for asthma have helped us plan and design this trial. Patients' representatives are also involved in the teams that oversee the running of the trial.

16. What if relevant new information becomes available?

Sometimes we get new information about asthma and the best treatment for asthma during the trial. If this happens 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 he/she may ask you to sign a new Informed Consent Form.

17. What happens at the end of the trial?

When the trial ends, your asthma treatment will continue as per usual treatment. If you withdraw from the trial, we will need to keep and use the data collected up to your withdrawal. 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

For further information please contact the RELIEF Team;

tim.harrison@nottingham.ac.uk (Chief Investigator)

Hugh.jarrett@nottingham.ac.uk (Senior Trial manager)

beverley.brown@nottingham.ac.uk (Trial Manager)

ms-relief@exmail.nottingham.ac.uk (Trial inbox)

Thank you for taking the time to read this participant information sheet. We hope that it has been helpful in enabling you to decide if you would like to participate in the RELIEF trial. Please ask us if you have any questions or would like more information about the trial.