CF STORM Adult Information Sheet

- You have been invited to take part in a research study, called CF STORM. CF STORM stands for Streamlining Treatment Or Reducing Medication. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully. You can ask a member of your clinical team if there is anything that is not clear, or if you would like more information. If you wish you can discuss it with friends, relatives and/or get independent advice via your local Patient Advice and Liaison Service (PALS) or equivalent. Taking part is voluntary. If you don't want to take part then you don't need to give a reason.

- CF STORM is a study which aims to find out if stopping certain daily nebulisers (dornase alfa (DNase), hypertonic saline or both) is safe for people with Cystic Fibrosis (CF) taking Kaftrio™.

- The study will compare two approaches to treatment:
  - **"CONTINUE"** where you will carry on taking your nebulisers.
  - **"STOP"** where you will stop taking the following daily nebulisers; dornase alfa, hypertonic saline or both.
- All other treatments will continue as usual and as agreed with your CF team.
- Patients that might be able to take part will have CF, be aged 6 years or over and will have been taking Kaftrio™ for at least 3 months.
- We will recruit 572 people with CF into the trial.

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PART 1: Purpose of the study and what will happen if you take

Why are we doing the CF STORM Study?

Over time, the number of treatments people with CF take on a daily basis can accumulate. It is important to know if these treatments could be safely reduced with reassurance that taking away any treatments does not have a negative impact on their health.

Most people with CF use daily nebulisers to help thin or clear mucus from the lungs (dornase alfa, hypertonic saline or they may use both). Some people with CF have also started a new treatment called Kaftrio™. It may be that some nebulisers are no longer necessary once people are taking Kaftrio™, but we do not know the impact of this on the lungs. This study aims to find out if those people taking Kaftrio™ can stop their daily nebulisers without causing a significant drop in lung function.

To be included in the study, you will be required to have been taking Kaftrio™ for at least 3 months and use one of these daily nebulisers (dornase alfa, hypertonic saline or both) to clear mucus from your lungs.

You will take part in the study for 52 weeks (although this could range from 51-55 weeks depending on the timing of your end of study clinic visit). At the end of the study you will revert back to standard care in discussion with your CF team.

The results from this study will be used to help us improve treatment burden for patients with CF.

Why have I been invited to take part?

You have been invited to take part because you;

- have been taking Kaftrio™ for over 3 months and you also take daily dornase alfa (DNase) or hypertonic saline (or both) nebulisers.
- have previously consented to be part of the UK CF Registry.
- you are able to do spirometry (respiratory function tests), either at home or in clinic.

Your condition is stable at the moment (no need for additional antibiotics in the past 2 weeks).

Do I have to take part?

No, taking part is voluntary. It is up to you to decide whether or not you want to take part. If you decide not to take part then you will still receive the usual treatment your hospital offers. Your Doctor can provide you with more information on this.

If you decide to take part you can also choose to stop taking part at any time without giving a reason.

The decision you make on whether to take part or not will not affect the standard of care you receive now or in the future.

What happens if I decide to take part?

A face to face or telephone/video appointment will be organised to arrange for you to provide your electronic consent (e-Consent). This can take place during one of your usual clinic appointments.

Following your consent and completion of a short quality of life questionnaire (EQ-5D-5L) and a CF specific quality of life questionnaire (CFQ-R), you will find out whether you are in the CONTINUE or STOP group by email and your CF team will discuss this with you.

We will follow your progress through the study using data collected during your routine appointments (face to face or by telephone/video call). After the first visit (where we obtain your e-Consent), the appointments should not be any longer than normal. Your progress will be recorded on the UK CF Registry and some of these results transferred to a CF STORM section for the purpose of this study.

During the course of your participation on the study we will send you three emails containing a link to a short survey to ask about your current treatments . We will also send you 4 emails with a link to the EQ-5D-5L questionnaire. (See study timeline). You may already complete the CFQ-R questionnaire as part of your usual care, and we will collect this data. However, your CF Team will also ask you to complete the questionnaire at the study start and end so you may end up completing more CFQ-Rs than you normally would.

You will not be required to attend any extra appointments for the study aside from those you would normally have.

During the study period we will collect the outcome from your spirometry tests (even if these tests are carried out by you at home). If you use a nebuliser that is able to measure when and how often you use it, we will request that we can record these results for three months before the study starts and during the study.

What will I have to do if I take part?

If you agree to take part, you will be asked to provide your email address so that a link to the e-Consent form can be emailed to you. Once you have completed the consent form, we will check and confirm that this study is suitable for you and you will be asked to follow the study plan (see study timeline). You will be emailed a copy of the completed e-Consent form to keep.

You will have to:

- Continue your usual CF clinic appointments and talk to your CF team about any change in symptoms, as you would even if you were not taking part in the study.
- Ensure you follow the correct treatment allocated to you (CONTINUE or STOP).
- Complete the questionnaires/ surveys in line with the study timeline.
- Ensure that you contact your CF Team if you are feeling unwell, experience any side effects or reactions.

What treatment is included in the study?

In this study we will be focussing on the use of daily nebulised dornase alfa and/or hypertonic saline for people taking the medicine Kaftrio™.

How will I know which treatment I'm going to have?

In research studies we often split patients up into groups to compare how different treatments work. In the CF STORM study those taking part will be split into two treatment groups at random:

One group will receive **"CONTINUE":**

- This means you would carry on taking all your nebulised treatments as directed by your Doctor.

The other group will receive **"STOP":**

- This means you would stop taking the following nebulised drugs:
  - *dornase alfa (also called DNase or Pulmozyme®)*
  - *hypertonic saline (also called Nebusal® or MucoClear®)*
  - *Or both dornase alfa and hypertonic saline*

It is really important that each group in the CF STORM study has a similar mix of people in it so we know that if one group does better than the other it is very likely to be because of the treatment and not because there are differences in the types of people in each group. We use a computer programme that puts people into groups 'at random' – you might hear this described as 'randomisation' or 'random allocation', but they all mean the same thing. Neither you nor your doctor choose which group you are in.

In the CF STORM study you are equally as likely to be in the "CONTINUE" group as you are in the "STOP" group.

Your healthcare team will let you know which group you are in as soon as possible following your completion of the EQ-5D-5L questionnaire that will be sent to you by email.

You will have 2 weeks to complete the EQ-5D-5L questionnaire. If you are unable to complete the questionnaire you will be informed of which group you are in following the two-week period after providing your consent.

Study Timeline

After you have consented to take part	You will receive a link via email to the EQ-5D-5L questionnaire which will take you 5 minutes to complete. Your CF centre will send you a CFQ-R questionnaire (10 minutes to complete) by post, email or they will provide a copy during one of your clinic visits.
7 and 10 days after consenting	*If we haven't received your response to the EQ-5D-5L we will send you a reminder email.*
Day 1: Allocated to either STOP or CONTINUE group	
At 12, 26, 39 weeks we will send you	A link via email to a survey of trial progress (2 minutes to complete)
At 17, 34, 50 weeks we will send you	A link via email to the EQ-5D-5L questionnaire (5 minutes to complete)
50 weeks	Your CF centre will send you a CFQ-R questionnaire (10 minutes to complete) by post, email or they will provide a copy during one of your clinic visits.
Day 1- week 52 (Regular clinics)	Your regular CF clinic appointments will not change but we will use some/all of the data taken recorded during these clinics. This will include any data from completion of the CFQ-R questionnaire during this period.
Week 52: End of your participation	

What are the alternatives for treatment?

If you chose not to take part in CF STORM, your usual CF care will continue as normal. Any decisions in relation to your current treatments should be fully discussed with your CF team.

What are the benefits and risks of taking part?

We do not currently know if it is safe to stop daily nebulised dornase alfa and/or hypertonic saline for people taking the medicine Kaftrio™.

If you are allocated to the "STOP" group this may reduce the burden of taking your daily treatments for the period of the study. However, stopping the use of the daily nebulisers dornase alfa / hypertonic saline may impact on the functioning of your lungs and your CF Team and people like you with CF need to be reassured that this is not the case.

If you "CONTINUE" to take your nebulisers, the common side effects you may already be familiar with are:

- *Dornase alpha (rare and mild side effects): Chest pain, high body temperature, conjunctivitis, indigestion, hoarseness; sore throat, inflammation of your voice box, runny nose, shortness of breath; fever; increased risk of infection; skin reactions.*
- *Hypertonic Saline: Temporary irritation; such as coughing, hoarseness, or reversible bronchoconstriction may occur.*

There will always be a member of your CF team that you can phone if you have any concerns.

We hope that the results from the study will help doctors and people with CF in the future when making decisions around the possibility of rationalising nebuliser use for people established on Kaftrio™.

What happens if I change my mind?

If at any point you decide to stop taking part in the study you will still receive treatment and the follow up usually offered by your hospital. If you do decide to stop taking part we will ask you if you would like to:

- allow us to carry on collecting your data from follow up visits **or**
- stop taking part with no more data collected for the study.

Information on how we will handle your information in the event of you withdrawing is detailed in Part 2 of this Information Sheet.

What if new information becomes available?

Sometimes during the course of a research project, important new information becomes available about the treatment/drug that is being studied. If this happens, your doctor will tell you about it and discuss with you whether you want to or should continue in the study. If you decide to withdraw your doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an

updated consent form. On receiving new information your doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue. If the study is stopped for any other reason you will be told why and your continuing care will be arranged.

What happens when the study stops?

At the end of your participation, you will return to your standard CF care in discussion with your CF team.

When all participants have completed their part in the study, it is intended that the results of the study will be presented at conferences and published in medical journals so that we can explain to the medical community what our research results have shown. They may also be used for research related to the development of pharmaceutical products, diagnostics or medical aids. Confidentiality will be ensured at all times and you will not be identified in any publication.

In addition, we will be working closely with the CF Trust and their community team to ensure that the results of the study are publicised and that people with CF can make informed decisions about their treatment options in partnership with their CF teams. We will send you an email at the end of the study to help direct you to the results.

Any information derived directly or indirectly from this research, as well as any patents, diagnostic tests, drugs, or biological products developed directly or indirectly as a result of this research may be used for commercial purposes. You have no right to this property or to any share of the profits that may be earned directly or indirectly as a result of this research. However, in signing this form for this research, you do not give up any rights that you would otherwise have as a participant in research.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information is given in Part 2 of this information sheet.

Will my taking part in the study be kept confidential?

Yes. All the confidential information about your participation in this study will be kept confidential. Detailed information on this is given in Part 2.

PART 2: Detailed Information about the conduct of the study

Who is running the study?

Alder Hey Children's NHS Foundation Trust is the Sponsor of this study and is responsible for managing it. They are based in the United Kingdom. They have asked that the day to day running of the study is carried out by a team based at the Liverpool Clinical Trials Centre (LCTC, part of the University of Liverpool). There are two doctors running the study, based at University of Liverpool and University College London. They are supported by a large team from across the UK, including adult and paediatric CF doctors, and health economics researchers from University of East Anglia (the central study team). LCTC collaborate with the UK CF Registry who provide the data collection system for your hospital site to record your data on.

The study has been reviewed by the Medicines and Healthcare Products Regulatory Authority, the Health Research Authority and the National Research Ethics Service Committee to make sure that the study is scientifically and ethically acceptable.

This study is funded by National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme.

Your doctor will not receive any payment for including you in this study.

How will my information be collected and handled?

Alder Hey Children's NHS Foundation Trust, University of Liverpool and University of East Anglia are the Data Controllers for this study and will need to use information from you or from your medical records for this research project.

This information will include your initials/ name/ email address/ DOB. People will use this information to do the research or to check your records to make sure that the research is being done properly.

Individuals from Alder Hey Children's NHS Foundation Trust, the LCTC and University of East Anglia and regulatory organisations may look at your medical and research records to check the accuracy of the research study. 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. The data stored in the CF Module on the CF Registry is currently held on servers in the Netherlands and London, however from February 2023 all data will be stored on servers in the UK. Your data will move from the CF STORM Module on the CF Registry (ran by the CF Trust) to LCTC. Some of your data will then be sent onto the University of East Anglia.

We will notify your GP that you will be taking part in the study for their information.

We will keep all information about you safe and secure. Once we have finished the study, we will keep the data for 25 years, so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are my choices about how my 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 the CF Registry. If you do not want this to happen, tell us and we will stop.

In some cases, however we may need to continue to collect limited information about any side-effects of the study treatment you may experience. We will only do this where we are required to do so by law. 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.

Information sharing for other research

When you agree to take part in a research study, the information about your health and care may be beneficial to researchers running other research

studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research, or equivalent standards**.**

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can I find out more about how my information is used?

You can find out more about how we use your information:

- at the study website: www.cfstorm.org.uk
- at www.hrs.nhs.uk/information-about-patients
- in the Health Research Authority leaflet available from www.hra.nhs.uk/patientdataandresearch
- by contacting the University of Liverpool Data Protection Officer (DPO) on LegalServices@liverpool.ac.uk.
- by contacting the Alder Children's Hospital NHS Trust DPO on info.gov@alderhey.nhs.uk
- by contacting the University of East Anglia DPO on dataprotection@uea.ac.uk.
- by asking someone from your CF Team

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with one of your research team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting local NHS Patient Advice and Liaison Service (PALS) or equivalent. Members of your local hospital team should be able to provide this information to you.

Every care will be taken in the course of this clinical study. However, in the unlikely event that you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated but you may have to pay for your legal costs. The normal National Health Service complaints procedures should be available to you.

If you wish to raise a complaint on how any research organisation has handled your personal data, you can contact the relevant Data Protection Officer who will investigate the matter. If you are not satisfied with their response or believe they are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (https://ico.org.uk/).

Thank you for taking the time to read and consider this information sheet. Should you decide to take part in the study, you will be emailed a copy of your signed e-Consent form to keep.