CF STORM Parent/ Guardian Information Sheet

- You have been given this information sheet as your child might be eligible to take part in this 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 child's 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 Child Advice and Liaison Service (PALS) or equivalent.
- 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 your child will carry on taking their nebulisers.
  - **"STOP"** where your child 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 child's CF team.
- People with CF that might be able to take part will be aged 12 years or over and will have been taking Kaftrio™ for at least 3 months.
- We will recruit 764 people.

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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 and clear mucus from the lungs (dornase alfa, hypertonic saline or they may use both). Some people with CF have started to take 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, your child will be required to have been taking Kaftrio™ for at least 3 months with the use of a daily nebuliser (dornase alfa, hypertonic saline or both) to clear mucus from their lungs.

If you agree, your child will take part in the study for 52 weeks (although this could range from 51-55 weeks depending on the timing of their end of study clinic visit). At the end of the study they will revert back to standard care.

The results from this study will be used to help us improve treatments for people with CF.

Why has my child been invited?

Your child has been invited to take part because they;

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

Their condition is stable at the moment (no need for additional antibiotics in the past 6 weeks).

Does my child have to take part?

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

If you decide that they will take part you can also change your mind at any time without giving a reason.

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

What happens if my child decides 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) and for your child to provide their assent (e-Assent). Assent is your child's agreement to take part. This can take place during one of your child's usual clinic appointments.

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

We will follow your child's progress through the study using data collected during their routine appointments (face to face or by telephone/video call). After the first clinic (where we obtain your e-Consent and your child's e-Assent), the appointments should not be any longer than normal. Your child's 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 child's 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 for your child to complete (See study timeline).

Your child may already complete the CFQ-R questionnaire as part of their usual care, and we will collect this data. However, their CF Team will also ask your child to complete the questionnaire at the study start and end so they may end up completing more CFQ-Rs than they normally would.

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

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

What will I and my child have to do if I decide they can take part?

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

Your child will have to:

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

What treatment is included in the study?

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

How will I know which treatment my child is going to have?

In research studies we often split patients up into groups to look at 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 they would carry on taking all their nebulised treatments as directed by their Doctor.

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

- This means they 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 child's doctor choose which group they are in.

Your child is equally as likely to be in the "CONTINUE" group as they are in the "STOP" group.

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

Your child will have 2 weeks to complete the EQ-5D-5L questionnaire. If they are unable to complete the questionnaire they will be informed of which group they are in following the two-week period after providing consent and assent.

Study Timeline

After you and your child have consented to take part	You will receive a link via email to the EQ-5D-5L questionnaire which will take you child 5 minutes to complete. Your CF centre will send your child a CFQ-R questionnaire (10 minutes to complete) by post, email or they will provide a copy during one of your child's clinic visits.
7 and 10 days after consenting	*If we haven't received your child's 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 for you and your child to complete (2 minutes to complete)
At 17, 34, 50 weeks we will send you	A link via email to the EQ-5D-5L questionnaire for your child to complete (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 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 decide against your child taking part in CF STORM, their usual CF care will continue as normal. Any decisions in relation to their current treatments should be fully discussed with their 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 your child is allocated to the "STOP" group this may reduce the burden of taking 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 their lungs and CF Teams and people with CF need to be reassured that this is not the case.

If your child "CONTINUE's" to take their nebulisers, the common side effects that 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 the 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 we change our mind?

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

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

Information on how we will handle yours and your child's information in the event of them 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,

the doctor will tell you about it and discuss with you whether you want your child to continue in the study. If you decide to withdraw your child their doctor will make arrangements for their standard CF care to continue. If you decide they should continue in the study you will be asked to sign an updated consent form. On receiving new information, the doctor might consider it to be in your child's best interests to withdraw them from the study. He/she will explain the reasons and arrange for their care to continue.

If the study is stopped for any other reason you will be told why and your child's 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 neither you nor your child will 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. Neither you nor your child have any 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, your child does not give up any rights that they would otherwise have as a participant in research.

What if there is a problem?

Any complaint about the way you or your child have been dealt with during the study or any possible harm they 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 child's 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 the hospital site to record your child's 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 child's doctor will not receive any payment for including them in this study.

How will my child's 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 your child or from their medical records for this research project.

This information will include your child's initials/ name/ email address/ DOB. People will use this information to do the research or to check your child's 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 child's medical and research records to check the accuracy of the research study. People who do not need to know who you and your child are will not be able to see yours or their name or contact details. Your child's data will have a code number instead. The data stored in the CF Module on the CF Registry is held on servers in the Netherlands and London. Your child's data will move from the CF STORM Module on the CF Registry (ran by the CF Trust) to LCTC. Some of your child's data will then be sent onto the University of East Anglia.

We will notify your child's GP that they will be taking part in the study for their information.

We will keep all information about you and your child 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 your child took part in the study.

What are my choices about how my child's information is used?

You can choose for your child to stop being part of the study at any time, without giving a reason, but we will keep information about you and your child that we already have. If you choose for your child to stop taking part in the study, we would like to continue collecting information about their 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 your child may experience. We will only do this where we are required to do so by law. We need to manage your child's 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 or your child.

Information sharing for other research

When you agree for your child to take part in a research study, the information about their 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 child's 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 for your child to take part in this study, you will have the option for them to take part in future research using their 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 yours and your child's 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/childdataandresearch
- 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 child's 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 the local 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 Child Advice and Liaison Service (PALS) or equivalent. Members of the 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 your child is harmed by taking part in this research project, there are no special compensation arrangements. If your child is harmed and this is due to someone's negligence, then they may have grounds for a legal action for compensation against the NHS Trust where they are being treated but they may have to pay for their legal costs. The normal National Health Service complaints procedures should be available to them.

If you wish to raise a complaint on how any research organisation has handled yours or your child's 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 yours or your child's 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 that your child can take part in the study, you will be emailed a copy of your signed e-Consent form and your child's signed e-Assent form to keep.