

# Can people with cystic fibrosis safely stop taking some of their nebulised treatments if they are established on the new modulator therapy, Kaftrio?

<b>Submission date</b> 22/02/2021	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 31/03/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 11/09/2024	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

For people with cystic fibrosis (pwCF), how to reduce treatment burden has been identified as the top priority research question. Nebulised treatments are identified by pwCF as burdensome. The CF STORM trial will recruit pwCF established on Kaftrio™ therapy to evaluate if stopping certain nebulised therapies is safe.

### Who can participate?

Patients with cystic fibrosis aged over 12 years of age who are established on the new therapy, Kaftrio™.

### What does the study involve?

Participants in the trial will have an equal chance of being allocated to either stop or continue their daily nebulised muco-active therapies (dornase alfa, hypertonic saline, or both). The trial is designed to provide confidence that stopping these nebulisers does not result in a significant decline in lung function over 12 months. This will be measured using spirometry (Forced Expiratory Volume in one second), a lung function test that pwCF are familiar with as part of their routine clinical care. In addition to collecting information about hospital admissions and additional antibiotic treatments, patients will be asked to complete short quality of life measures. All clinical outcomes will be collected on the national CF Registry, and the trial will not involve extra visits outside of normal clinical care. The trial has been designed to be conducted remotely if necessary. This includes the informed consent process for taking part in the trial, and opportunity for remote monitoring of lung function. For patients with nebuliser devices that enable electronic data capture, we will request these data to monitor how participants are managing their nebuliser regimens during the trial. This is in addition to other initiatives that will monitor and encourage participants to comply with the trial group they were allocated to (stopping or continuing muco-active nebulisers).

What are the possible benefits and risks of participating?

The results of the study will guide people with CF and their CF team to make informed choices with respect to their treatment pathway.

Patients in the trial will be monitored carefully but there is a potential risk that patients allocated to stop their nebulised therapies may have a deterioration in their respiratory condition. Participants and CF teams will be aware of this and will restart therapies if necessary.

Where is the study run from?

Alder Hey Children's NHS Foundation Trust (UK) will run the trial and analysis of results. The UK Cystic Fibrosis Trust (UK) will run the national registry on which data for the trial will be collected and will support enrolment into the study through their Clinical Trials Accelerator Programme (CTAP).

When is the study starting and how long is it expected to run for?

From September 2020 to July 2024

Who is funding the study?

The National Institute for Health Research (NIHR) (UK)

Who is the main contact?

Prof Kevin Southern, [cfstorm@liverpool.ac.uk](mailto:cfstorm@liverpool.ac.uk)

### **Study website**

[cfstorm@liverpool.org.uk](mailto:cfstorm@liverpool.org.uk)

## **Contact information**

### **Type(s)**

Scientific

### **Contact name**

Prof Kevin Southern

### **ORCID ID**

<http://orcid.org/0000-0001-6516-9083>

### **Contact details**

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## **Additional identifiers**

**EudraCT/CTIS number**

2020-005864-77

**IRAS number**

293186

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

CPMS 48177, IRAS 293186

## **Study information**

**Scientific Title**

A randomised open-label trial to assess change in respiratory function for people with cystic fibrosis (pwCF) established on triple combination therapy (Kaftrio™) after rationalisation of nebulised mucoactive therapies (the CF STORM trial)

**Acronym**

CF STORM

**Study objectives**

For people with cystic fibrosis established on triple therapy (Kaftrio™), stopping their nebulised muco-active therapies does not result in a significant reduction in their respiratory condition.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 03/03/2021, London -London Bridge Research Ethics Committee (Skipton House, 80 London Road, London SE1 6LH; +44 (0)207 104 8019, +44 (0)207 104 8124; londonbridge.rec@hra.nhs.uk), ref: 21/LO/0080

**Study design**

Open-label randomized controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

## Participant information sheet

Available when the trial goes live at [www.cfstorm.org.uk](http://www.cfstorm.org.uk)

## Health condition(s) or problem(s) studied

Cystic fibrosis

## Interventions

CF STORM will be a randomised open-label trial, undertaken on a national patient registry, to evaluate whether people with cystic fibrosis (pwCF) can rationalise their daily treatment without a significant reduction in their respiratory function. Patients established on triple therapy, elexacaftor-tezacaftor-ivacaftor (Kaftrio™), for more than three months will be enrolled and randomly allocated to either stop or continue their nebulised muco-active treatment (dornase alfa, hypertonic saline, or both). Patient allocations will be irrevocably generated upon completion of the web-based randomisation form by a delegated member of the trial research team. Allocation concealment will be ensured as the service will not release the randomisation code until the patient has been recruited into the trial; this takes place after all baseline measurements have been completed.

Percent predicted Forced Expiratory Volume in One Second (ppFEV1), need for extra antibiotic treatment, quality of life (QoL), and weight will be collected on the national UK Cystic Fibrosis (CF) Registry. In addition, eligibility will be assessed, electronic consent recorded, and randomisation will be undertaken on the registry. This provides an opportunity for pwCF to be recruited remotely, in line with delivery of care during the COVID-19 pandemic.

During the 12 month trial period the participants will be asked to complete two short surveys, the first evaluating how they are doing with respect to maintaining their allocation and the impact on their treatment and a second evaluating their general quality of life. The surveys will be emailed to them, the first survey, four times and the second, three times during the study. For participants using a nebuliser device that enables the download of data, we will ask to collect these results to monitor how patients are doing with their treatments for 3 months before and during the trial. The results of CF STORM together with data from the SIMPLIFY trial (a shorter non-pragmatic trial being undertaken in the US) will inform the knowledge transfer exercise that will be undertaken by the CF STORM team at the end of the trial, co-ordinated by the PPI leads.

## Intervention Type

Drug

## Phase

Not Applicable

## Drug/device/biological/vaccine name(s)

ivacaftor/tezacaftor/ellexacaftor

## Primary outcome measure

Change in percent predicted Forced Expiratory Volume in One Second (ppFEV1) measured using spirometry at baseline, 52 weeks, and any other relevant encounters during the trial period

## Secondary outcome measures

1. Change in respiratory function measured as the incidence of Forced Expiratory Flow between 25-75% of vital capacity using spirometry at baseline and 52 weeks

2. Need for extra antibiotic treatment measured using the number of courses and the total number of days of extra antibiotics (oral, intravenous and nebulised) at baseline and 52 weeks
3. Need for extra chronic medications measured using the number of courses and the total number of days of chronic medications (oral and nebulised) at baseline and 52 weeks
4. Number and proportion of respiratory cultures positive for significant pathogens measured using respiratory cultures at baseline and 52 weeks and any other relevant encounters during the trial period
5. Need for hospital admission measured from the number of separate hospital inpatient stays at 52 weeks and any other relevant encounters during the trial period
6. Change in nutritional status measured using Body Mass Index (BMI) calculated from weight (kg) and height (cm) at baseline and 52 weeks
7. Number of clinician-determined pulmonary exacerbations measured from participant records at baseline and 52 weeks and any other relevant encounters during the trial period
8. Change in disease-specific Quality of Life measured using Cystic Fibrosis Questionnaire-Revised (CFQ-R) at baseline and 52 weeks
9. Adverse events relating to a large drop in respiratory function or treatment of pulmonary exacerbation with IV antibiotics measured using spirometry to calculate ppFEV1 and use of intravenous antibiotics (including dates and drug name) within 4 weeks of the event and at 52 weeks
10. Costs to the NHS measured using treatment costs and compliance to allocation at 52 weeks and any other relevant encounters during the trial period
11. To determine if the 'STOP' intervention represents value for money measured using Incremental cost per QALY gained compared to 'CONTINUE' arm, estimated using the EQ-5D-5L QoL measure at baseline, 17, 34, 50, and 52 weeks

**Overall study start date**

30/09/2020

**Completion date**

31/07/2024

## Eligibility

**Key inclusion criteria**

1. Clear diagnosis and clinical features of Cystic Fibrosis
2. One or two Phe508del variants
3. Established on daily mucoactive nebulised therapy (hypertonic saline or Dornase alfa or both) for at least 3 months
4. Aged  $\geq 12$  years
5. Established on Kaftrio™ for at least 3 months
6. Enrolled in the UK CF Registry
7. Able to undertake spirometry
8. No need for extra antibiotics (oral or intravenous) in the previous six weeks
9. Completed informed consent and assent if applicable obtained from the participant, participant's parent, or legal representative and agreement of participant to comply with the requirements of the study

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

Planned Sample Size: 764; UK Sample Size: 764

**Key exclusion criteria**

1. Significant adverse reaction to Kaftrio™ requiring dose change during the previous 3 months
2. ppFEV1 below 40% after Kaftrio™ therapy at any point during the previous 3 months
3. History of solid organ transplant or placed on the active transplant waiting list
4. Other non-CF condition that, in the opinion of the local CF team, significantly impacts on clinical progress
5. Participation in another Clinical Trial of an Investigational Medicinal Product (CTIMP) within the previous 3 months (the 3-month period does not apply to open-label Kaftrio™ CTIMPs)
6. Prescribed Mannitol dry powder for inhalation as part of usual daily CF care within the previous 6 weeks

**Date of first enrolment**

01/04/2021

**Date of final enrolment**

31/07/2024

## **Locations**

**Countries of recruitment**

England

Northern Ireland

United Kingdom

**Study participating centre**

**Alder Hey Hospital**

Alder Hey Children's NHS Foundation Trust

Eaton Road

West Derby

Liverpool

United Kingdom

L12 2AP

**Study participating centre**

**John Radcliffe Hospital**

Oxford University Hospitals NHS Foundation Trust

Headley Way

Headington  
Oxford  
United Kingdom  
OX3 9DU

**Study participating centre**

**Great Ormond Street Hospital**

Great Ormond Street Hospital For Children NHS Foundation Trust  
Great Ormond Street  
London  
United Kingdom  
WC1N 3JH

**Study participating centre**

**Liverpool Heart And Chest Hospital**

Liverpool Heart And Chest Hospital NHS Foundation Trust  
Thomas Drive  
Liverpool  
United Kingdom  
L14 3PE

**Study participating centre**

**Manchester University NHS Foundation Trust**

Cobbett House  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**Belfast City Hospital**

A Floor  
Belfast Health & Social Care Trust  
Lisburn Road  
Belfast  
United Kingdom  
BT9 7AB

**Sponsor information**

**Organisation**

Alder Hey Children's NHS Foundation Trust

**Sponsor details**

Eaton Road  
Liverpool  
England  
United Kingdom  
L12 2AP  
+44 (0)151 252 5570  
Richard.Kirk@alderhey.nhs.uk

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.alderhey.nhs.uk/>

**ROR**

<https://ror.org/00p18zw56>

**Funder(s)****Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

**Results and Publications**

Publication and dissemination plan



We have a detailed knowledge transfer plan following study end, that involves our PPI team and working closely with other research groups in the US. We will co-ordinate our findings to ensure clear messages are generated.

Outcomes of the trial will be published in open-access peer-review journals, as standard. We will also work closely with the CF Trust to ensure people with CF and their healthcare teams have clear outcomes from the trial in order to best inform their future care pathways

**Intention to publish date**

30/09/2025

**Individual participant data (IPD) sharing plan**

CF STORM is a registry-based trial. The anonymised data will be available on the UK Cystic Fibrosis Registry through an application process.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No