ISRCTN14081521 https://doi.org/10.1186/ISRCTN14081521

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

Submission date
22/02/2021

Recruitment status
No longer recruiting

Registration date
31/03/2021

Overall study status
Completed

Last Edited
30/09/2026

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] 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 6 years or older 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 a 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 an 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 August 2025

Who is funding the study?
The National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Mrs Abigail Williams (Trial Manager), cfstorm@liverpool.ac.uk
Dr Gwyneth Davies (Co- Chief Investigator), gwyneth.davies@ucl.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Gwyneth Davies

Contact details
UCL Great Ormond Street, Institute of Child Health, 30 Guilford Street
London
United Kingdom
WC1N 1EH
+44 20 7405 9200
gwyneth.davies@ucl.ac.uk

Type(s)
Public, Scientific

Contact name
Mrs Abigail Williams

Contact details
Liverpool Clinical Trials Centre, 2nd Floor, Institute in the Park, Alder Hey Children’s NHS Trust, Eaton Road
Liverpool
United Kingdom
L12 2AP

+44 151 794 9764
cfstorm@liverpool.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2020-005864-77

Integrated Research Application System (IRAS)
293186

Central Portfolio Management System (CPMS)
48177

National Institute for Health and Care Research (NIHR)
131889

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 (KaftrioTM), 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

Primary study design
Interventional

Study design
Open-label randomized controlled trial

Study type(s)
Treatment

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 3 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, coordinated by the PPI leads.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ivacaftor/tezacaftor/elexacaftor

Primary outcome(s)
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

Key secondary outcome(s)
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

Completion date
26/08/2025

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 25/09/2025:
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. 6 years of age or older
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 2 weeks
9. Completed informed consent and assent if applicable, obtained from the participant, participant's parent, or legal representative and agreement of the participant to comply with the requirements of the study

Previous 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 ≥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 6 weeks

9. Completed informed consent and assent if applicable, obtained from the participant, participant's parent, or legal representative and agreement of the participant to comply with the requirements of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
6 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
591

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
21/07/2021

Date of final enrolment
30/05/2024

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Study participating centre
Alder Hey Hospital
Alder Hey Children's NHS Foundation Trust
Eaton Road
West Derby
Liverpool
England
L12 2AP

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
Great Ormond Street Hospital
Great Ormond Street Hospital For Children NHS Foundation Trust
Great Ormond Street
London
England
WC1N 3JH

Study participating centre
Liverpool Heart And Chest Hospital
Liverpool Heart And Chest Hospital NHS Foundation Trust
Thomas Drive
Liverpool
England
L14 3PE

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
England
M13 9WL

Study participating centre
Belfast City Hospital
A Floor
Belfast Health & Social Care Trust
Lisburn Road
Belfast
Northern Ireland
BT9 7AB

Sponsor information

Organisation
Alder Hey Children's NHS Foundation Trust

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

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?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results		29/09/2026	30/09/2026	No	Yes
Protocol file	version 6.0	13/02/2025	25/09/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes