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Real world health outcomes in people with cystic fibrosis after initiation of a new combination treatment

Submission date
22/10/2020

Recruitment status
Recruiting

Registration date
16/12/2020

Overall study status
Ongoing

Last Edited
12/08/2025

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cystic fibrosis is an inherited condition that causes sticky mucus to build up in the lungs and digestive system. This causes lung infections and problems with digesting food.
In recent years, a number of new exciting medications have been developed that treat the underlying genetic defect in Cystic fibrosis (CF).
In August 2020 the next generation of potent CF medications Elexacaftor/Tezacaftor/Ivacaftor (ETI) was approved for patients with CF in Europe (having previously been approved by the FDA. This presents a unique opportunity for us to plan a real-world study involving all Irish centres in people six years and above with CF. In the summer of 2025, a new triple combination modulator Vanzacaftor/Tezacaftor/Deutivacaftor (VTD), was licensed for use in the UK and Ireland. A new 1-year arm was added to the study at this time, looking at any potential side effects from participants switching from ETI to VTD.

Who can participate?
People with cystic fibrosis who are suitable for treatment with triple combination modulator therapy can partake in this study.

What does the study involve?
The study will examine clinical outcomes over a seven-year period for each age cohort (6-11 years and 12+ years) across eight pediatric and adult CF centers in Ireland and the UK. Participants will be prescribed ETI. They will attend appointments to provide measurements at the start of the study and then every 3 months for the first 2 years and then annually until the end of the study.

What are the possible benefits and risks of participating?
The subject may benefit from the information obtained during the study. Depending on the usual practice of performing tests and investigations at your local centre, the subject may have more diagnostic tests performed that can be used by the local team. People in research studies see their CF team more than those not involved in research studies. This could be associated with better outcomes.

Almost all medical investigations and treatments have some risks. The following tests are associated with mild discomfort: Nasal lavage (irritating, like doing a nasal rinse). Sputum induction – the subject is encouraged to cough after having nebulised hypertonic saline (can cause excessive coughing). Blood tests (we will endeavour to collect blood for RECOVER only when it is already needed for clinical care - annually).
The subject may have CT scans as part of the advanced tests required for this study. They would not have these scans if they did not take part in the study. These procedures use ionising radiation to form images of the lungs. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. We are all at risk of developing cancer during our lifetime. This will happen to about 50% of people at some point in their lives. Taking part in this study will increase the chances of this happening from 50% to 50.1 %.

Where is the study run from?
RECOVER will be coordinated through the Royal College of Surgeons in Ireland.

When is the study starting and how long is it expected to run for?
January 2020 to June 2029

Who is funding the study?
1. Cystic Fibrosis Foundation (USA)
2. Cystic Fibrosis Trust (UK)
3. Cystic Fibrosis Ireland

Who is the main contact?
RECOVER study team, recover@rcsi.ie
RECOVER project manager, Rachel Cregan rachelcregan@rcsi.ie

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000922-85

Integrated Research Application System (IRAS)
279116

ClinicalTrials.gov (NCT)
NCT04602468

Protocol serial number
IRAS 279116, CFF OOC – 2019

Study information

Scientific Title

Real world clinical outcomes with novel modifier therapy combinations in people with cystic fibrosis

Acronym
RECOVER

Study objectives
Current study hypothesis as of 12/08/2025:
1. Use of Triple Combination Modulator (TCM) in routine clinical practice is associated with significant and sustained improvements in airway and gastrointestinal outcomes and quality of life in children and adults with cystic fibrosis
2. Adherence to routine therapies will decrease after initiation of Elexacaftor/Tezacaftor /Ivacaftor (ETI)

Previous study hypothesis as of 20/03/2024:
1. Use of Elexacaftor/Tezacaftor/Ivacaftor (ETI) in routine clinical practice is associated with significant and sustained improvements in airway and gastrointestinal outcomes and quality of life in children and adults with cystic fibrosis
2. Adherence to routine therapies will decrease after initiation of Elexacaftor/Tezacaftor /Ivacaftor (ETI)

Previous study hypothesis:
1. Use of TCMT in routine clinical practice is associated with significant and sustained improvements in airway and gastrointestinal outcomes and quality of life in children and adults with cystic fibrosis
2. Adherence to routine therapies will decrease after initiation of TCMT

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 22/03/2021, London - City & East Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)2071048033/53; cityandeast.rec@hra.nhs.uk), ref: 21/LO/0224
2. Approved 11/03/2020, Children's Health Ireland at Crumlin Medical Research Committee (Crumlin, Dublin 12, D12N512 , Ireland; +353 (0)14096243; ethics. committee2@childrenshealthireland.ie), ref: Gen/807/20
3. Approved 30/06/2020, Children's Health Ireland at Temple Street ethics committee, now Children's Health Ireland at Crumlin Medical Research Committee (Research Office, Temple Street Children’s University Hospital, Temple Street, Dublin 1, D01 XD99, Ireland; +353 (0)1 892 1787; research@cuh.ie), ref: 20.020
4. Approved 17/08/2020, Children's Health Ireland at SJH/TUH Research Ethics Committee, now Children's Health Ireland at Crumlin Medical Research Committee (Tallaght University Hospital, Dublin 24, D24 TN3C, Ireland; +353 (0)1-414 2199; researchethics@tuh.ie), ref: 2020-07
5. Approved 11/06/2020, University Hospital Limerick ethics (Research Ethics Committee, UL Hospitals Group, USE, Unit 2, Loughmore Avenue, Raheen Business Park, Limerick, V94P7X9, Ireland; +353 (0)61 482519; nicola.moloney@hse.ie), ref: 055/2020
6. Approved 27/08/2020, St Vincent’s Healthcare Group Ethics and Medical Research Committee (Education and Research Centre, Elm Park, Dublin 4, D04T6F4, Ireland; +353 (0)1-2214117; svhgethics@ucd.ie), ref: RS20-047

7. Approved 30/07/2024, Beaumont Hospital Ethics (Medical Research) Committee (Beaumont Road, Dublin 9, D09 C562, Ireland; N/A; beaumontethics@rcsi.com), ref: 24/13

Study design
Multicenter clinical trial of an investigational medicinal product in UK clinical sites, multicenter observational cohort study in Irish sites

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Cystic fibrosis

Interventions
Current interventions as of 12/08/2025:
RECOVER is a real-world observational study examining the impact of Triple Combination Modulator therapy in the treatment of people with cystic fibrosis. The RECOVER parent study commenced in 2020 in people aged 12 and over who were prescribed Elexacaftor/Tezacaftor /Ivacaftor clinically. In 2022, when the drug was prescribed for children aged 6 to 11, they were recruited into the study. The parent study ran for two years. The duration of the extension study is five years for each cohort. The extension study for the older cohort and the parent study for the younger cohort will run concurrently. New participants will be recruited to the study when Vanzacaftor/Tezacaftor/Deutivacaftor is licensed for use in 2025.

The FDA approved VTD for use on 20/12/2025, with the EMA expected to approve in quarter two 2025. This provides a unique opportunity to collect data on mental health and liver response of participants starting on VTD. RECOVER will collaborate with the RETRIAL study to assess these outcomes globally. RETRIAL is a prospective longitudinal observational multi-site study designed to observe what happens when PwCF aged 6 and up start taking VTD and have a history of new or worsening mental health symptoms while on ETI requiring discontinuation or change from standard dosing or liver-related intolerance to ETI requiring discontinuation. Existing RECOVER participants and new participants switching from ETI to VTD will take part in this arm of the study.

Our aim with RECOVER is to examine the clinical impact of TCM on key clinical outcomes in people with CF in a real-world setting. For this study, in addition to some of the more traditional ways of monitoring clinical outcomes in people with CF such a standard lung function, nutrition, exacerbations and liver disease, we are proposing to include some novel outcome measures not typically used in clinical trials such as lung clearance index (LCI) and spirometry-controlled chest CT.

By implementing an extensive study protocol that will include important outcomes in a number of areas of health in people with CF, and matching this to a comprehensive biosample collection plan we will have the power in RECOVER to gain important insight into how TCM works, and what impact it has on rescue of CFTR function in this group of people.

The study will operate in collaboration with our academic and clinical partners and the CF registries in Ireland and the UK. The study is supported by the European CF Society Clinical Trials

Network (ECFS-CTN). The study is being run as a CTIMP in the UK clinical sites as classified by the regulatory authority, the MHRA. The Irish regulatory authority, the HPRA, has determined this study to be an observational research study and will be run as one at the Irish sites.

Prior to any study assessments being complete, the participant will be contacted by a member of the study team provided information on the study in age-appropriate information leaflets, and request the participant to review. If the participant is happy to take part in the study, a team member will arrange a day for the participant to come to the clinical study site where the investigator will take informed consent. Once consent has been obtained, the participant will have their eligibility assessed. In the UK, this will include a pregnancy test for women of childbearing potential prior to any other study assessments. The subject will be enrolled if they meet all inclusion criteria and no exclusion criteria. They will then undergo several tests at -3 month visit and baseline prior to starting on commercially available ETI (at the dosage decided by their clinician).

Previous interventions as of 20/03/2024:
Our aim with RECOVER is to examine the clinical impact of ETI on key clinical outcomes in people with CF in a real-world setting. For this study, in addition to some of the more traditional ways of monitoring clinical outcomes in people with CF such a standard lung function, nutrition, exacerbations and liver disease, we are proposing to include some novel outcome measures not typically used in clinical trials such as lung clearance index (LCI) and spirometry controlled chest CT.

By implementing an extensive study protocol that will include important outcomes in a number of areas of health in people with CF, and matching this to a comprehensive biosample collection plan we will have the power in RECOVER to gain important insight into how ETI works, and what impact it has on rescue of CFTR function in this group of people.

The study will operate in collaboration with our academic and clinical partners and the CF registries in Ireland and the UK. The study is supported by the European CF Society Clinical Trials Network (ECFS-CTN). The study is being run as a CTIMP in the UK clinical sites as classified by the regulatory authority, the MHRA. The Irish regulatory authority, the HPRA, has determined this study to be an observational research study and will be run as one at the Irish sites.

Subject participation is 7 years. Prior to any study assessments being complete, the participant will be contacted by a member of the study team provided information on the study in age-appropriate information leaflets, and request the participant to review. If the participant is happy to take part in the study, a team member will arrange a day for the participant to come to the clinical study site where the investigator will take informed consent. Once consent has been obtained, the participant have their eligibility assessed. In the UK, this will include a pregnancy test for women of child bearing potential prior to any other study assessments. The subject will be enrolled if they meet all inclusion criteria and no exclusion criteria. They will then undergo several tests at -3 month visit and baseline prior to starting on commercially available ETI (at the dosage decided by their clinician). Once the participant has started this triple combination modulator therapy, they will be monitored at 3 monthly intervals for the first 2 years and then annually after this.

Previous interventions as of 29/04/2021:
Our aim with RECOVER is to examine the clinical impact of Kaftrio on key clinical outcomes in people with CF in a real-world setting. For this study, in addition to some of the more traditional ways of monitoring clinical outcomes in people with CF such a standard lung function, nutrition, exacerbations and liver disease, we are proposing to include some novel outcome measures not

typically used in clinical trials such as lung clearance index (LCI) and spirometry controlled chest CT.

By implementing an extensive study protocol that will include important outcomes in a number of areas of health in people with CF, and matching this to a comprehensive biosample collection plan we will have the power in RECOVER to gain important insight into how Kaftrio works, and what impact it has on rescue of CFTR function in this group of people.

The study will operate in collaboration with our academic and clinical partners and the CF registries in Ireland and the UK. The study is supported by the European CF Society Clinical Trials Network (ECFS-CTN). The study is being run as a CTIMP in the UK clinical sites as classified by the regulatory authority, the MHRA. The Irish regulatory authority, the HPRA, has determined this study to be an observational research study and will be run as one at the Irish sites.

Subject participation is 27 months. Prior to any study assessments being complete, the participant will be contacted by a member of the study team provided information on the study in age-appropriate information leaflets, and request the participant to review. If the participant is happy to take part in the study, a team member will arrange a day for the participant to come to the clinical study site where the investigator will take informed consent. Once consent has been obtained, the participant have their eligibility assessed. In the UK, this will include a pregnancy test for women of child bearing potential prior to any other study assessments. The subject will be enrolled if they meet all inclusion criteria and no exclusion criteria. They will then undergo several tests at -3 month visit and baseline prior to starting on commercially available Kaftrio (at the dosage decided by their clinician). Once the participant has started this triple combination modulator therapy, they will be monitored at 3 monthly intervals, which will coincide with the patients 3 monthly clinic visits.

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Previous interventions:

Our aim with RECOVER is to examine the clinical impact of Kaftrio on key clinical outcomes in people with CF in a real-world setting. For this study, in addition to some of the more traditional ways of monitoring clinical outcomes in people with CF such a standard lung function, nutrition, exacerbations and liver disease, we are proposing to include some novel outcome measures not typically used in clinical trials such as lung clearance index (LCI) and spirometry controlled chest CT.

By implementing an extensive study protocol that will include important outcomes in a number of areas of health in people with CF, and matching this to a comprehensive biosample collection plan we will have the power in RECOVER to gain important insight into how Kaftrio works, and what impact it has on rescue of CFTR function in this group of people.

The study will operate in collaboration with our academic and clinical partners and the CF registries in Ireland and the UK. The study is supported by the European CF Society Clinical Trials Network (ECFS-CTN).

Subject participation is 27 months. Prior to any study assessments being complete, the participant will be contacted by a member of the study team provided information on the study in age-appropriate information leaflets, and request the participant to review. If the participant is happy to take part in the study, a team member will arrange a day for the participant to come to the clinical study site where the investigator will take informed consent. Once consent has

been obtained, the participant will undergo several tests at -3 month visit and baseline prior to starting on commercially available Kaftrio (at the dosage decided by their clinician). Once the participant has started this triple combination modulator therapy, they will be monitored at 3 monthly intervals, which will coincide with the patients 3 monthly clinic visits.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Elexacaftor/Tezacaftor/Ivacaftor (ETI), Vanzacaftor/Tezacaftor/Deutivacaftor (VTD)

Primary outcome(s)
Current primary outcome measures as of 12/08/2025:
1. Lung clearance index (LCI or multiple breath washout) is measured to determine the effect of treatment on pulmonary function. It will be measured at -3 months, baseline, 6 months, 12 months, 18months and annually until the end of the study.
2. Spirometry-controlled CT will assess the effect of Elexacaftor/Tezacaftor/Ivacaftor (ETI) on the CT scores. It is for patients on the advanced testing group only. It will be measured at baseline, 12 months and 24 months and at years four and six at sites doing routine clinical CT. Scan at year six for sites not performing biennial CT.
3. Height/weight/BMI will be used for pulmonary function and to determine the effects of nutrition. It is measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and annually until the end of the study.
4. FEV1 (spirometry) is measured to determine the effect of treatment on pulmonary function. It is measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and annually until the end of the study.
5. Airway sampling (microbiology) will be used to measure the effect on ETI on airway infection and inflammation in children and adults with CF. It will be measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and annually until the end of the study.
6. Nasal lavage will be used to measure the effect of TCTM on airway infection and inflammation. It is measured on patients in the advanced testing arm only. This will be measured at baseline, 6 months and annually until the end of the study.
7. FeNO (exhaled nitric oxide) is used to measure airway infection and inflammation. It is measured at -3 months, baseline, 6 months and 12 months.
8. Liver function testing will be used to determine the effect of ETI on nutrition, gastrointestinal symptoms, gut inflammation and pancreatic function in children and adults over a 2-year period. It is measured at baseline, 3 months, 6 months and annually until the end of the study.
9. Liver ultrasound will be used to determine ETI on nutrition, gastrointestinal symptoms, gut inflammation and pancreatic function. It will be measured annually until the end of the study.
10. Sputum sample collection is for the advanced testing group only. This will be used to determine ETI effect on airway infection and inflammation. It will be measured at baseline, 6 months and annually until the end of the study.
11. Liver examination will be performed annually for the parent study, as part of the nutritional, gastrointestinal, gut inflammation and pancreatic function aim
12. Effect of ETI on digestive tract by stool sample collection will be performed at baseline, 1 month, 6 months and annually until the end of the study.
13. Serum blood sample collection will occur annually until the end of the study. A once

collected EDTA blood sample will be used for genetic modifiers of treatment response by our collaborators in Toronto.
14. Abdominal symptom questionnaire and score will be used for nutritional and gastrointestinal symptoms outcomes. It is measured at -3 months, baseline, 1 month, 2 months, 6 months and annually until the end of the study.
15. CFQ-R questionnaire will be administered at baseline, 6 months and and annually until the end of the study. This has components on digestion, respiratory and quality of life
16. Pharmacy records (medication pick-up rates) will be reviewed at baseline, 12 months and 24 months to assess the impact of the introduction of ETI on antibiotic treatment of pulmonary disease and on adherence
17. Adherence and barriers to adherence questionnaires will be collected at - 3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and 24 months. This will assess adherence impact with overall medical treatments for CF.
18. MEMs caps reading will be at 12 months and will assess adherence to ETI
19. Antibiotic use (through prescribed treatment plan and pharmacy pick up rates) will be measured at baseline, 12 months and 24 months, and will assess the impact of the introduction of ETI on antibiotic treatment for pulmonary disease
20. Effect of ETI on sweat, sweat chloride will be measured at baseline, 6 months and annually until the end of the study.
21. Mental Health Questionnaires will be carried out at year 3 and annually until the end of the study. This is an aim for the 5-year extension study only.

Additional questionnaires will also be collected when a participant switches from ETI to VTD:
22. Cognitive function will be assessed using the NIH Toolbox when a participant switches from ETI to VTD.

Previous primary outcome measure as of 20/03/2024:
1. Lung clearance index (LCI or multiple breath washout) is measured to determine the effect of treatment on pulmonary function. It will be measured at -3 months, baseline, 6 months, 12 months, 18months and annually until the end of the study.
2. Spirometry-controlled CT will assess the effect of Elexacaftor/Tezacaftor/Ivacaftor (ETI) on the CT scores. It is for patients on the advanced testing group only. It will be measured at baseline, 12 months and 24 months and at years four and six at sites doing routine clinical CT. Scan at year six for sites not performing biennial CT.
3. Height/weight/BMI will be used for pulmonary function and to determine the effects of nutrition. It is measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and annually until the end of the study.
4. FEV1 (spirometry) is measured to determine the effect of treatment on pulmonary function. It is measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and annually until the end of the study.
5. Airway sampling (microbiology) will be used the measure the effect on ETI on airway infection and inflammation in children and adults with CF. It will be measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and annually until the end of the study.
6. Nasal lavage will be used to measure the effect of TCTM on airway infection and inflammation. It is measured on patients in the advanced testing arm only. This will be measured at baseline, 6 months and annually until the end of the study.
7. FeNO (exhaled nitric oxide) is used to measure airway infection and inflammation. It is measured at -3 months, baseline, 6 months and 12 months
8. Liver function testing will be used to determine the effect of ETI on nutrition, gastrointestinal symptoms, gut inflammation and pancreatic function in children and adults over a 2-year period. It is measured at baseline, 3 months, 6 months and annually until the end of the study.

9. Liver ultrasound will be used to determine ETI on nutrition, gastrointestinal symptoms, gut inflammation and pancreatic function. It will be measured annually until the end of the study.
10. Sputum sample collection is for the advanced testing group only. This will be used to determine ETI effect on airway infection and inflammation. It will be measured at baseline, 6 months and annually until the end of the study.
11. Liver examination will be performed annually until the end of the study as part of the nutritional, gastrointestinal, gut inflammation and pancreatic function aim
12. Effect of ETI on digestive tract by stool sample collection will be performed at baseline, 1 month, 6 months and 24 months and annually until the end of the study.
13. Blood sample collection will occur annually until the end of the study. The EDTA blood sample will be used for genetic modifiers of treatment response by our collaborators in Toronto
14. Abdominal symptom questionnaire and score will be used for nutritional and gastrointestinal symptoms outcomes. It is measured at -3 months, baseline, 1 month, 2 months, 6 months and annually until the end of the study.
15. CFQ-R questionnaire will be administered at baseline, 6 months and and annually until the end of the study. This has components on digestion, respiratory and quality of life
16. Pharmacy records (medication pick up rates) will be reviewed at baseline, 12 months and 24 months to assess the impact of the introduction of ETI on antibiotic treatment of pulmonary disease and on adherence
17. Adherence and barriers to adherence questionnaires will be collected at - 3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and 24 months. This will assess adherence impact with overall medical treatments for CF.
18. MEMs caps reading will be at 12 months and will assess adherence to ETI
19. Antibiotic use (through prescribed treatment plan and pharmacy pick up rates) will be measured at baseline, 12 months and 24 months, and will assess the impact of the introduction of ETI on antibiotic treatment for pulmonary disease
20. Effect of ETI on sweat, sweat chloride will be measured at baseline, 6 months and annually until the end of the study.
21. Mental Health Questionnaires will be carried out at year 3 and annually until the end of the study. This is an aim for the five year extension study only.

Previous primary outcome measure:
1. Lung clearance index (LCI or multiple breath washout) is measured to determine the effect of treatment on pulmonary function. It will be measured at -3 months, baseline, 6 months, 12 months, 18 months and 24 months
2. Spirometry controlled CT will assess the effect of triple combination modulator therapy (TCMT) on the CT scores. It is for patients on the advanced testing group only. It will be measured at baseline, 12 months and 24 months
3. Height/weight/BMI will be used for pulmonary function and to determine the effects of nutrition. It is measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and 24 months
4. FEV1 (spirometry) is measured to determine the effect of treatment on pulmonary function. It is measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and 24 months
5. Airway sampling (microbiology) will be used the measure the effect on TCMT on airway infection and inflammation in children and adults with CF. It will be measured at -3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and 24 months
6. Nasal lavage will be used to measure the effect of TCTM on airway infection and inflammation. It is measured on patients in the advanced testing arm only. This will be measured at baseline, 6 months and 12 months
7. FeNO (exhaled nitric oxide) is used to measure airway infection and inflammation. It is

measured at -3 months, baseline, 6 months and 12 months
8. Liver function testing will be used to determine the effect of TCMT on nutrition, gastrointestinal symptoms, gut inflammation and pancreatic function in children and adults over a 2-year period. It is measured at baseline, 3 months, 6 months, 12 months and 24 months
9. Liver ultrasound will be used to determine TCMT on nutrition, gastrointestinal symptoms, gut inflammation and pancreatic function. It will be measured at baseline, 12 months and 24 months
10. Sputum sample collection is for the advanced testing group only. This will be used to determine TCMT effect on airway infection and inflammation. It will be measured at baseline, 6 months, 12 months and 24 months
11. Liver examination will be performed at baseline, 12 months and 24 months as part of the nutritional, gastrointestinal, gut inflammation and pancreatic function aim
12. Effect of TCMT on digestive tract by stool sample collection will be performed at baseline, 1 month, 6 months and 24 months as above
13. Blood sample collection will occur at baseline, 12 months and 24 months. The EDTA blood sample will be used for genetic modifiers of treatment response by our collaborators in Toronto
14. Abdominal symptom questionnaire and score will be used for nutritional and gastrointestinal symptoms outcomes. It is measured at -3 months, baseline, 1 month, 2 months, 6 months, 12 months and 24 months
15. CFQ-R questionnaire will be administered at baseline, 6 months, 12 months and 24 months. This has components on digestion, respiratory and quality of life
16. Pharmacy records (medication pick up rates) will be reviewed at baseline, 12 months and 24 months to assess the impact of the introduction of TCMT on antibiotic treatment of pulmonary disease and on adherence
17. Adherence and barriers to adherence questionnaires will be collected at - 3 months, baseline, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months, 21 months and 24 months. This will assess adherence impact with overall medical treatments for CF
18. MEMs caps reading will be at 12 months and will assess adherence to TCMT
19. Antibiotic use (through prescribed treatment plan and pharmacy pick up rates) will be measured at baseline, 12 months and 24 months, and will assess the impact of the introduction of TCMT on antibiotic treatment for pulmonary disease
20. Effect of TCMT on sweat, sweat chloride will be measured at baseline, 3 months, 12 months and 24 months

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
30/06/2029

Eligibility

Key inclusion criteria
Current inclusion criteria as of 12/08/2025
There are two study populations.
1. Those previously on RECOVER prescribed ETI
2. Those not previously on RECOVER who are switching from ETI to VTD

Participants may only be selected for inclusion in RECOVER if they have been independently determined by their treating physician to be suitable for treatment with TCM in compliance with the official marketing authorization and summary of product characteristics (SPC). The decision to include participants in the study is independent of the decision to prescribe TCM. Participants

will receive treatment only through prescription by their physician through usual clinical treatment pathways.

Subjects on TCM:
In exceptional circumstances where baseline clinical data have been collected prior to the start of treatment, either through clinical care or ethically approved research projects (including a cohort of subjects initially recruited to this study on the understanding that it was a non-regulated observational study), subjects already receiving ETI may be recruited to this study and undergo on-treatment visits. Any additional patient data can only be added with written informed consent from the patients/parents concerned.

All subjects must have a signed informed consent form and/or signed assent form when appropriate, as determined by the subject's age and individual site and country standards.

Male and female participants of childbearing potential must agree to adhere to contraception requirements as detailed in the local TCM SmPC and in line with the standard of care.

As this is a real-world study, all eligible subjects, including those with FEV1 values lower than 40% or greater than 90% and/or those with significant comorbidity or multi-resistant or atypical organisms, will also be included in the study.

As the study is observational in Ireland, contraception requirements are not needed for study participation.

Previous inclusion criteria as of 20/03/2024:
Inclusion Criteria for Parent Study (UK CTIMP Sites)
1. Participants may only be selected for inclusion in RECOVER if they have been independently determined by their treating physician to be suitable for treatment with ETI in compliance with the official marketing authorization and summary of product characteristics (SPC). The decision to include participants in the study is independent of decision to prescribe ETI. Participants will receive treatment only through prescription by their physician through usual clinical treatment pathways.

Inclusion Criteria for Subjects on ETI
1. In exceptional circumstances where baseline clinical data has been collected prior to the start of treatment either through clinical care or ethically approved research projects (including a cohort of subjects initially recruited to this study on the understanding that it was a non-regulated observational study) subjects already receiving ETI may be recruited to this study and undergo on-treatment visits. Any additional patient data can only be added with written informed consent from the patients/parents concerned.

2. All subjects must have a signed informed consent form and/or signed assent form when appropriate, as determined by the subjects age and individual site and country standards.

3. Male and female participants of childbearing potential must agree to adhere to contraception requirements as detailed in the local ETI SmPC and in line with the standard of care.

Inclusion Criteria for Extension Study (UK CTIMP Sites)
1. Children and adults with CF who have completed two years participation on the parent study, and are willing to provide informed consent for continued data and bio-sample collection for a period of five years.

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Previous inclusion criteria as of 29/04/2021:

Inclusion Criteria for RECOVER CTIMP (UK clinical sites only):
1. People with CF aged 12 years and over: Participants may only be selected for inclusion in RECOVER if they have been independently determined by their treating physician to be suitable for treatment with Kaftrio in compliance with the official marketing authorization and summary of product characteristics (SPC). The decision to include participants in the study is independent of decision to prescribe Kaftrio. Participants will receive treatment only through prescription by their physician through usual clinical treatment pathways
2. Children aged 6-11 years will be included in the study only if and when Kaftrio is licenced, approved and funded for this age group. Participants may only be selected for inclusion in RECOVER if they have been independently determined by their treating physician to be suitable for treatment with Kaftrio in compliance with the official marketing authorization and summary of product characteristics (SPC). The decision to include participants in the study is independent of decision to prescribe Kaftrio. Participants will receive treatment only through prescription by their physician through usual clinical treatment pathways.
3. In exceptional circumstances where baseline clinical data has been collected prior to the start of treatment either through clinical care or ethically approved research projects (including a cohort of subjects initially recruited to this study on the understanding that it was a non-regulated observational study) subjects already receiving Kaftrio may be recruited to this study and undergo on-treatment visits. Any additional patient data can only be added with written informed consent from the patients/parents concerned.
4. All Subjects (people with CF aged 12 years and over, children aged 6-11 years and subjects on Kaftrio) must be taking the full dose of Kaftrio (in accordance with the age-appropriate posology in the SmPC).
5. All subjects must have a signed informed consent form and/or signed assent form when appropriate, as determined by the subjects age and individual site and country standards.
6. Male and female participants of childbearing potential must agree to adhere to contraception requirements as detailed in the local Kaftrio SmPC and in line with the standard of care.

Inclusion Criteria for RECOVER Observational Study (Irish Sites Only):
1. Children and adults with CF independently determined to commence on triple combination CFTR modulator treatment as covered by the license given by the manufacturer.
2. As this is a real-world study, all eligible subjects, including those with FEV1 values lower than 40% or greater than 90% and/or those with significant comorbidity or multi-resistant or atypical organisms will also be included in the study.
3. Subjects must be taking the full dose of the triple combination compound.

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Previous inclusion criteria:

1. Children and adults with CF and starting on triple combination CFTR modulator treatment
2. Subjects must be taking the full dose of the triple combination compound.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
6 years

Sex
All

Total final enrolment
206

Key exclusion criteria
Current exclusion criteria as of 12/08/2025:
1. Patients not willing to comply with study procedures or assessments.
2. Individuals on clinical trials of investigational CFTR modulators.
3. Clinical instability at baseline assessments. Subjects undergoing an active exacerbation and at the beginning of their treatment should be excluded from the study as this is likely to skew the data.
4. Any contraindication to TCM treatment as per the local approved SmPC.
5. Severe hepatic impairment.
6. Pregnant and breastfeeding women.

Previous exclusion criteria as of 20/03/2024:

Exclusion Criteria for Parent Study (UK CTIMP Sites)
1. Patients not willing to comply with study procedures or assessments.
2. Individuals on clinical trials of investigational CFTR modulators.
3. Clinical instability at baseline assessments. Subjects undergoing an active exacerbation and at the beginning of their treatment should be excluded from the study as this is likely to skew the data.
4. Any contraindication to ETI treatment as per the local approved SmPC.
5. Severe hepatic impairment.
6. Pregnant and breastfeeding women.

Exclusion Criteria for Extension Study (UK CTIMP Sites)
1. Participants not willing to comply with study procedures or assessments.

Previous exclusion criteria as of 29/04/2021:

Exclusion Criteria for RECOVER CTIMP (UK clinical sites only):
1. Patients not willing to comply with study procedures or assessments
2. Individuals on clinical trials of investigational CFTR modulators
3. Clinical instability at baseline assessments. Subjects undergoing an active exacerbation and at the beginning of their treatment should be excluded from the study as this is likely to skew the data
4. Any contraindication to Katrio treatment as per the local approved SmPC
5. Severe hepatic impairment
6. Pregnant and breastfeeding women

Exclusion Criteria for RECOVER Observational Study (Irish Sites Only):
1. Patients not willing to comply with study procedures or assessments. Individuals on clinical trials of investigational CFTR modulators.
2. Clinical instability at baseline assessments. Subjects undergoing an active exacerbation and at the beginning of their treatment should be excluded from the study as this is likely to skew the data.

Previous exclusion criteria:
1. Patients not willing to comply with study procedures or assessments
2. Individuals on clinical trials of investigational CFTR modulators.

Date of first enrolment
01/08/2020

Date of final enrolment
01/08/2026

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Ireland

Study participating centre
Children's Health Ireland at Crumlin
Crumlin
Dublin
Ireland
D12 N512

Study participating centre
Children's Health Ireland at Temple Street
Temple Street
Dublin
Ireland
D01 YC67

Study participating centre
Children's Health Ireland at Tallaght
Tallaght

Dublin
Ireland
D24 NR0A

Study participating centre
University Hospital Limerick
Children's Arc
Butterfly ward
St. Nessans Rd
Dooradoyle
Limerick
Grenada
V94 F858

Study participating centre
St. Vincent's University Hospital
Merrion Road
Dublin
Ireland
D04 N2E0

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Sydney St
Chelsea
London
United Kingdom
SW3 6NP

Study participating centre
Royal Belfast Hospital for Sick Children
274 Grosvenor Rd
Belfast
United Kingdom
BT12 6BA

Study participating centre
Beaumont Hospital
Beaumont Road
Beaumont
Dublin 9

Ireland
D09 C562

Sponsor information

Organisation
Royal College of Surgeons in Ireland

ROR
https://ror.org/01hxy9878

Funder(s)

Funder type
Charity

Funder Name
Cystic Fibrosis Foundation

Alternative Name(s)
CF Foundation, CFF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Funder Name
Cystic Fibrosis Trust

Funder Name
Cystic Fibrosis Ireland

Results and Publications

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/11/2023	20/03/2024	Yes	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 7.0	09/01/2024	20/03/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes