ECFS CTN 2022 Annual Report

2022/
Annual Report

Clinical Trials Network

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Message from the CTN Director

Damian Downey

We are excited to share with you the 2022 year report of the ECFS-CTN (European Cystic Fibrosis Society - Clinical Trial Network). This report gives you an overview of our work in 2022, clinical trials that we have supported, a description of the European projects we are involved in, and specific activities including the COVID-19 Antibody Responses in CF (CAR-CF) study.

During 2022 we supported 32 studies to help bring new therapies closer to people with CF. This would not have been possible without people with CF taking part in clinical trials facilitated by all our research teams across Europe. We will continue to support new and novel therapies to ensure all people with CF have effective treatments.

The Investigator Trial Committee in the CTN oversees the CAR-CF study across our European sites. It is our first investigator led study and demonstrates the agility of the CTN to develop new studies to answer important questions for the CF community. We are very thankful for your incredible support to date, and we hope to publish some preliminary results next year.

We are indebted to the patient organisations and people with CF who have provided their feedback and ideas. The various quotes in the report from people with CF, actively involved in the CTN, highlight the important work undertaken within our network. The patient-centred project, Pro-CF (Patient reported outcomes in CF) continues to move forward under the guidance of Isabelle Sermet and Kate Hill from our Standardisation Committee.

We gratefully acknowledge our partners for their sustained funding of our network, including the patient organisations from France, UK, Italy, Belgium, the Netherlands, Switzerland, Luxemburg, Germany, Poland, Israel and Ireland. We are also very thankful for the financial support of the Cystic Fibrosis Foundation (US) for supporting, additional research staff in many of our sites, the CTN Core Centre in Leuven, and the CAR-CF study.

Our network could not have achieved the current level of success without a strong and engaged team. I would like to thank Veerle Bulteel, Anne Verbrugge and Katia Reeber as well as our Executive Committee members for their unwavering support and engagement. The management of complex data and the development of this excellent report would not have been possible without Fiona Dunlevy, quality manager of the CTN. We are also appreciative of the support from our partner networks, the Therapeutics Development Network (TDN) in the US and the CF Canadian Accelerating Clinical Trials Network (CanACT).

Finally, we are so thankful for all your support. Please give us your feedback on this report and contact us if you have any comments or items you would like to have included in future reports. Feel free to share this report with your teams!

Yours sincerely,

Damian Downey
Director ECFS-CTN

Clinical Trials Network

2022 OUR YEAR IN NUMBERS

1914 PEOPLE with CF
newly enrolled into trials

Feasibility checks for **9** **trials**

x15 **protocols**
from 9 sponsors
reviewed by people with CF, their families, doctors, research coordinators & statisticians.

3
EU
projects ongoing

1400
enrolled into **CAR-CF**
COVID-19 antibody response in CF
to measure **Covid-19** antibodies

32 active trials supported

CFTR modulator (25)
Anti-infective (2)
Mucociliary clearance & airway surface liquid (1)
None (4)

102 **Happy People** at face to face training and meetings in June 2022

1 **scientific** **PUBLICATION** published

ECFS-CTN

Organisation

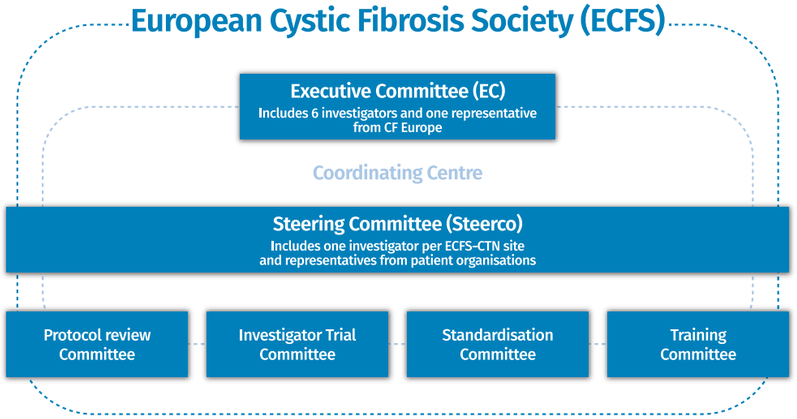
Our mission

Visit **www.ecfs.eu/ctn** to learn more about how ECFS-CTN speeds up clinical trials of new therapies for CF.

How we work

ECFS-CTN was founded in 2008 and aims to intensify clinical research in CF and to bring new medicines to people with CF as quickly as possible.

ECFS-CTN is made up of 57 sites in 17 countries and a central coordinating centre in Leuven, Belgium.



ECFS-CTN is run by:

- the Executive Committee, who meet by teleconference twice monthly. They develop network policies, steer actions to different committees and approve clinical trials to add to the CTN portfolio following protocol review.
- the Steering Committee (Steerco) is made up of 1 doctor from each member site, a representative from each of the funding patient organisations, executive committee members and CTN staff. Steerco members meet in person twice yearly to discuss CTN activities, strategies and common challenges.

The CTN Coordinating Centre has 5 staff members who organise the daily activities of CTN and support the various committees.

Our sites

ECFS-CTN

Executive Committee

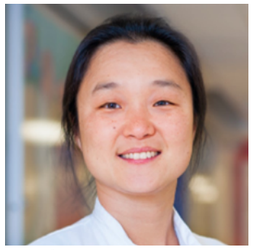
The executive team in 2022

Damian Downey
A doctor caring for adults with CF in Belfast, Northern Ireland.

Lieven Dupont
A doctor caring for adults with CF in Leuven, Belgium.

Nicholas Simmonds
A doctor caring for adults with CF in London, England.

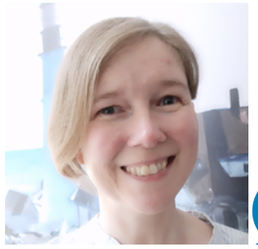
Thank YOU to Hettie who ended her term in December 2022



Hettie Janssens
A doctor caring for children with CF in Rotterdam, the Netherlands.

Dario Prais
A doctor caring for children with CF in Petah Tikva, Israel.

Philippe Reix
A doctor caring for children with CF in Lyon, France.



Jutta Bend
Coordinator of the German Clinical Trials Network and representing the patient voice in the ECFS-CTN.

CTN activities

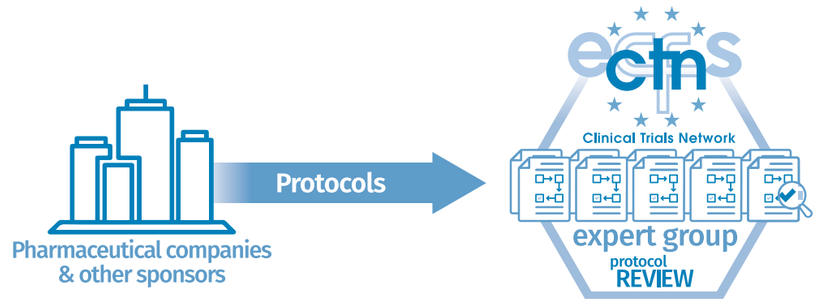
Supporting new trials

Protocol review & feasibility

Find out more on our website
www.ecfs.eu/ctn

Pharmaceutical companies who want to run clinical trials in ECFS-CTN sites must have their protocol reviewed by the ECFS-CTN protocol review team, including expert groups of CF doctors, research coordinators, academic researchers and people with CF and their families.

In 2022, we reviewed 13 commercial protocols from 8 different companies. We also reviewed 2 protocols for the HIT-CF European project.



The ECFS-CTN asked for clarifications or modifications for 7 protocols before approval. In total 11 protocols were approved, 3 were deferred, awaiting a second round. 1 protocol was not approved by the ECFS-CTN.

When a protocol is reviewed and approved, we tell all ECFS-CTN sites that the protocol had a successful review and whether we consider it high, medium or low priority.

In 2022, we coordinated feasibility checks for 9 trials (4 sponsors).

CTN activities

Protocol review

Protocol review

Every protocol is reviewed by a person with CF, or a family member of a person with CF. Three of our community protocol reviewers tell us why it's so important that people with CF review clinical trial protocols.

“ I think it is very right that people who personally know the ins and outs of the CF regime are commenting on the draft study. Patient representatives can judge whether a study can be at all compatible with the treatment regimen, whether the study is attractive enough for potential participants to take part.”

(Milan, Czech Republic)

“ As patient representatives, we are concerned with whether the design of the study fits the reality of the patients' lives, whether the effort is reasonable and justified, and whether there are suggestions for improvements above. There are always aspects that can be better assessed with the experience of more than 5 decades with my own cystic fibrosis than by a biologist or medical doctor.”

(Stephan, Germany)

“ While a family member/CF patient may not be the perfect medical expert, we are the experts when it comes to living with CF. I am convinced that our insights can help to make study designs more practical and easier to integrate.”

(Anne, Germany)

CTN activities

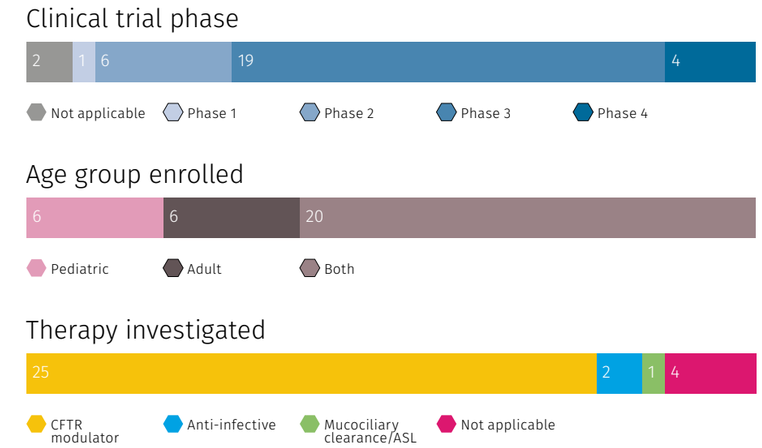
Clinical trials in 2022

Trials in ECFS-CTN member sites

Across ECFS-CTN there were 32 studies active during 2022. Most studies were assessing CFTR modulators and most studies were phase 3.

You can find a full list of the studies we supported in the appendix.

These graphs describe the 32 studies active in 2022, by clinical trial phase, by age group enrolled and by therapy investigated.



Find details of all trials we support (and results) at:
www.ecfs.eu/ctn/clinical-trials

CTN activities

Clinical trials in 2022

a clinical TRIAL

In the words of people with CF who participated

Tamir, an adult with cystic fibrosis from Israel, participated in a phase 2 trial of a compound for nonsense mutations in CFTR.

“ I participated in a trial with hopes to feel better and that it will help me and others with CF to find a solution for our disease. Unfortunately, the trial was not successful and did not have had a great influence or effect. However, I am happy that I could contribute to the research and the efforts to find a solution. I will participate in futures clinical trials and researches.”

Sara, an adult with cystic fibrosis from Wales, took part in a trial for a CFTR modulator.

“ I chose to take part in clinical trials as taking part in potentially groundbreaking research is exciting and rewarding, particularly knowing that this could benefit future generations, as well as myself. It gives me hope knowing that so much research is going on into improving CF care and trying to find a cure / treatments for the cause of CF, instead of just treating the symptoms. As someone who was born in the 80s when the life expectancy was early teens, this is huge progress!

I was lucky enough to have access to Kaftrio much earlier than the general CF population through a trial, which hugely stabilised my health at a time where I was on the brink of IVs / a hospital admission again. I feel very lucky to have been given this opportunity.

I completely trust my CF team, and the research team to tell me all the potential benefits and risks of the trial to allow me to make an informed decision about taking part with no pressure. My team make me feel well supported and they are there if I have any questions or worries about anything. I feel confident that I can withdraw from the study at any time if I change my mind or experience negative side effects, and know this wouldn’t affect my care going forward.

I’ve also found it positive that travel expenses have been covered in the trials I have taken part in, so I haven’t ended up out of pocket financially.

I would consider participating in any future trials that I felt able to and would recommend to anyone interested.”

CTN activities

Clinical trials in 2022

a clinical TRIAL

In the words of people with CF who participated

Sophie, an adult from France, participated in a study of an ENaC inhibitor.

Why did you participate in the trial?

I participated in the study to help with research, but also to have a treatment that could improve my quality of life.

Did it take a lot of time and effort to participate in the trial?

I took a lot of time to participate in this study (close visits, extra aerosol time…) But it didn’t take me any more effort. I’ve been using aerosols for a long time.

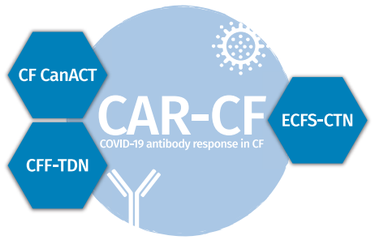
Would you participate in another trial in the future?

Yes, of course. I will gladly return to studies to advance research, and always with the goal of improving my quality of life. My genetic mutations mean that I do not have many proposals to take part in studies and so access to treatment is later.

CTN activities

Our Covid-19 response

Covid-19 antibody response in CF (CAR-CF)



CAR-CF is an investigator-initiated trial supported by ECFS-CTN. We are collecting blood samples from people with CF across Europe to detect whether the person had Covid-19 or not. We are working with patient organisations in Europe, Canada (CanAct) and the USA (CFF-TDN), who will do similar research in their countries. The project, called CAR-CF, will also look at how well people with CF develop immunity to Covid-19 after vaccination.

By the end of 2022, 39 sites in 13 countries were open to enrolment and 1400 people with CF were enrolled.

You can find the up-to-date number of recruited patients per site on https://www.ecfs.eu/ctn/projects/CAR-CF. The first results are expected in 2024.

CAR-CF received a research grant from the Cystic Fibrosis Foundation (CFF). French and Dutch sites received extra financial support from their national patient organisations.

A big thank you to the people with CF participating in the study, and to the patient organisations, investigators, and research coordinators.

CTN activities

Our Covid-19 response

Helen Groves

Helen Groves, a doctor in Belfast, explains her role in the CAR-CF project.

“ I am a paediatrician currently working in Belfast and am part of the research team for the CAR-CF project. The CAR-CF project, which was launched in 2021, is a very exciting and important study to look at the antibody responses to COVID-19 in people with CF. At the start of COVID-19 pandemic I was working at The Hospital for Sick Children in Toronto, Canada and worked with the research team involved in setting up the CAR-CF study in Canada. Using my connections to Belfast I was privileged to link in with Prof. Downey and subsequently became part of the team leading the European aspect of CAR-CF study. My initial involvement included study design and protocol development as well as helping to write study information and consent leaflets. Thereafter I have also been involved in recruiting patients for the study at the Children’s hospital in Belfast.

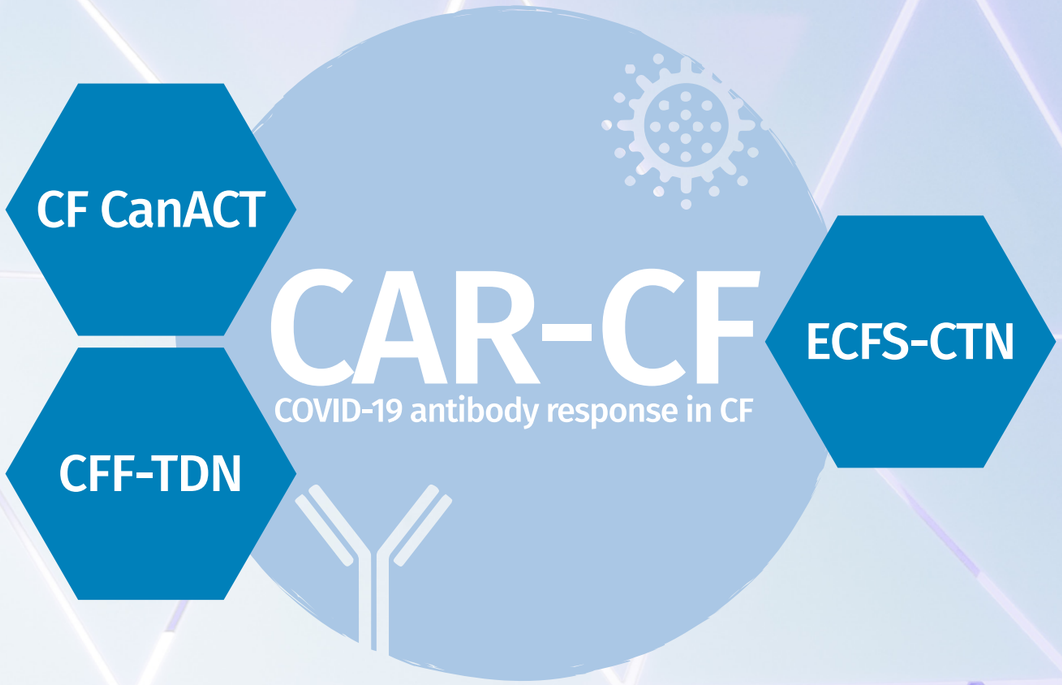
Another part of my role in the CAR-CF study has been to develop Case Report Forms and to set up the electronic database for collecting the study information for each participant. This has required a lot of work to set up and there has been some trouble-shooting and new processes to be developed to make sure all the information is properly collected. Alongside the study monitor I continue to regularly review the study database to make sure the data is entered correctly and to help solve any problems that arise.

This is the first time I have been part of a research project supported by the ECFS-CTN (European Cystic Fibrosis Society - Clinical Trials Network) and it has been very exciting to see the amazing work the ECFS-CTN does. It is wonderful to work alongside so many outstanding colleagues across the network and I am eager to see how the CAR-CF results can help people with CF. ”

CAR-CF

Timeline for a clinical trial

January 2020	July 2020	Aug-Dec 2020	February 2021	March 2021	May 2021	June 2021	July 2021	2022	2024
Plan to setup a CTN Investigator Trial Committee (ITC)	ITC first meeting – decided to launch CAR-CF study	Protocol review and feasibility	Country leads selected, regular teleconferences started	First ethics submission	First site activation	First person with CF included	Investigator meeting	Recruitment ongoing	Planned study end and publication of results



Beth, a person with CF from Wales, explains why she is taking part in CAR-CF

"I participated in the trial as I believe it's incredibly important to collect data on this topic. Hopefully it will help others and we can better understand what covid does to our bodies. This was such a straight forward trial to take part in, took no time or effort at all. Bloods were taken at regular appointments and I literally had to do nothing extra. I will always participate in further trials, certainly ones as straightforward as this."

Closer links with the ECFS Patient Registry

Combining our strengths

Stronger together

In 2022, we started working more closely with the ECFS Patient Registry (ECFSPR). As special projects of ECFS, our two groups have complementary expertise. Combining our strengths will help us perform powerful research projects. As well as discussing how to work together on research, we aligned our visual identities to show that we are sister groups within ECFS, who work closely together.

Closer links with the ECFS Patient Registry

Combining our strengths

Andreas Jung,
pediatric doctor and director of the ECFSPR

Andreas Jung, a pediatric doctor from Zurich and director of the ECFSPR from 2020 to 2023, explains why working together makes sense.

“ The ECFS-CTN and the ECFSPR are the biggest working groups of the ECFS. Their main common interest is to promote and conduct CF research, by clinical trials, epidemiological data analyses and pharmacovigilance trials. As research fields are overlapping and both working groups benefit from each others experience and acitivities, the CTN and ECFSPR Executive Committees have intensified their collaborative work over the recent years, to define future research priorities and undertake research projects. Eventually, this fruitfull collaboration will be of benefit for all people with CF in Europe. ”

Fiona Dunlevy,
quality manager in ECFS-CTN

Fiona Dunlevy, quality manager in ECFS-CTN, agrees.

“ Collaboration between patient registries and clinical trials is becoming more common in medical research. Patient registries such as ECFSPR already collect a huge amount of information, in a very structured way. Designing and running clinical trials via patient registries can greatly reduce the burden of clinical trial participation for patients, and reduce workload for medical staff in the CF centre.

The ECFSPR has already achieved accreditation from the European Medicines Agency to run studies investigating how recently approved medicines perform in the real world, in terms of safety and effectiveness. ECFS-CTN and ECFSPR now meet regularly to discuss how we can design and perform low-burden clinical trials that use registry data and data collection software. As well as discussing research ideas, patient priorities and trial designs, we have lots of challenges to overcome. For example, how to handle consent, regulations, data protection, as well as the daily practicalities of running and financing a big project.

Regulators such as the European Medicines Agency are open to hearing how patient registries can contribute to clinical trial design. It’s an exciting opportunity for ECFS-CTN and ECFSPR to combine our strengths and advance research into therapies for CF. ”

CTN activities

Our work

Training

For the first time since Covid-19, we had a face to face training day in June 2022. We brought together 102 happy investigators and research coordinators for a day of lectures, discussions and training.

Thea Pugatsch from Israel is a research coordinator and member of the ECFS-CTN training committee. She led a training session on Good Clinical Practice. Here, she explains why this is important for safe clinical trials.

“ Good clinical practice (GCP), isn’t that obvious?

Research that involves humans should be scientifically sound and ethical. Two sets of rules help ensure this: the Declaration of Helsinki and the Guidelines for Good Clinical Practice (GCP). Together these rules ensure ethical and scientific quality in designing, conducting, recording and reporting trials that involve humans. In addition, adhering to these rules allows comparison of studies regardless of where in the world the trials were conducted.

All members of a clinical trial team need to perform GCP exams and renew their certificate every few years. Adhering to GCP helps protect participants by ensuring a high level of quality for each trial conducted. The standards also ensure accurate reporting of study results and protect against fraudulent or misleading data.

Research Coordinators (RCs) are at the core of each and every study, and must be GCP experts.

Therefore, at the training day for RCs in Rotterdam, in 2022, we decided to test the knowledge of RCs.

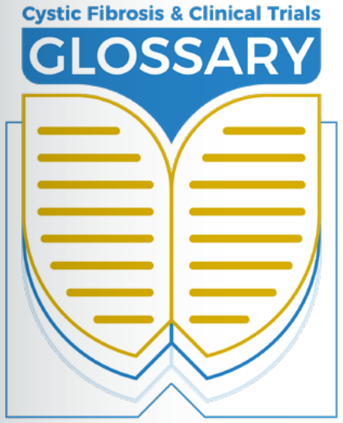
The participants formed groups, found a catchy name and worked together to answer 15 questions in our GCP quiz. Three possible and plausible answers were provided for each question. The questions ranged from rather easy to very tricky, which led to some lively discussions.

Congratulations to the “Rotterdam Research Rockets” who won first prize. At the end of the meeting, all questions were discussed, and the answers explained. The session was a learning experience for both organizers and RCs.”

CTN activities

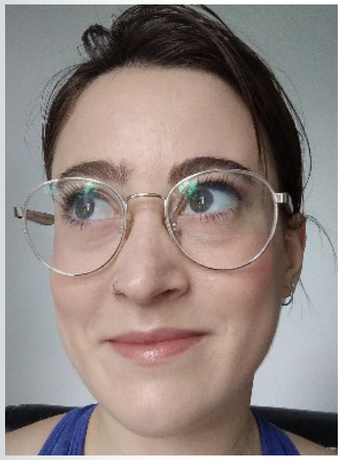
Our work

Plain language glossary



ECFS-CTN worked with CF Europe and its member patient organisations to create a plain language glossary of scientific terms that are often used in clinical trials. We secured funding from Queen’s University, Belfast to help promote the project and launched the glossary and a blog at the ECFS conference in June 2022.

Check out the glossary to learn more about words commonly used in clinical trials.



Jade Ashton

Jade Ashton, who lives with CF, is a freelance health science writer working on the glossary.

“ Accessibility of information is valued by people with CF and their families, particularly information about new research. It is my hope that anyone doing research in CF recognises the importance of involving the end-user, and finds the glossary useful to achieve this. Equally, as the glossary grows I hope we can help anyone wishing to learn more about CF, just as learning about my condition started my journey of empowerment. ”

CTN activities

Standardisation

Standard operating procedures

ECFS-CTN writes and shares guidance known as Standard Operating Procedures (SOPs), detailed documents explaining the steps to follow for measuring clinical trial outcomes.

In 2022, we published a scientific paper about how to isolate, cultivate and use primary nasal epithelial cells obtained by nasal brushing or tissue samples (polyp or lung).

Central Reading Core Facilities for Lung Clearance Index and Lung Imaging

We make sure that all our trial network sites work in a similar way when it comes to some of the special techniques needed for the clinical trials. We train and certify sites using some “central core” facilities. For example, for a measure of lung efficiency called Lung Clearance Index and for CT scanning.

To find out more, visit:

https://www.lungclearanceindex.com/

https://lunganalysis.erasmusmc.nl/

For general enquiries for all our SOPs , core reading facilities and standardisation group, please contact Kate Hill at:

k.hill@qub.ac.uk or the coordinating centre at ecfs-ctn@uzleuven.be

CTN activities

Standardisation

Patient-reported outcomes

PROMS

In 2019, ECFS-CTN started working with CF Europe (the European Federation of CF patient organisations) and a group of people with CF, to create a new quality of life questionnaire, also called a patient reported outcome measure. During 2021/2 we began the ‘validation’ of the questionnaire, that is, the testing of the tool with a group of people with CF, to see if the content and structure of the questionnaire was valid to use in both clinical and research settings. Using funding secured from the French patient organisation called the Association Gregory Lemarchal, the expert team based at Université Paris Descartes, have been analysing the data collected by colleagues Dr Trudy Havermans, Prof Lieven Dupont and staff. The results of this analysis will help to refine the questionnaire and make it easy to use in clinical trials and in everyday care.

Dr Simona Caldani and team have also been working on the development of a paediatric tool for ages 6 to 12 years of age and a tool for children less than 6 years of age which uses an emoji-based format for these younger children.

CTN Imaging in CF Special Interest Group

To enhance our understanding of lung imaging, the ECFS-CTN also set up an Imaging Special Interest Group in 2021, which continued to meet monthly through 2022 via teleconference. Led by Prof Harm Tiddens of Erasmus MC, Rotterdam, this group seeks to coordinate research in this important area of CF research.

The group is comprised of radiologists, medical physicists, paediatric and adult CF specialists, CTN and CF Europe representatives. In 2022, its 3 sub-teams have continued work on the development of guidance on each of the 3 areas:

1. CT Monitoring Strategies: to develop guidance for the CT examination of children and adults with CF, in partnership with our colleagues in the European Respiratory Society. This group is led by Michael Fayon (Bordeaux, France), Barabra Messore (Torino, Italy) and Luca Riberi (Torino, Italy).

2. Defining core sets of MRI sequences for use in a clinical setting. This group is led by Pierluigi Ciet (Rotterdam, Netherlands) and Jens Vogel-Claussen (Hannover, Germany).

3. Guidance on low dose strategies for CT. This group is led by Michael Maher (Cork, Ireland).

Putting lungs in the picture

Standardising lung imaging

In the picture with lung imaging

A picture speaks a thousand words - and this holds true for the lungs as well. There are many ways of testing how well a person's lungs are working, including the classic spirometry tests of lung function. Technological advances over the last 30 years have improved to a point where radiographers can now peer inside the lungs and take pictures of unprecedented detail. This practice, known as "imaging," has become so widespread and accessible that ECFS-CTN recently decided to agree on, or "standardize" the way to take and analyse lung images. Standardisation means that we can compare a person's lung images year after year to monitor for changes. Or we can compare lung images before and after a treatment, to look for any changes. Harm Tiddens is a professor of paediatric respiratory medicine at Erasmus MC Hospital in Rotterdam, the Netherlands, and has been championing lung imaging for over 30 years. Here, he tells us about the different types of images used to monitor lung health, and explains how ECFS-CTN is moving the field forward.

The limitations of chest X-rays

When Tiddens first started out as a CF physician, chest radiographs (also known as x-rays) were the most common way of sneaking a peek at the lungs. But, as Tiddens explains, this only gives a basic 2D snapshot of the lung, plus bits of the image are blocked by the heart and diaphragm. One day back in 1996, Tiddens stood around a light box with a radiologist, both peering at a chest X-ray film. "I couldn't see anything of interest", recalls Tiddens. Nor could the radiologist, who suggested that a CT scan might give more information.

CT scanning

CT (computed tomography) also uses radiation to image organs inside the body. Unlike traditional X-rays, a CT scanner takes multiple pictures in slices, that are then combined by a computer to give a detailed 3D image. "When a patient comes in, I can listen to the symptoms, I can use my stethoscope," says Tiddens, "I can't look in the lungs, I need the image to understand."

Tiddens and his team joined the ranks of several other European centres that were routinely imaging the lungs of people with CF using a CT scanner. The routine CT scans revealed often hidden lung problems, sometimes in patients who seemed to be in good health, and who had good results with lung function tests like spirometry. "We were really startled by the discrepancy," recalls Tiddens.

It turns out that a person with relatively normal lung function can be hiding structural problems in their lungs. The clear images and information from CT scans help patients participate in clinical decision making, by showing why a new treatment might be needed, even when lung function tests don't show up a problem.

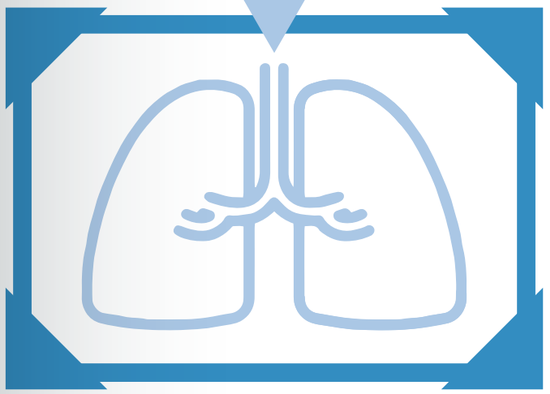
"I can't look in the lungs,

I need the image to understand"

Tackling the limitations of CT scans

The value of CT scanning was becoming clear. However, CT scans were more expensive, and reports, Tiddens explains, were "not reproducible between observers." In other words, radiologits and CF doctors obtained and interpreted the images differently in each hospital.

Tiddens and his colleagues set about developing a sensitive system to score signs of CF lung disease on CT scans. Their system, called the PRAGMA-CF score, turned CT scanning from a qualitative evaluation where each person makes their own expert interpretation into a quantitative evaluation, where a reproducible analysis method spits out a number at the end. "We started validating this system in 2002 and now have about 30 publications about it," says Tiddens, "So you're not fooled by FEV1 being stable, while progression of the structural lung damage is present on the CT."



Tiddens and his team put their expertise into practical use, with the LungAnalysis Core Facility based at Rotterdam Erasmus Hospital. A core facility offers specialised services to other researchers in academia or industry. The Lung Analysis core centrally analyses lung CT scans from hospitals all over Europe during clinical trials in various respiratory diseases.

Imaging in clinical trials

ECFS-CTN has been working with Tiddens over the years in various projects related to lung imaging in clinical trials. The SciFi project trained and certified ECFS-CTN sites in standardised CT scanning, to prepare them for using CT scanning in clinical trials. Then sites put their certification to work in the SHIP-CT clinical trial. "This was the first phase three study where CT imaging was the primary outcome measure," says Tiddens. "We showed that hypertonic saline was effective to improve the abnormalities on chest CT using the PRAGMA CF scoring system." As ECFS-CTN grew and expanded in 2018 and 2020, the SciFi2 project trained the new ECFS-CTN sites in standardised CT scanning, with the help of ECFS-CTN funding. In an ambitious new project, The LungAnalysis team is working with the ECFS Patient Registry, to add data from CT scans to the data collected and analysed by the registry. The team want to use these data to see the impact of CFTR modulator medicines on lung structure. "Quantitative information classifying the severity of the structural damage will now be part of the registry," says Tiddens. "In the long term, I think this study will also greatly help us to understand more risk factors for progression [of disease], and help us personalise monitoring."

A new standardisation group

This flurry of activity and progress in lung imaging also highlighted gaps in knowledge, protocols and know-how. This is where the structure of the ECFS-CTN Standardisation Committee came into play. In 2021, researchers, radiologists and doctors interested in lung imaging came together to form the Imaging Standardisation Special Interest Group.

The aptly named "How low can you go?" group is tackling issue of radiation risk. Repeated imaging using radiation based techniques, such as chest x-ray or CT scanning is an issue, because with every dose of radiation, a person accumulates their risk of the radiation causing damage to DNA, which could lead to cancer. Again technology advances are helping here. "The radiation used is coming down and down and down," says Tiddens, to the point that a CT scan now uses about the same radiation as a regular chest X-ray. The "how low can you go?" group, led by Prof Michael Maher from Ireland, is trying to define the lowest possible dose of radiation that still produces a useful CT scan. This should help allay worries about repeated exposure to radiation over a patient's lifetime.

"The radiation used is coming

down and down and down,"

Another team, led by Prof Michael Fayon from France, is looking at how to tailor CT monitoring plans to each person with CF, based on their risk of lung problems. This approach is known as stratified, or personalised monitoring. Right now, hospitals use a one size fits all approach, scanning all patients every year or two. But, as Tiddens explains, "maybe, we can get away with a CT scan every three years for low-risk patients, but maybe high risk patients need a CT scan every year."

Putting lungs in the picture

Standardising lung imaging

MRI

The third topic being tackled by the Imaging Standardisation Special Interest Group looks at a different kind of imaging, called MRI, short for magnetic resonance imaging. MRI uses a completely different approach to take pictures of the inside of the body. It uses powerful magnets to align water molecules in the body, then sends radio waves to capture the image. A computer then makes sense of all the data generated to build up a series of images. This method of imaging is particularly good for peeking at soft parts of the body like organs and tissues. The catch is that the method relies on the body part being imaged having plenty of water and minimal air. The lungs however have plenty of air and minimal water, which traditionally made it challenging to produce a clear MRI image. Technology has advanced though, allowing better definition of lung MRI images. You can also see mucus with MRI, an advantage when looking at CF lungs. A big advantage of MRI is that it doesn't use radiation. For this reason, MRI is sometimes called a dose-sparing technology.

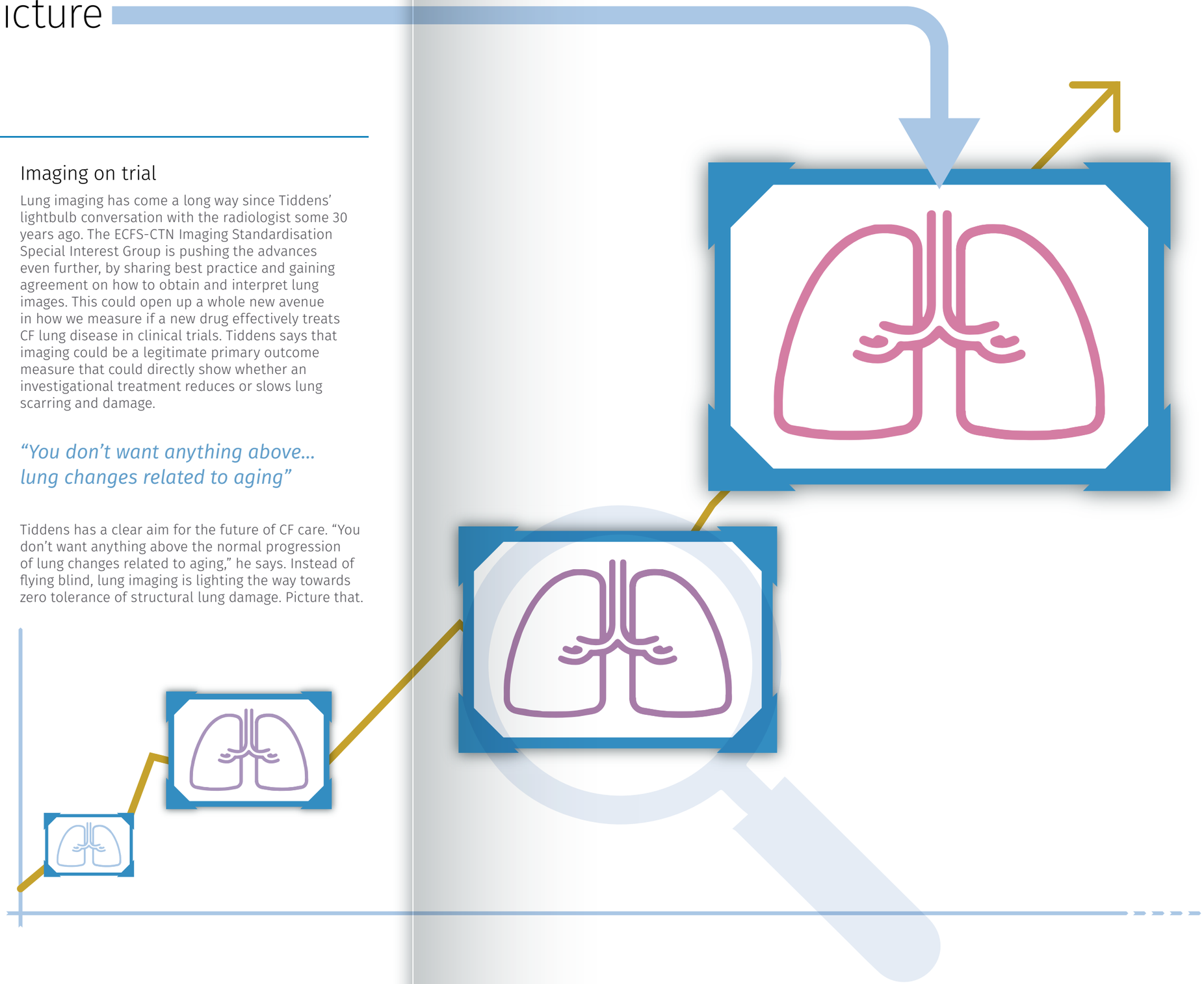
Like any other imaging method, MRI has its own set of advantages and limitations. One limitation is that many different types of machines exist. Plus every hospital has their own way of adjusting the machine's settings to obtain the image. The ECFS-CTN group is asking experts from different hospitals to share how they adjust their MRI settings (known as sequences, in imaging lingo) to get the best lung images. Agreeing on a common procedure to get the best lung image is the first step in being able to use MRI in clinical trials, to see if a new drug works as hoped. "One of the committees within the ECFS Clinical Trials Network is now defining a set of sequences for centres who want to start MRI," says Tiddens. This group, run by radiologist Pierluigi Ciet from the Netherlands, is hard at work developing expertise and recommendations. Another issue is that the MRI machines in most hospitals are already running at full capacity. "Now we're banging on the radiologist's door saying, listen we also want slots for our CF patients," says Tiddens, "the capacity of MRI is very competitive, and its very expensive."

Imaging on trial

Lung imaging has come a long way since Tiddens' lightbulb conversation with the radiologist some 30 years ago. The ECFS-CTN Imaging Standardisation Special Interest Group is pushing the advances even further, by sharing best practice and gaining agreement on how to obtain and interpret lung images. This could open up a whole new avenue in how we measure if a new drug effectively treats CF lung disease in clinical trials. Tiddens says that imaging could be a legitimate primary outcome measure that could directly show whether an investigational treatment reduces or slows lung scarring and damage.

"You don't want anything above... lung changes related to aging"

Tiddens has a clear aim for the future of CF care. "You don't want anything above the normal progression of lung changes related to aging," he says. Instead of flying blind, lung imaging is lighting the way towards zero tolerance of structural lung damage. Picture that.



CTN activities

Increasing & maintaining research capacity

Financial support to sites

Additional Research Capacity (ARC) award (2017-2020)

The CFF awarded $3,049,953 to fund additional research personnel in ECFS-CTN sites meeting certain criteria, as well as some structural support between 2017 and 2020. This funding allowed sites to take on more trials, and in some cases more complicated trials. The funding also allowed sites to dedicate more staff time to existing trials.

Continued Research Capacity (CRC) award (2021-2023)

As a continuation of the ARC award, the CFF kindly awarded 3 more years of funding worth $3 million for 2021-2023 to maintain the capacity at sites and the CTN coordinating centre and to support training and software. We are all extremely grateful to the CFF for providing this support!

European research projects

ECFS-CTN is a partner in several EU projects

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement no 777389. The Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Collaborative network for European clinical trials for children (c4c)

c4c is facilitating new and safer medicines for children by building a European network for paediatric clinical trials (in all diseases, not just CF).

Our role in this vast project is in the education work package. We helped revise and tailor some general clinical trials training to paediatric clinical trials. When preparing the annual report (March 2022), we received the news that the cASPerCF trial has been prematurely ended.

https://www.imi.europa.eu/

https://conect4children.org/

European Reference Network-LUNG

ECFS-CTN is a core network within ERN-LUNG and provides advice to groups who are setting up new clinical trial networks for other lung diseases.

https://www.ern-lung.eu/

European research projects

ECFS-CTN is a partner in several EU projects

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no 755021.

The HIT-CF Europe project

HIT-CF Europe is a research project which aims to provide better treatment and better lives for people with CF and rare mutations. To do this, drug candidates of several companies are tested in the laboratory on patient-derived mini-intestines (called organoids). Secondly, based on the reaction in the organoids, a smaller group of patients will be assigned to clinical trials with the drug candidates. All participating sites are part of the ECFS-CTN.

In 2020, despite Covid-19, organoids were screened with the CFTR modulating drug candidate from Proteostasis Therapeutics, Inc. (PTI). Plans for the clinical trial (called "CHOICES") progressed and 52 participants whose organoids show a variety of responses will be invited to take part.

The HIT-CF community has had to deal with the characteristic high volatility of the biotech and pharmaceutical industries. The HIT-CF consortium is confident that new partners will fully support the efforts of the community to bring new drugs to people with CF with ultrarare mutations.

https://www.hitcf.org

European research projects

News from HIT-CF

Elise Lammertyn,
Head of research at CF Europe

Elise Lammertyn is head of research at CF Europe, the European umbrella organisation of national patient organisations. She gives an update on HIT-CF.

“ 2022 turned out to be a year full of uncertainties for the HIT-CF project. In spring, the team initiated the procedure to obtain permission from the national competent authorities to run the CHOICES trial. The goal of this clinical trial is to evaluate the efficacy and safety of new drug candidates in people with rare CF mutations selected through preliminary tests in the laboratory on their organoids. Since 31 January 2022, the procedure of applying for permission to run a trial is harmonized throughout Europe via the Clinical Trials Information System or CTIS. The advantage of this is that one procedure leads to one decision applicable for all countries in which you want to run the trial, instead of having to submit a clinical trial application in every country separately. This increases efficiency and allows for a trial to start at the same time in different countries. Even though this centralized approach was well received by the HIT-CF team, familiarizing yourself with a new procedure takes time and it could leave you with unpleasant surprises. Indeed, in November 2022, the team was notified that the CHOICES protocol was rejected, mainly because some older data had to be updated and additional testing was required.

Fortunately, the consortium did not hold back. While additional funding was secured to guarantee the start-up and continuation of CHOICES, the team is now preparing CTIS resubmission. Meanwhile, the team made sure to share its learnings around the CTIS procedure with the clinical trial community during the ECFS-CTN Steering Committee meeting in January 2023. ”

Financial report 2022

Income & expenses

ECFS-CTN is funded by grants and by charging fees for scientific services to pharma companies.

ECFS-CTN helps pharma companies improve the design of clinical trials. It is important that we are not financially dependent on pharma companies so that we have no conflict of interest when giving scientific advice on clinical trials. Therefore, we limit our earnings from services to pharma, and rely on the generous support of other stakeholders to make up the shortfall. ECFS-CTN is grateful to the following organisations for funding our work in 2022: CFF and European patient organisations (from France, Germany, UK, Italy, Belgium, the Netherlands, Luxembourg, Switzerland, Ireland, Israel and Poland). We also thank CF Europe for coordinating the contributions from national patient organisations.

Financial report 2022

Income & expenses

Reflects book-keeping year 1 Jan – 31 Dec 2022:

CTN - Income & expenses 2022	Euro €
ECFS Support	100,000.00
National CF associations	118,037.50
Services to companies	165,211.40
LCI Core Centre	39,973.47
EU projects	40,815.51
Trial Management System license	3,493.28
Total Income	***467,531.16***
Travel / Meetings	8,190.00
Human resources	281,414.14
Computer & Software / Office equipment	2.866.73
Publication	7,693.75
Telecommunication	968.16
Training - Research Coordinators Support	14,807.00
Software Development / Maintenance	27,537.75
Dedicated server	14,071.00
CHEST-CT support	15.547.64
CAR-CF support	9.252,79
Miscellaneous	48.00
Total Expenditures	***382,396.97***
CTN result 2022	
Year result	**85,134.19**

Appendix

Studies supported by ECFS-CTN in 2022

RESTORE CFTR FUNCTION

New Phase 3 efficacy and safety testing of VX-121 combination therapy in people with CF who have one F508del mutation and one minimal function mutation. (VX20-121-102)

New Phase 3 efficacy and safety testing of VX-121 combination therapy in people with CF who have one of the following combinations of mutations 1) two F508del mutations, 2) one F508del mutation and one gating or residual function mutation, 3) no F508del mutation and at least one mutation responsive to triple combination therapy. (VX20-121-103)

New Phase 3 open-label long-term efficacy and safety testing of Kaftrio in people with CF aged 2 years and older (VX20-445-112)

New Phase 3 open-label long-term safety evaluation of Kaftrio in people with CF (VX20-445-121)

New Quality of Life in people with CF treated with Orkambi or Symkevi and their primary caregivers in the UK (Vertex VX20-CFD-004)

New Phase 3 efficacy and safety testing of Kaftrio in people with CF aged 6 years and older with a non-F508del mutation that is responsive to Kaftrio (Vertex VX21-445-124)

New A long term evaluation of how Kaftrio impacts people with CF in Europe (VX20-CFD-005)

Phase 3b open-label testing extension testing of Kaftrio in people with CF (Vertex, VX19-445-115; parent study =VX18-445-109)

Real World Clinical Outcomes with Novel Modulator Therapy Combinations in People with CF (Recover, Royal College of Surgeons in Ireland)

Phase 3b open-label testing of the effects of Kaftrio on cough and physical activity in people with CF aged 12 years and older with 1 F508del mutation and 1 minimal function mutation (Vertex VX18-445-126)

Phase 2 study of Galicaftor/Navocaftor/ABBV-119 Combination Therapy in people with CF with 1 or 2 F508del mutations. (Abbvie M19-771)

Phase 3b open-label testing extension testing of Kaftrio in people with CF (Vertex, VX19-445-115; parent study =VX18-445-109)

Phase 3b open-label testing of the effects of Kaftrio on glucose tolerance in people with CF and abnormal glucose metabolism (Vertex, VX19-445-117)

Phase 3 safety and efficacy testing of Kaftrio in children with CF aged 2-5 years. (Vertex VX19-445-111)

Phase 3b open-label safety and efficacy testing of the effects of long-term treatment with Kaftrio in people with CF aged 6 years and older with 1 F508 del mutation and 1 minimal function mutation (Vertex VX18-445-119)

Phase 2 testing of ABBV-3067 alone or in combination with ABBV-2222 in people with CF aged 18 and older with 2 F508del mutations. (Abbie M19-530)

Phase 2 safety and drug behaviour testing of ELX-02 in people with CF aged 16 years and older, with1 or 2 G542X mutations. (Eloxx EL-004)

Phase 3 testing of ivacaftor in children with CF aged under 2 years with a gating mutation (Vertex VX15-770-126)

Phase 2 open-label long-term observation of Orkambi's effect on CF progression in children aged 2-5 years with 2 F508del mutations (Vertex VX16-809-121)

Phase 3 testing of ivacaftor in children with CF aged under 2 years with a gating mutation (Vertex VX15-770-124)

Phase 3 open-label extension testing of Kaftrio in people aged 12 years and older with 1 or 2 F508del mutations (Vertex VX17-445-105; parent studies: VX17-445-102 and VX17-445-103)

Long term rollover testing of VX-661 in combination with ivacaftor in people aged 12 years and older with 1 or 2 F508del mutations (Vertex VX14-661-110)

Phase 3 open-label extension observation of long-term treatment with Symkevi in children aged 6 years and older with 1 or 2 F508del mutations (Vertex VX16-661-116; parent studies: VX16-661-113 and VX16-661-115)

Phase 3 open-label extension observation of long-term treatment with Kaftrio in people with CF with 1 F508del mutation and 1 gating or residual function mutation (Vertex VX18-445-110; parent study: VX18-445-104)

Phase 3 open-label extension observation of long-term treatment with Kaftrio in people with CF aged 6 years and older (Vertex VX19-445-107; parent study: VX18-445-106 Part B)

Long term safety testing of VX-445 combination therapy in unblinded phase 3 testing of in people with CF aged 12 years and older. (Vertex VX18-445-113)

ANTI-INFLAMMATORY

ANTI-INFECTIVE

Phase 1 study to evaluate safety and tolerability and to find the right dose of hypothiocyanite (OSCN-), bovine lactoferrin (bLF) and their combination (ALX-009) in males without CF and then in adults with CF and non-CF bronchiectasis. (ALX-009-CL-038)

Early Phase 1b/2a safety and efficacy testing of nebulised phage treatment of chronic lung infection with Pseudomonas aeruginosa in people with CF. (BMX-04-001)

Kaftrio = elexacaftor, tezacaftor and ivacaftor Orkambi = lumacaftor and ivacaftor Symkevi = tezacaftor and ivacaftor

Appendix

Studies supported by ECFS-CTN in 2022

MUCOCILIARY CLEARANCE

Phase 2 testing of safety and efficacy of inhaled SNSP113 in adults with CF. (Synspira SNSP113-19-201)

OTHER

A trial to see if people with cystic fibrosis taking Kaftrio have changed respiratory function after reducing nebulised mucoactive therapies (the CF STORM trial)

Covid-19 Antibody Responses in Cystic Fibrosis (CAR-CF): a study to measure antibodies to SARS-CoV-2 in blood samples from people with CF.

A study to assess how many children in Europe have signs of Aspergillus infection in their sputum (CASPerF, Ospedale Pediatrico Bambino Gesù)

Phase 4 remote evaluation of a wearable cough monitor in adults with CF taking Kaftrio (Vertex VX20-445-118)

Kaftrio = elexacaftor, tezacaftor and ivacaftor Orkambi = lumacaftor and ivacaftor Symkevi = tezacaftor and ivacaftor

ecfs Clinical Trials Network

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