2021/
Annual Report

Clinical Trials Network

www.ecfs.eu/ctn
ecfs-ctn@uzleuven.be
Tel : +32-479 983839

Contents

DOWNLOAD your personal version in PDF

www.ecfs.eu/ctn

Message from the CTN Director

Damian Downey

We are excited to share with you the 2021 year report of the ECFS-CTN (European Cystic Fibrosis Society - Clinical Trials Network). This report will give you an overview of our work in 2021, 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 2021 we supported 28 studies to help bring new therapies closer to people with CF. Our work over the last number of years has supported the introduction of CFTR “triple therapy” which has been a momentous achievement. This would not have been possible without people with CF taking part in clinical trials facilitated by all our research teams across Europe. Our journey does not stop here, as we continue to support new therapies in development to ensure all people with CF avail of effective treatments.

We continue to witness the Covid-19 pandemic, which has been an incredibly challenging time for the CF community. We continue our fantastic collaboration with the ECFS-Patient Registry in order to publish updates of Covid-19 in CF. The Investigator Trial Committee in the CTN has overseen the initiation of 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. It has been an enormous undertaking, with many challenges, but we are confident it will provide valuable clinical data. We are very thankful for all your support.

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 Hayes 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 and Germany. We are also very thankful for funding from 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, Kate Hayes 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

2021 OUR YEAR IN NUMBERS

4 **scientific PUBLICATIONS** published

529 PEOPLE with CF newly enrolled into trials

Feasibility checks for **10** **trials**

x10 protocols

from 6 companies

reviewed by people with CF, their families, doctors, research coordinators & statisticians.

3 **EU** projects ongoing

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

28 active trials supported

- Restore CFTR function (18)
- Anti-infection (3)
- Mucociliary clearance & airway surface liquid (1)
- Other (6)

ECFS-CTN

Organisation

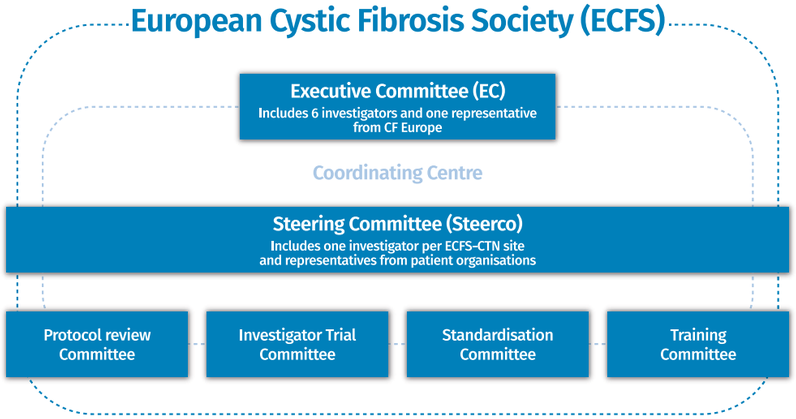
Our mission

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

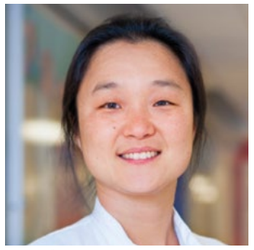
Executive Committee

The executive team in 2021

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.



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

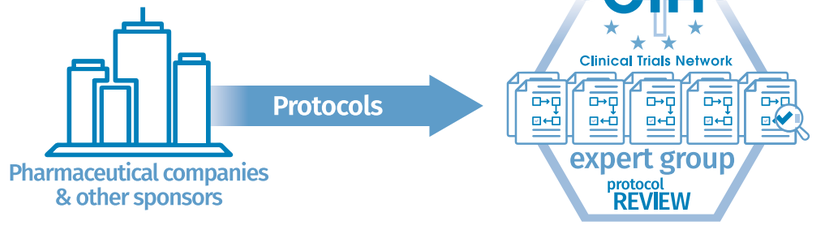
Supporting new trials

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 2021, we reviewed 10 commercial protocols from 4 different companies.



The ECFS-CTN asked for clarifications or modifications for 5 protocols before approval. In total, 10 protocols were approved, one with a contingent approval. 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.

After a protocol has been approved to run in ECFS-CTN, we help the sponsor identify appropriate sites to participate in the trial. In 2021, we coordinated feasibility checks for 10 trials (for 4 sponsors).

CTN activities

Clinical trials in 2021

Protocol review

Stephan, an adult with CF from Germany is a member of the protocol review committee, and explains what's involved.

I have been a member of the board of the German Cystic Fibrosis Organization (Mukoviszidose e.V., www.muko.info) for a very long time, namely since 1991. As a cystic fibrosis patient, but also as a natural scientist (I am a physicist), I have always been interested in research in the field of cystic fibrosis. So I gladly agreed when I was asked to join the ECFS Clinical Trials Network protocol review committee.

Sometimes it is difficult and time-consuming to read the study protocol and to find the relevant parts in the large number of pages. 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. For each protocol review, I invest about three long evenings to read and familiarize myself, and then to answer the questions.

Of course, it is very interesting to see how such studies are set up, the many issues which have to be taken into account, and the scientific questions they are supposed to answer. 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. Therefore, I very much welcome the fact that the ECFS Clinical Trials Network (ECFS-CTN) involves family members and patients in the review.

CTN activities

Clinical trials in 2021

Protocol review

Anne, an adult with CF from Germany is a member of the protocol review committee, and explains what's involved.

What motivated you to join the protocol review committee?

I am happy to have a chance to support scientific research and to be able to help in a small way to improve the treatment for CF.

Is it difficult to read a scientific protocol?

Once you are familiar with the general structure and recurring medical terms it's ok. However, it can be challenging sometimes.

Is it a lot of work?

Per review I need between 2 and 4 hours, depending on the complexity. This includes researching some of the medical terms, procedures, etc. I also try to find out if similar studies have already been done somewhere else.

What is interesting about participating in the protocol review committee?

For me the most fascinating part is to get an insight on current scientific developments. Sometimes the protocols are quite challenging - I love to dive into the descriptions and explanations and to finally understand them.

Why is it important that the protocol is reviewed by a family member?

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. Sometimes researchers are not aware of other CF factors - so we can bring in that perspective and make sure it is not overlooked.

Do you have any other remarks about protocol review?

I think it would be cool to have a Zoom get together of all the reviewers, just to get to know each other and exchange review experiences.

I am very proud to be part of this European group!

CTN activities

Clinical trials in 2021

Protocol review

Milan, an adult with CF from the Czech Republic is a member of the protocol review committee, and explains what's involved.

What motivated you to join the protocol review committee?

I wanted to help something completely unique and hugely beneficial - the development of new types of drugs for CF. It can make an incredible difference in the lives and destinies of people, not only with this disease, but also their families and friends.

Is it difficult to read a scientific protocol?

Yes, it is usually dozens of pages of technical text, which is often about detail. On the other hand, the Patient Reviewer is not there to evaluate the medical merits of the study.

Is it a lot of work?

Overall, it is several hours of work.

What is interesting about participating in the protocol review committee?

You are one of the first to know about future treatment options. Moreover, you are able to have very detailed information about new drugs. And finally, you have the opportunity to actively influence some sub-aspects of testing.

Why is it important that the protocol is reviewed by a family member?

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. Whether it contains too many obligations and conditions that cannot be fulfilled.

Do you have any other remarks about protocol review?

I have to appreciate the great professionalism of the whole process. From the initial approach to verify my interest in being an evaluator to the final feedback on my comments. You know exactly what is expected of you and you can see that your work is meaningful.

CTN activities

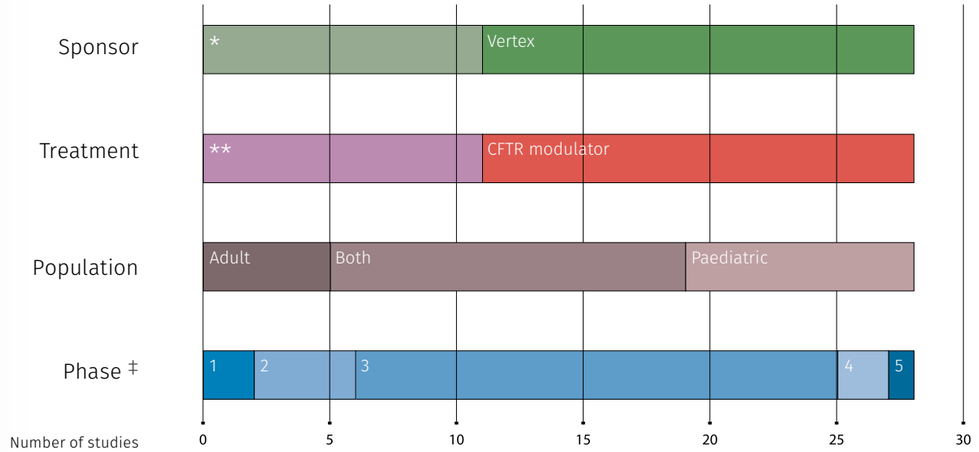
Clinical trials in 2021

Trials in ECFS-CTN member sites

The 28 studies included in this year's analysis were mostly assessing CFTR modulators. Studies were mostly phase 3.

Between November 2020 and November 2021, ECFS-CTN sites enrolled 529 people with CF into clinical trials. Three quarters of the people enrolled were adults.

You can find a full list of the studies we supported in the appendix (p. 36-37)



* Ospedale Pediatrico Bambino Gesu (OPBG) sponsored the 2 cASPerCF studies. AbbVie sponsored 2 studies. The following sponsors had 1 study each: Royal College of Surgeons in Ireland (RCSI), UMC Erasmus, Synspira, Alaxia, Alder Hey NHS and Eloxx. CAR-CF has multiple national sponsors.

**mucociliary clearance and airway surface liquid (2 studies), ENaC inhibitor (1 study), anti-infective (2 studies), real-world evidence (3 studies) and no therapy (3 studies).

‡ CAR-CF does not have a phase.

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

CTN activities

Clinical trials in 2021

a clinical TRIAL

In the words of people with CF who participated

Leonoor

Marian and her daughter Leonoor are from the Netherlands. They describe their experience of Leonoor's participation in a trial for a CFTR modulator triple therapy.

" Years ago when our daughter Leonoor was diagnosed with cystic fibrosis one of our first thoughts was that she was going to die too young too soon. We were told that the developments in terms of drug research were very promising and that we should not despair. However, most drugs that were being developed were suitable for the most common mutations. Unfortunately, Leonoor has a rare mutation and I think that I do not have to explain that having a rare mutation within a rare disease is not the 'uniqueness' you want to have in life... Of course we had heard of all promising developments like Orkambi, and eventually Kaftrio. However, to protect ourselves mentally we embraced the thought that we would be just fine without any treatment suitable for her mutation. In the meantime we participated in almost every research project conducted by our hospital as long as it was not too invasive or burdensome for Leonoor. If the results from the research would not help her, it still might help somebody else.

To our astonishment we received a call in the fall of 2020 that Leonoor belonged to a small group of patients that met the criteria to participate in the Kaftrio trial and that out of that small group she had been randomly selected. Did we want to participate? Even though this was a chance that we never even had dared to dream of we still had to think about it. Of course we were jumping with joy by the thought that she could be one of the first kids under 12 in the Netherlands with access to Kaftrio. However quality of life turned out to be just as important. For ourselves we decided that we could make it work from a practical point of view. Scheduling the hospital visits on days on which one of us was working from home (Covid-19 also had some advantages...) so that the other kids were taken care of. But in the end the most important thing was Leonoor's opinion. We decided that if she said no we would not do it. We explained the advantages that she might have from

CTN activities

Clinical trials in 2021

a clinical TRIAL

In the words of people with CF who participated

Kaftrio and we told her what would be expected from her in terms of hospital visits and tests, and then she said yes!

The first phase of the trial was a challenge due to the high frequency of the hospital visits and the lengthy days, which were tiring for Leonoor. Luckily we are now in the second phase and on a somewhat looser visit scheme. In hindsight having to incorporate three new pills in our daily routine turned out to be the most difficult part of this trial. In the morning everything goes smoothly. We have our breakfast routine and those two pills are simply part of it. In the evening all goes well unless a play-date turns into staying over for dinner or a spontaneous sleep-over. Those unexpected events have proven to be our bottle-neck because they are not part of our rhythm. In the meantime we are getting the hang of it even with such unexpected events.

We will continue participating in research because it is so important. Nevertheless participation in a new trial is something we'll have to think about, or as Leonoor says herself:

"I sometimes find it annoying that we have to go to the hospital so often. Then I miss school and on Fridays are all the fun things. I like the heart film (for the ECG) the most, the stickers are nice and tickling! I find the LCI measurement the most stupid. I don't know if I would like to participate in another study, it depends on how often we have to go to the hospital." "

CTN activities

Our Covid-19 response

The impact on people with CF and CF clinical trials

In 2021, we continued to work with the ECFS Patient Registry to collect information about the number of people with CF who had Covid-19. We published regular updates on the ECFS website and published a scientific paper about the risk factors for poor outcomes.

We also published a scientific paper about how clinical trial sites can mitigate the impact of the pandemic on clinical trials. This paper was based on ideas collected from ECFS-CTN sites via regular surveys throughout 2020 and 2021.

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

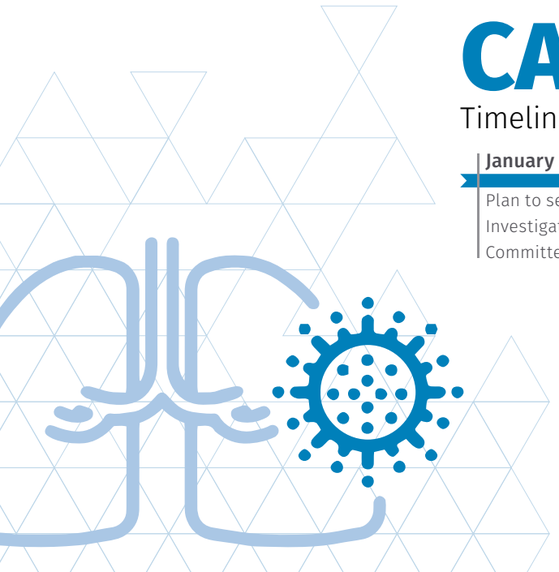
CAR-CF is an investigator-initiated trial supported by ECFS-CTN. We are collecting blood samples from people with CF across Europe to detect whether the person had Covid-19 or not. We are working with patient organisations in Europe, Canada (CanAct) and the USA (CFF-TDN), who will do similar research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

It will run in 14 countries in Europe, plus in Canada and the USA, and we hope to collect blood samples from thousands of people with CF.

By the end of 2021, 19 sites in 9 countries were open to enrolment and 317 people with CF were enrolled. 40 other sites in 5 countries were busy doing all the administrative preparations to start the study.

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

Timeline for a clinical trial

January 2020
Plan to setup a CTN Investigator Trial Committee (ITC)

July 2020
ITC first meeting – decided to launch CAR-CF study

Aug-Dec 2020
Protocol review and feasibility

February 2021
Country leads selected, regular teleconferences started

March 2021
First ethics submission

May 2021
First site activation

June 2021
First person with CF included

July 2021
Investigator meeting

2022
Planned end of inclusion

2024
Planned study end and publication of results

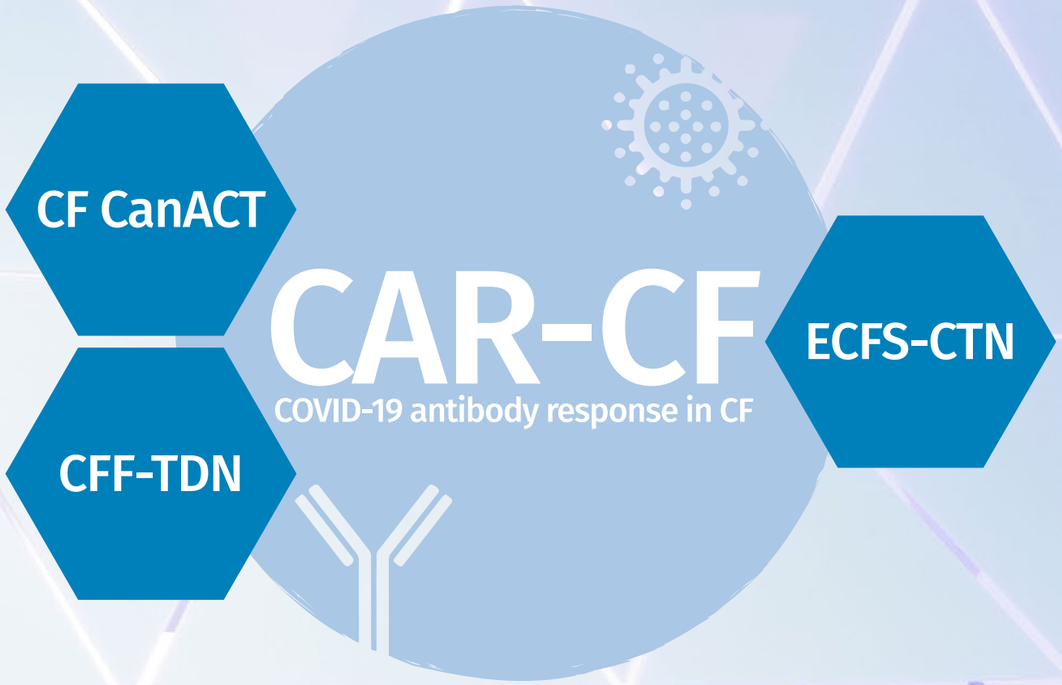
CTN activities

Our Covid-19 response

Jutta Bend

Jutta Bend is the coordinator of the German Clinical Trials Network which is run by the German patient organisation "Mukoviszidose eV". She represents the patient voice on the Investigator Trial Committee (ITC).

" It is a great opportunity and honour for me to represent the patient organisations as a member of the ITC, because this way patient-centered research can be realised. CAR-CF – the first investigator-initiated trial (IIT) project of the ITC – was launched in 2021. The pandemic still impacted all our lives and made planning of a multicenter, multinational study a tremendous challenge. I am proud however, that the first patients could be included into the study in Germany. This was achieved following a very good cooperation between the clinical trial site in Cologne and the German patient organisation I am working with. We translated and adapted the patient information documents needed for submission to Ethic committee and for informing people with CF in an appropriate way about CAR-CF and the possibility to take part. Other countries followed with similar cooperation between physicians and patient organisations: by the end of 2021, clinical trial sites in 12 countries had started and approx. 300 patients were included. There were lots of issues to be solved and processes to be developed: Examples are the agreements for data and material transfer, the electronic Case Report Form for the documentation of the data and the entry of the study into the trials register www.clinicaltrials.gov. Great progress was made and it is amazing to see people with CF and doctors working together to make this project a reality. "



Vincent, a person with CF from Germany. He explains why he is taking part in CAR-CF

"Fantastic that a study like the CAR-CF study was initiated! The Covid-19 pandemic affected us all very much - with a special threat to all patients with chronic lung diseases like CF. So gaining scientific knowledge out of this trial is essential. And to hear that this trial is performed as a huge European study is great as we need this unification especially in these currently very difficult times. I am proud to be a part of it."

CTN activities

Our work

Training

Usually, we hold a training day for investigators and research coordinators in June, just before the ECFS conference. Unfortunately the Covid-19 pandemic meant that the 2021 conference, and all our training activities, had to be held online.

January 2021: steering committee meeting with 91 investigators participating (including speakers and panel).

June 2021: steering committee meeting with 74 investigators participating (including speakers and panel).

June 2021: research coordinator training with 139 research coordinators and investigators participating (including speakers and panel), focused on clinical trial audit. For the interactive workshop 57 research coordinators joined in real time.

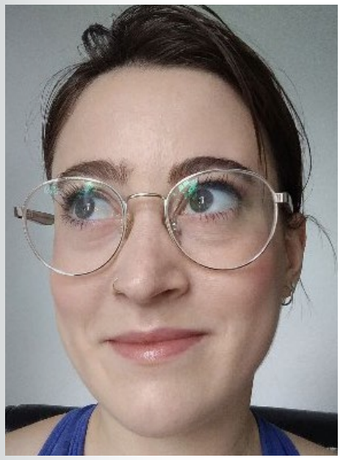
October 2021: we had a 3-part webinar about real world evidence, including speakers from academia and industry, as well as regulatory and reimbursement agencies. We had 329 participants for the 3 webinars, with some teams participating via one computer connection.

CTN activities

Our work

Plain language glossary

ECFS-CTN is working with CF Europe and its member patient organisations to create a plain language glossary of scientific terms that are often used in clinical trials. In 2020 we created a pilot glossary of 11 terms. In 2021, we asked people with CF and people from the general public for their feedback and advice on improving the glossary. We secured funding from Queen's University, Belfast to help promote the project and launch the glossary at the ECFS conference in June 2022.



Jade Ashton

Jade Ashton, who lives with CF, is a freelance health science writer.

" I have had the privilege to be part of this project, both as a reviewer and subsequently as a writer, for just over a year now. It has been wonderful to work with such a fantastic team on a project that will have an impact on people in the CF community. Accessibility of information is valued by people with CF and their families, particularly information about new research – hearing about ongoing research provides a good amount of hope for the future, and showcases how fundraising and donations can have positive effects on people's lives. 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 and associated blogs provide context, I hope we can help anyone wishing to learn more about CF, just as learning about my condition started my journey of empowerment. I give my thanks to all who are making this project possible. "

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.

During 2021:

- We wrote a new SOP about how to isolate, cultivate and use primary respiratory epithelial cells obtained by nasal brushing or polyp or lung explants (May 2021)
- We updated an existing SOP about Sweat Induction and Collection Macroduct® Advanced (this SOP does not replace the existing Sweat test SOP, but is for the sites using the newer equipment) (December 2021)
- We also published a paper in JCF article about sputum biomarkers.

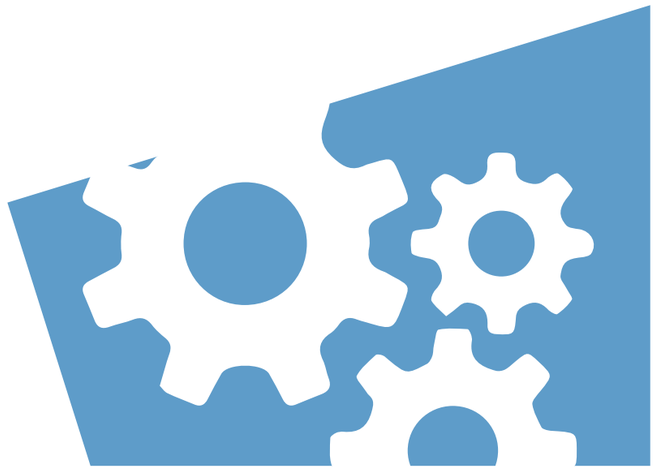
CTN activities

Standardisation

CTN Imaging in CF Special Interest Group

In 2021 the Imaging in CF Special Interest Group, led by Prof Harm Tiddens of Erasmus Medical Center, Rotterdam, met monthly via teleconference to coordinate research in this important area of CF research. Its aim is to produce recommendations/guidelines for CT and for MRI protocols that could potentially be used by CF centres and people with CF. The group includes radiologists, medical physicists, paediatric and adult CF specialists, CTN and CF Europe representatives. It is made up of 3 sub-teams who also meet monthly and are exploring the following areas:

1. CT Monitoring Strategies: to develop guidelines for CT examinations for children and adults, in partnership with our colleagues in the European Respiratory Society. This group is led by Michael Fayon (Bordeaux), Barbara Messore and Luca Riberi (Torino)
2. Defining core sets of MRI sequences for use in a clinical setting led by Jens Vogel-Claussen (Hannover) and Pierluigi Ciet (Rotterdam)
3. Low dose strategies for CT: led by Michael Maher (Cork)



CTN activities

Core Facilities

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.

Lung Clearance Index Core Facility

In July 2014, the CTN Lung Clearance Index Central Core Facility was established to set standards and assess traces submitted by CTN member sites, qualifying and certifying those sites who meet pre-set quality criteria.

The LCI Core Facility is co-led by Prof Jane Davies and Clare Saunders at the Royal Brompton/Imperial College London and their research team. They have extensive experience in multiple breath washout testing and interpretation of results.

This core facility offers expert consultation regarding standardisation of LCI procedures and staff training for clinical trials. To date they have trained and certified 45 CTN sites (179 operators) and in collaboration with core facilities in North America and Australasia have supported 22 clinical trials.

Any queries regarding the Core Facility at the Royal Brompton/Imperial College London, please contact: c.saunders@imperial.ac.uk or LCICore@rbht.nhs.uk or visit https://www.lungclearanceindex.com/

The LCI Team: Chris Short, Gina Rivellini, Clare Saunders, Jane Davies, Mary Abkir, Sophie Pinnell.

“It has been encouraging to see the impact the ECFS CTN Core Facility has been able to have in the adoption of LCI into clinical trials over the last few years. Until now mainly used in paediatrics, it seems likely that more sensitive outcome measures such as this will be increasingly helpful in the adult population on CFTR modulators.”

Prof Jane Davies

CTN activities

Core Facilities

Lung Imaging Core Facility

To ensure that all our CTN sites are following similar practice and following the 2019-2020 consultation across all ECFS-CTN sites, the Lung Analysis lab of the Erasmus Medical Centre in Rotterdam is now standardising chest-CT scans across all ECFS-CTN sites.

25 sites have been certified by the central lab with a further 16 in the process.

Website: https://lunganalysis.erasmusmc.nl/

Any queries, please contact Jorien at: j.vandeputtelaar@erasmusmc.nl

For general enquiries for all our SOPs and group, please contact Kate Hayes at: k.hayes@qub.ac.uk or the coordinating centre at ecfs-ctn@uzleuven.be for details of these SOPs and all the others too!

CTN activities

Increasing & maintaining research capacity

Financial support to sites

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

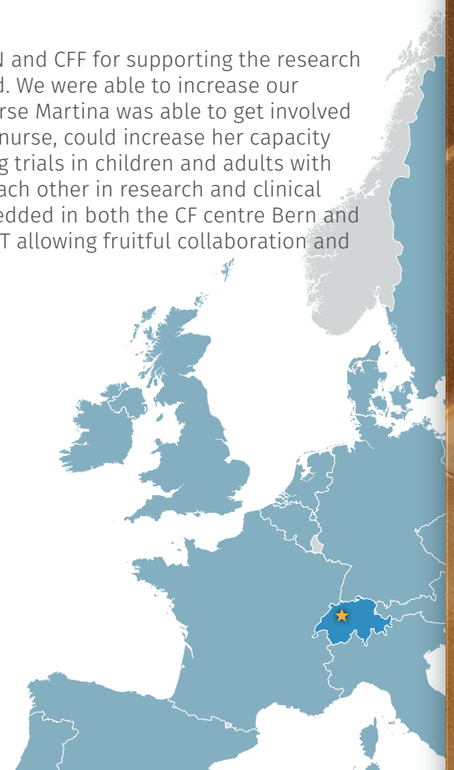
The CFF awarded $3,049,953 to fund additional research personnel in ECFS-CTN sites meeting certain criteria, as well as some structural support between 2017 and 2020. This funding allowed sites to take on more trials, and in some cases more complicated trials. The funding also allowed sites to dedicate 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 totalling $3,063,615 for 2021-2023 to maintain the capacity at sites and the CTN coordinating centre. We are all extremely grateful to the CFF for providing this support!

Florian Singer, the principal investigator in Bern, Switzerland explains how the CRC award helped his site.

“ We are very grateful to the ECFS-CTN and CFF for supporting the research capacity at our site in Bern, Switzerland. We were able to increase our personnel resources. Our clinical CF nurse Martina was able to get involved in research. Barbara, another CF study nurse, could increase her capacity and provide more support for upcoming trials in children and adults with CF. Barbara and Martina complement each other in research and clinical aspects. Barbara and Martina are embedded in both the CF centre Bern and the paediatric research network PEDNET allowing fruitful collaboration and knowledge exchange. ”



ecfs ctn

Clinical Trials Network

Patient-reported outcomes

A joint project with ECFS-CTN and CF Europe

PROMS

Why measure quality of life?

There are many ways of measuring whether a person's CF is stable, getting better or getting worse. One deceptively simple way is to just ask the person – after all nobody knows CF better than those living with it. However, turning the question "how are feeling?" into something that doctors and researchers can track, measure and compare is an altogether bigger task.

And this task is becoming more and more important, since the agencies in charge of approving licensing and reimbursement of new medicines take into account changes in "quality of life."

Agencies such as the European Medicines Agency will only accept quality of life data if it was collected using an agreed questionnaire, also called a patient-reported outcome measure (PROM). These questionnaires are developed and tailored to the condition itself and the age of the patient group taking part in the study. Researchers must "validate" the questionnaire to make sure that the right questions are included and that everyone understands the questions in the same way. Another important step in validation is to check if changes in the questionnaire results mirror changes in symptoms or other aspects of the condition. It is very important to validate questionnaires properly, so that their results can be used to help bring new medicines to patients.

Why do we need a new questionnaire in CF?

In CF, the most common quality of life measure is a questionnaire called the "Cystic Fibrosis Questionnaire-Revised" or the CFQ-R for short. This questionnaire has been used for many years and has featured in many clinical trials. However, some of the questions are a bit old-fashioned these days. For example, the availability of online banking means that a question about feeling well enough to go to the bank is now obsolete.

People with CF have been asking for a questionnaire that's more adapted to modern day life. 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.

The group met monthly via teleconferences over the course of 2 years, reviewing existing patient reported outcome measures used in CF. The group linked their findings with the results of another PROMs project, an interview-based study of 125 people with CF and their families to see what topics they would like to be included in a new questionnaire. We also surveyed clinical CF sites across Europe to see what tools and questionnaires they use in clinic visits.

2019:

Established patient advisory group

Collected information about PROMs used across Europe

2020:

Draft questionnaire developed, called PRO-CF

Pilot testing

2021:

Grant received to fund validation phase of PRO-CF

Experts hired to validate survey

Next:

Validation studies will be planned, performed and published

Final goal:

A validated, easy-to-use questionnaire that can be used in medicines development and in everyday care

Patient-reported outcomes

A joint project with ECFS-CTN and CF Europe

PROMS

A team behind the survey

The group then developed a new patient-created questionnaire and called it the PRO-CF (Patient-reported outcomes in CF). This questionnaire aims to more accurately assess people with CF's quality of life and allow them to report their symptoms, including areas not previously captured in existing tools.

During 2020, we did a big survey to check that the questionnaire was accurate and easy to understand. We used the expert patient feedback to improve and refine the questionnaire. We also published a research paper in the Journal of Cystic Fibrosis, outlining the importance and the process of the patient-created questionnaire (see Journal of CF paper and the lay summary). "There is a real need for a more adapted tool for PROMS in CF. And who could talk better about quality of life than the patients themselves?" says Audrey Chansard, France, who lives with CF and was author on the scientific paper.

In 2021, we reached the stage where we needed to validate the questionnaire. This validation step will make sure that the PRO-CF questionnaire can be used to support the development, licencing and reimbursement of new medicines. This is a very technical task, and we decided that we needed expert help. We successfully applied for funding from a patient organisation in France called the Association Gregory Lemarchal. The funding was used to hire experts in validating PROM questionnaires.

Simona Caldani, Emmanuel Devouche and Emilie Cappe, based at the Université Paris Descartes, are the experts who are working on the validation of the new questionnaire.

"It's so important to have people with CF create the new questionnaire, to truly represent the experiences of living with CF and to understand what works well and what needs to be improved in assessing quality of life," says Kate Hayes ECFS-Clinical Trial Network PROMs Project Coordinator. "The patient involvement in this project lets us plan and carry out this research in a way that is meaningful to people with CF."

Kate Hayes

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 "Health, demographic change and well-being" under grant agreement no 755234.

The European Commission (via H2020) is funding a clinical trial of the orphan drug OligoG CF-5/20 in CF

This is a clinical trial of the orphan drug OligoG CF-5/20 to help airway clearance in CF. Preparations in 2020 when the Covid-19 pandemic started were well advanced for this clinical trial in countries across Europe. However, the availability of new CFTR modulator medicines for people with CF in some European countries changed the treatment landscape in respiratory Cystic Fibrosis treatment. Therefore AlgiPharma and the clinical investigators in the study consortium have decided to pause further preparations and stopped the HORIZON 2020 project. Extensive reworking of a new trial design with OligoG is needed to fit into the new CF treatment landscape beyond the scope and time of the current EU grant.

https://oligogpivotalcf.eu/

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 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. In December 2020, PTI merged with Yumanity Therapeutics, which is now the formal owner of the CF portfolio and Eloxx merged with Zikani. The HIT-CF consortium is confident that these 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 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

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 from the CF Europe perspective.

“ 2021 was a demanding year for both the HIT-CF team and the whole CF community, requiring a great deal of flexibility and creativity. Covid-19 continued to test our patience, both in our personal and professional lives. The fact that we could not meet was frustrating and meant that we moved forward slower than hoped. But forward we went! At the end of 2020, the CHOICES trial was at risk because HIT-CF industry partner Proteostasis merged with Yumanity, which had no focus on CF. However in 2021, we were extremely happy to welcome the Dutch start-up company FAIR Therapeutics. They were able to obtain an exclusive license on the CF drug portfolio from Yumanity. Consequently, FAIR Therapeutics has made it its mission to bring drugs to people with rare forms of CF at affordable prices. Good news also reached us from our teams in the labs: they obtained excellent results with the primary and secondary organoid screen. Not only was there superb agreement between the first and the second screening, which strongly underlines the reliability of the results, also a number of organoids of HIT-CF participants responds quite well to the tested CFTR modulators. This means that we are all ready to start the next HIT-CF chapter: the CHOICES trial, for which preparations are in full swing.

At CF Europe, we are also very happy with Santhera joining the consortium. This gives options and alternatives to HIT-CF participants whose organoid did not respond well to the test modulators, and to the CF community as a whole. We eagerly await the first results of their clinical trial with neutrophil elastase inhibitor lonodelestat. We look forward to 2022 with great confidence, and we hope you share our excitement. ”

Financial report 2021

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 2021: CFF and European patient organisations (from France, Germany, UK, Italy, Belgium, the Netherlands, Luxembourg, and Switzerland). We also thank CF Europe for coordinating the contributions from national patient organisations.

Financial report 2021

Income & expenses

Reflects book-keeping year 1 Jan – 31 Dec 2021:

CTN - Income & expenses 2021	Euro €
ECFS Support	100,000.00
National CF associations	113,750.00
Services to companies	233,432.81
EU projects	37,769.60
LCI Core Centre	59,407.28
Trial Management System license	3,516.72
Total Income	***547,876.41***
Human resources	355,483.04
Chest CT coordinator support	25,912.70
Travel / meetings / courses	720.60
Software Development / Maintenance	1,089.00
Manuscript	1,331.25
Dedicated Server	12,522.29
Office equipment	1,452.67
Designer year report	2,550.00
Subscriptions online tools	820.72
Other	168.22
Total Expenditures	***402,050.49***
CTN result 2021	
Year result	**145,825.92**

Appendix

Studies supported by ECFS-CTN in 2021

RESTORE CFTR FUNCTION

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

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

New 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)

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

New 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 F508del mutation and 1 minimal function mutation (Vertex VX18-445-119)

Phase 3 safety and efficacy testing of Kaftrio in children with CF aged 6-11 years with 1 F508del mutation and 1 minimal function mutation. (Vertex VX19-445-116)

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. (Abbvie 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

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

New A clinical trial to assess a new dosing regime of an anti-fungal medicine called posaconazole (cASPerCF, Ospedale Pediatrico Bambino Gesù)

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)

MUCOCILIARY CLEARANCE

Inhaled hypertonic saline in preschoolers (UMC Erasmus SHIP-002)

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

OTHER

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

New 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.

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

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

New Quality of life in people with CF taking Orkambi or Symkevi and in their primary caregivers (Vertex VX20-CFD-004)

New 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)

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

Clinical Trials Network

www.ecfs.eu/ctn
ecfs-ctn@uzleuven.be
Tel : +32-479 983839