2019/ Annual Report

Clinical Trials Network

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Contents

Message from the CTN Executive Director

Silke van Koningsbruggen-Rietschel
Director ECFS-CTN

Dear Friends,

We are pleased to share with you the 2019 year report of the ECFS-CTN (European Cystic Fibrosis Society - Clinical Trial Network).
This report gives you an overview of our work in 2019 including general information about clinical trials and the role of the CTN, specific activities within our network, a list of all clinical trials run via our network in 2019, and a description of the various European projects – just to name some of the topics.

This report again is the result of excellent collaboration with patients and patient organisations who have provided their expert feedback and ideas. The various quotes in the report from patients who are actively involved in the CTN underline the important work that has been performed within our network. A new collaboration has been started with CF Europe focusing on trial results and their dissemination. Also, the patient-centred project on PROMS (Patient Reported Outcome Measures) is moving forward successfully under the guidance of Kate Hayes. Thank you very much for all your great commitment!

2019 has been a very busy year again: 26 studies were performed in our network, 15 protocols were reviewed, and 11 feasibilities conducted. Most studies were Phase III studies showing the successful progress of compounds moving through the pipeline; however, many Phase I and II studies were also conducted advancing new compounds through their clinical development.

We all worked very hard in 2019 and have accomplished major milestones of our mission: we have intensified clinical research in CF and we will have again, brought new medicines to our patients as soon as the “triple therapy” will be licensed in Europe. Although this triple therapy is a major milestone we are not done! The ultimate goal is to restore CFTR function in every individual patient (regardless of their mutation or home country), but also to reduce the remaining infection and chronic inflammation.
In the near future, many compounds are expected to evolve from the preclinical and early clinical phase which will need our full engagement: CFTR modulators with higher efficacy, antisense oligonucleotides (ASOs), gene and m-RNA/t-RNA therapies, read-through agents, ENaC-blockers, agents activating alternative chloride channels, anti-inflammatory compounds, antibiotics, biofilm disrupting agents, etc. Therefore, we will all still be very busy!

To manage these future challenges our network will further expand to 58 sites in 17 European countries caring for ca. 22000 CF patients. A Principal Investigator from a new site/country (Adrien Halasz from Budapest, Hungary) will explain what it means to become a CTN site.

We gratefully acknowledge our partners for their sustained and reliable funding of our network: the Patient Organisations from France, UK, Italy, Belgium, the Netherlands, Switzerland, Luxemburg and Germany, as well as the ECFS.
We are also very thankful for the general financial support of the Cystic Fibrosis Foundation (USA) for building up additional research capacity in many of our sites as well as in the CTN Core Centre in Leuven, Belgium.

“This report again is the result of excellent collaboration with patients and patient organisations...”

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 all thank her for her brilliant work within our network.

Our network could not have achieved the current level of success without a very engaged and strong team. I would like to thank the co-ordinating team Veerle Bulteel, Anne Verbrugge and Katia Reeber as well as our Executive Committee members Damian Downey, Lieven Dupont, Nick Simmonds, Nadine Dufeu, Hettie Janssens, Dorota Sands and Paola de Carli for their unwavering support and engagement. Last but not least the CTN would not be so successful without all your loyal commitment.

Let's keep on this good path and this excellent teamwork to further develop therapies for all our patients!

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,

Silke van Koningsbruggen-Rietschel
Director ECFS-CTN

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2019 OUR YEAR IN NUMBERS

CTN 10th birthday

2 scientific **PAPERS** published about trial measurements

New TRIAL RESULTS collaboration

CF Europe

475 PEOPLE with CF newly enrolled into trials

Feasibility checks for **11** trials

CTN is expanding **15** new sites in 11 countries

3 ★★★ EU projects ongoing

15 protocols

from **9** companies reviewed by people with CF, their families, doctors, research coordinators and statisticians

26 active trials supported

Restore CFTR function (22)

Anti-infection / inflammation (1)

Mucociliary clearence (3)

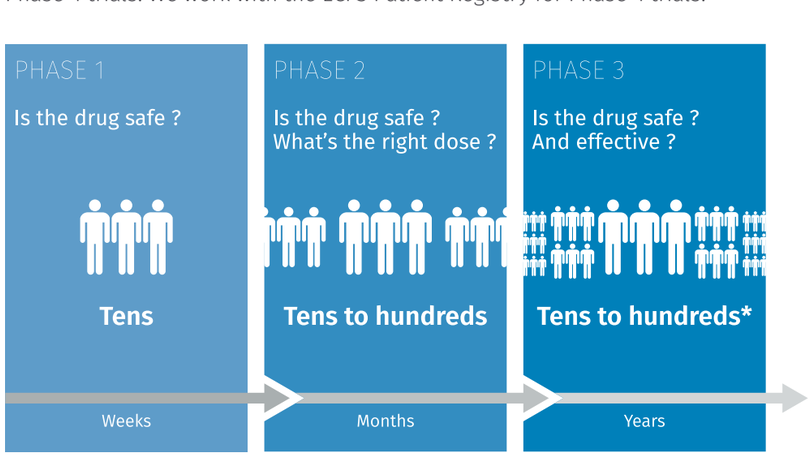
Clinical trials and CTN

How does it work ?

What are clinical trials?

In clinical trials, people without CF and/or people with CF take a new medicine to help researchers assess whether the medicine is safe and effective at treating the disease in question.

All medicines, including those for CF, are tested in several clinical trials from phase 1 to phase 3. Once licensed, “real world” safety testing continues in Phase 4 trials. We work with the ECFS Patient Registry for Phase 4 trials.



*As trial design improves for rare diseases, fewer patient are needed to test the drug.

Where can I find out more about clinical trials?

Check out this leaflet from the CF Trust in the UK: https://www.cysticfibrosis.org.uk/get-involved/clinical-trials/taking-part-in-clinical-trials

Ask your national patient organisation for information in your language.

ECFS-CTN

Our mission

How does a European network streamline research?

The aim of ECFS-CTN is to intensify clinical research in the area of CF and to bring new medicines to people with CF as quickly as possible.

- Increases cooperation between the whole CF community (people with CF, patient organisations, pharmaceutical industry and academic researchers)
- Shares expertise across countries to standardise research procedures and measures
- Gives a stronger voice to member sites in case of issues with clinical trials
- Encourages high quality research by training staff and monitoring site performance

When was ECFS-CTN founded?

ECFS-CTN was founded in 2008 by ECFS and EuroCareCF, a project funded by the EU. The Cystic Fibrosis Foundation (CFF) in the USA had already set up a successful clinical trials network (CFF-Therapeutic Drug Development Network (CFF-TDN) and they helped us in setting up ECFS-CTN.

CTN structure

The organisation

What sites are involved and why?

What if my city isn't on the map? Can I still participate in trials?

Ask your CF care team about clinical trials happening in your area

In 2019 there were 43 CTN sites across 15 countries in Europe. Member sites have a good track record in clinical trials, highly trained staff and good infrastructure. Check the map on the next page to see which sites are involved.

We launched a call for new member sites to join CTN in 2018. After carefully evaluating the applications we selected 15 new sites from 11 countries to become official CTN member sites from January 2020. We are delighted to welcome the following sites to ECFS-CTN:

- Amsterdam, the Netherlands
- Bern, Switzerland
- Brno, Czech Republic
- Brussels, Belgium
- Budapest, Hungary
- Cardiff, UK
- St Vincents & Our Lady's Childrens' Hospitals, Dublin, Ireland
- Ghent, Belgium
- Glasgow, UK
- Grenoble, France
- Heidelberg, Germany
- Innsbruck, Austria
- King's Hospital London, UK
- Manchester, UK
- Turin, Italy

Our sites

Amsterdam
Barcelona
Belfast
Berlin
Bern
Birmingham
Bordeaux/Toulouse
Brno
Brussels UZB
Brussels ULB
Budapest
Cambridge
Cardiff
Cologne
Copenhagen
Dublin
Dublin (Vincent's & Our Lady's)
Essen/ Bochum
Florence
Frankfurt
Genoa
Ghent
Glasgow
Gothenburg
Grenoble
Hanover
Heidelberg
Innsbruck
Jena
Jerusalem
Leeds
Leuven
Lille
Lisbon
London Brompton
London Kings
Lyon
Manchester
Milan
Mucomed (Montpellier, Marseille, Nice)
Munich
Nottingham
Paris (Cochin, Debré and Necker hospitals)
Petah Tikva
Prague
Reims
Rome Bambino Gèsu
Rome Sapenzia
France Northwest (Roscoff, Rennes, Nantes)
Rotterdam
Rouen
Southampton
Stockholm
Turin
Utrecht
Verona
Warsaw
Zurich

Joining CTN

A new site explains why they joined CTN

Adrien Halász,
Principal investigator of the Budapest site

1. Why were you motivated to join ECFS-CTN?

With the financial support of the Hungarian government, in 2015 a new CF center was built in the National Koranyi Institute of Pulmonology in Budapest, Hungary. Due to the growing number of adults among the Hungarian CF population, there was a great need to develop the adult CF care. Since we created the center for the patients, we immediately recognized that we would have to work closely with the CF patients' association, if we intend to understand and service their needs. From the very beginning we always discussed every important decision with our patients, and carried out our development projects through joint applications for financial awards. Striving for the best CF care, we organized our CF center strictly following the guidelines of the ECFS. At the same time we recognised that it was not enough to get state-of-the-art medical instruments, equipment and medication for CF treatment, but we must also gain up to date knowledge, and understand the new possibilities for improving treatment. We have realized that the accumulation of knowledge cannot only be acquired by our own findings and experience, but from the international expert community. Apart from getting access to the latest medication for our patients, this was the main reason, which motivated us to join the ECFS-CTN.

When we started our work in the new CF center, there were 80 CF patients treated in the hospital. Nowadays we have 140 patients, which is more than two third of the Hungarian adult CF population. We have become the largest CF center in Hungary.

2. What benefits do you hope ECFS-CTN membership will bring for your patients?

The quality of life for the CF patients relies mostly on their treatment. We consider ourselves lucky in Hungary since our CF patients get their medication free of charge. Pulmozyme, inhaled antibiotics and daily medications are all provided. There are ongoing negotiations on CFTR modifying therapy, as well. Yet since the number of new drugs for CF are continuously rising, it is increasingly difficult to gain early access to these products. The only possible way to do so is to participate in clinical trials. Our patients often feel that they have no time to waste, and effective medication should be given as soon as possible. Since most of our patients are young adults, they read about the new medications and are eager to get them. They know about clinical trials, how these can change their lives and are willing to participate in them. By joining ECFS-CTN our patients have the opportunity to receive the newest medication, or to opt out if they feel uncertain. Hence, we can give them a choice and the power to decide their own treatment process.

We are proud to be chosen as a member of ECFS-CTN and we are positive that this membership will benefit our CF patients by giving them access to the best available treatment.

CTN governance

The organisation

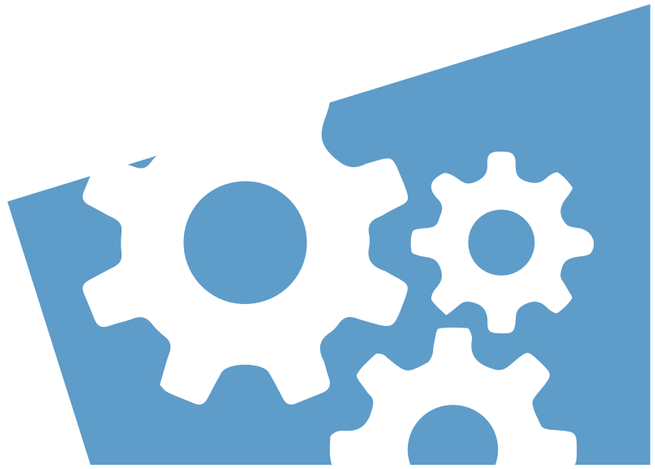
How does CTN work?

ECFS-CTN is an ECFS project and is run by:

- the Executive Committee (6 doctors from different countries and 1 patient organisation representative) 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 in carrying out their tasks.



Funding

Maintaining independence

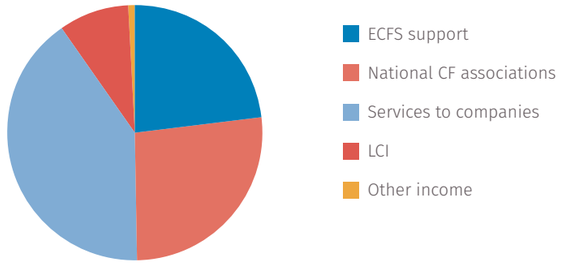
ECFS-CTN is funded by grants and by charging fees for scientific services to pharma companies.

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 ECFS and patient organisations to make up the shortfall.

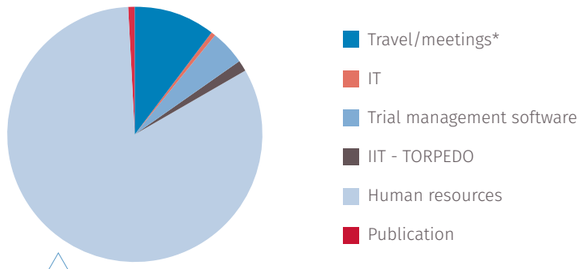
ECFS-CTN is grateful to the following organisations for funding our work in 2019: ECFS, CFF, European patient organisations (from France, Germany, UK, Italy, Belgium, the Netherlands, Luxemburg, and Switzerland). We also thank CF Europe for coordinating the contributions from national patient organisations.

You can find our 2019 financial report at the end of this document.

Income



Spending



"If one day the drug gets to patients, I'll be happy to say that thanks to me, you have this medicine. I have the impression that, since a few years, patients see new medicines arriving and they say 'what about me, what about my mutation?' So they go looking for trials. A few years ago it wasn't at all like that, patients waited until the new medicine arrived. But now it's more the patients who go looking for information. They're very keen on clinical trials at the moment - they know things are moving and they want to participate."

Audrey, person with CF from France

CTN activities

Protocol review / What we do

Protocol review

A clinical trial should answer a scientific question (e.g. is the medicine safe and effective?), should be well planned so that hospital staff can work efficiently, and should ask only what is reasonable from participants.

Our protocol review system gives people with CF a voice in setting the research agenda and makes sure that trials take the patient experience into account.

The protocol is the “handbook” for a clinical trial and describes in detail how the medicine will be tested, how patients will be involved and how the data will be analysed. The pharmaceutical company developing the medicine is responsible for designing the clinical trial and writing the protocol.

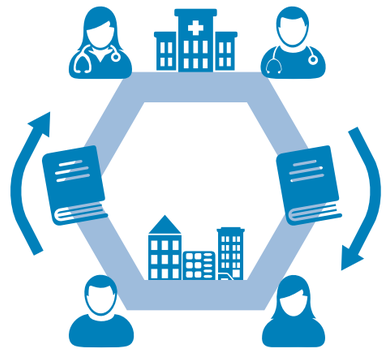
Designing a good clinical trial is a team effort and needs input from all the main players involved – that is from doctors, research coordinators, statisticians, and of course people with CF and their families.

Protocol review

At ECFS-CTN, we coordinate the review of new clinical trial protocols by expert groups of CF doctors, research coordinators, academic researchers and people with CF and their families.

They check that the research question is worthwhile, the practical plan is well thought out and that the demands of participation in the trial are reasonable for participants.

ECFS-CTN strongly encourages sponsors to update the protocol based on the advice provided by the review.



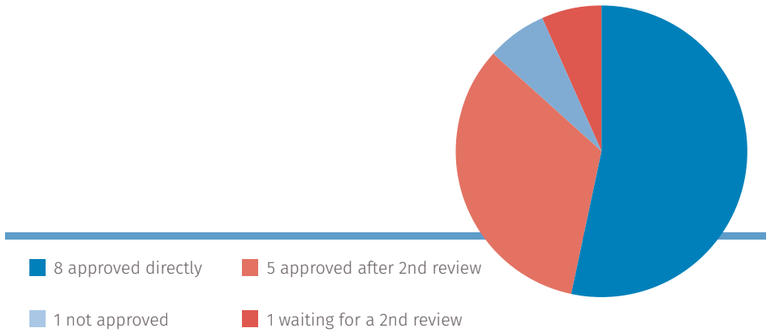
Clinical trials in CF often include participants across different cities, countries and even continents. For trials planned to run in Europe and the USA, a joint “global” protocol review is sometimes performed with our partner clinical trial networks in the US and Canada. In 2019, all three networks collaborated to improve and streamline this process.

CTN activities

What we do

Protocol review

In 2019, we reviewed 15 protocols from 9 different companies. ECFS-CTN asked for clarifications or modifications for 7 protocols before approval. In total, 13 protocols were approved, 1 was not adopted, and 1 is awaiting feedback from the sponsor and a second-round review.



When a protocol is reviewed and approved, we tell all the sites in ECFS-CTN that the protocol had a successful review.

Also, in 2019 6 reviewers with CF (or reviewers from families with CF) from 4 countries joined the protocol review committee, bringing the total to 23 CF community reviewers from 11 countries. We are very grateful to all CF community reviewers for sharing their time and expertise.

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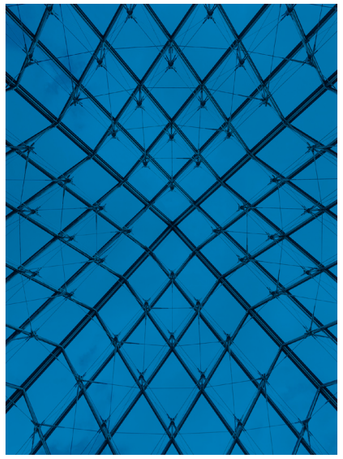
Clinical Trials Network

CTN activities

Marc, from the Netherlands, lives with CF and explains what's involved in reviewing a protocol



What motivated you to join the protocol review committee?

The science and knowledge around CF have taken a huge step in the right direction last years. This is fantastic news for all patients with CF. It could give you back a future.

When I was young, the doctors said to my parents that I would not live older than 15. Luckily, they were wrong and my health has gotten better and better in the last couple of years. I think that without science and the good healthcare system we have in Europe this would not have been possible.

I hope that my contribution to the review committee helps the experts and doctors to solve the puzzle of CF and that young patients can have the health that I have right now, preferably even better health.

Is it difficult to read a scientific protocol?

Every protocol has a summary where they explain in plain text what the study is about. This summary gives you enough background to read the entire protocol and link the in-depth technical terms with what was said in the summary. The first protocol is the hardest. Reviewing a protocol takes me around 60 - 90 minutes depending on the subject / complexity of the study.

What is interesting about participating in the protocol review committee?

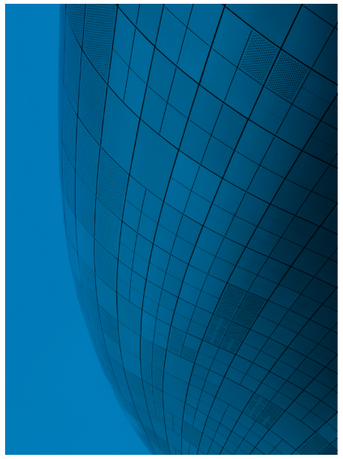
Every review I do, I learn more about the world behind CF. It gives me inside in my own disease and I find that very fascinating.

Why is it important that a person with CF, or a family member reviews the clinical trial protocol?

It's very good that the studies are reviewed from different angles, I see other things than a family member and so do they. Combined we could give feedback to the study how to improve or how to get a better acceptance for the study.

CTN activities

Bart, the parent of a person with CF in Belgium, recounts his experience of reviewing protocols with ECFS-CTN



What motivated you to join the protocol review committee?

I joined the protocol review committee for several reasons:

- the possibility to deliver a (hopefully) valuable contribution to the CF community (in return for the excellent care we are receiving on a continuous basis)
- the opportunity to represent the voice of a patient (or parent of a patient)
- the idea to form a counterbalance to the purely scientific approach of a clinical trial (the "human touch")
- the chance to get a unique insight (albeit under strict confidentiality obligations) in the efforts that are being invested in the search for a more effective treatment of CF

Is it difficult to read a scientific protocol? Is it a lot of work?

On the one hand, it is good to know that the structure of a protocol is always similar. Once you are used to it, it is not too difficult to know which parts are most relevant to read from a patient's point of view and which parts you can skip. The training we got before we started reviewing was very useful and relevant in this respect.

On the other hand, protocols are usually written in a scientific language, a jargon. Apart from a basic knowledge of the most commonly used concepts and terms, also a proficient knowledge of English is required in order to have a sufficient understanding of the protocol.

Protocols are often quite lengthy documents. Although the template form with guiding questions (made available by ECFS-CTN) helps to keep the right focus, it quickly takes a few hours to review the (relevant parts of the) protocol and write down your feedback.

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

For the simple reason that the impact of a study on the existing burdensome treatment of a CF patient, often seems not to be the first concern of the scientific research professionals. Review by a family member adds some empathy...

The importance of the patient's voice cannot be overestimated. Sometimes I wonder whether we really have impact on the study protocols. A 'before' and 'after' comparison would be very clarifying in this respect ;-)

CTN activities

Our work

Standardisation of procedures and clinical trial measures

In research, it is important that we all work in the same way, so that the results from clinical trials are reliable and so that we can compare results from different clinical trials.

ECFS-CTN brings together experts from all over Europe to agree the best way to perform clinical tests and measurements in clinical trials. We also work jointly with our American and Canadian colleagues on some projects.

We published 2 new papers in 2019 :

- one on *Pseudomonas aeruginosa*

and

- one on CT scans

The ECFS-CTN Standardisation Committee has produced 37 standard operating procedures and 12 peer reviewed publications in scientific journals, we have also produced an information leaflet for people with CF and their families about the sweat test (available in 17 languages) and a paediatric advice leaflet for sputum induction (which was translated during 2019 into extra languages – now available in 14 languages).

ECFS-CTN also supports the training and certification of site staff in the following measurements for clinical trials: multiple breath washout, spirometer-controlled chest CT scanning, nasal potential difference, sweat test and intestinal current measurement.

PROMS

Patient Reported Outcomes

2019 update

In 2017, ECFS-CTN started a project to develop patient reported outcome measures (PROMs), in collaboration with patient organisations.

PROMs cover issues of concern to patients and the data can often be collected by self-administered questionnaires. These are of particular importance as they supply important patient-reported information about daily life which cannot be captured by usual measures. This can include quality of life measures such as patients' resilience, coping strategies, and perception of their future and disease. In clinical trials they can provide a reliable way to gain the patients' perspective regarding the benefits and limitations of a specific treatment.

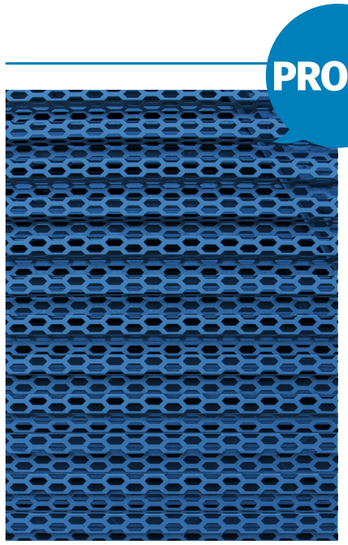
A survey of all CTN sites was conducted in 2019 to assess what quality of life/PROM/symptom report tools are used in current clinical practice. 120 interviews were also conducted with people with CF and their caregivers. The results from both of these projects have been summarised and are currently getting ready for publication: entitled: We have to keep asking questions: Patient Reported Outcome Measures in Cystic Fibrosis: A Qualitative Study of People with Cystic Fibrosis and their Caregivers.

In 2019, ECFS-CTN continued the work (started in 2018) with our patient organisation partners through CF Europe to explore patient priorities and to look more deeply into the issues identified by patients. To do this, we formed a Patient Advisory Group, comprising people with CF, family members and representatives of both ECFS-CTN and CF Europe. During monthly conference calls, existing quality of life questionnaires were assessed and proposals for improvement were discussed. This hands-on approach has led to recommendations on how to assess patient reported outcomes, first in clinical trials and eventually also during routine clinic visits. A draft CF-specific questionnaire has now been created and the next steps involve wider scale testing.

We are always looking for enthusiastic and motivated people with CF and carers to help guide our research. If you would be interested in getting involved in this patient-centred project, please get in touch with Kate Hayes, one of our CTN staff (k.hayes@qub.ac.uk)

CTN activities

Diana, a person with CF from Germany, explains what it's like to be involved in the PROMS project



How did you get involved in the PAG Group/PROMs project?

I was asked by the German Cystic Fibrosis Association Mukoviszidose e.V., whether I would be interested in working in a multidisciplinary team within a very important European project. They looked for people with CF with a certain level of understanding, good English skills and experience with the disease. I am on the Federal Board of the Association and was at that time at home most of the time waiting for my pension. And of course, it might have helped to have CF myself and that I have already been through two double-lung transplants. :-)

What motivated you to participate?

PRO questionnaires are so important and should be even more so. A good lung function and relatively normal blood values help you to feel more confident, but most of the time you will notice an improvement or decline in a more subtle way that cannot be measured accurately during an examination at a CF centre. Also, the mostly used "old" questionnaires do a lot of comparison and I simply hate that fact. Improvement or decline should always be a feeling for oneself and in no way be connected with the performance level of others.

What does participation involve? (What happens?)

The start was a bit tough for me, to be honest. I am known for my very forward nature and at the first meetings, I could not see where we would be heading, what our goals were and how the group would work, since we only had phone calls and few members of the group were native English speakers. However, I think we did a good start. We compared many existing questionnaires and feedback on the French questionnaire to get a starting point. From that point on, we went through all important categories such as physical or emotional function. We talked about the style of questions we wanted to use and the positive connotation we wanted to imply. And so, we met month after month by phone, later via Zoom, and discussed these topics. As the work was getting more and more definite, we decided to have extended weekend meetings.

Why is the PROMs project important?

This is easy to answer: The existing questionnaires do not reflect the everyday life of us CF patients and are much too unspecific. Especially with regard to the evaluation of new drugs the "old" questionnaires do not seem suitable to get a good feeling for the improvement of the patients.

How do you hope it will help people with CF?

Reflecting about one's own state of health is a particularly important part in the daily routine of us CF patients. Being "forced" to answer a negatively connotated questionnaire or one that does not reflect my sorrows, seems to be simply a waste of my time and will not help anybody. So, creating a questionnaire that is easy to answer and very relatable for many patients could be a big improvement for both the patients and their doctors. In addition, a good questionnaire can help to improve and speed up the development of new drugs.

How do you find working with a diverse group of people including scientists and doctors?

I loved the different team members. We all have different backgrounds and can contribute totally different views of living with CF. And having "our" doctors and scientists, helped me to remain focused on what we wanted to do. They do have the expertise in both CF and scientific methods for questionnaires. And besides the professional aspect, I am always amazed about the heart and soul that all of them put into this project. So thanks a lot, to everybody, especially to Kate who coordinated everything and also had the time and energy to make us feel welcome and appreciated.

Do you enjoy working on such a project?

I am surprised how much I enjoyed working on this project as the months flew by. Getting to know so many different people and most importantly to start a refreshed version of a PRO questionnaire to be maybe a little help for CF patients. So yes, I enjoyed it very much.

Do you recommend other people with CF getting involved in shaping research?

Absolutely, as long as you are speaking English, just try it. It is not that hard as it might seem at the beginning. You expand your horizons by simply helping others (and of course yourself) and you will love it!

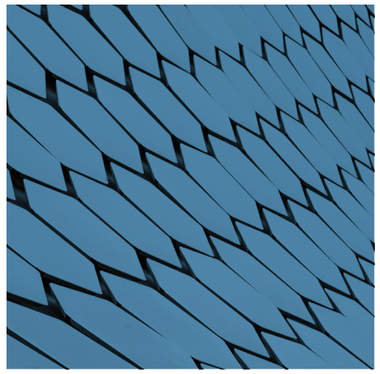
CTN activities

Our work

Quality & training

We monitor sites participating in ECFS-CTN approved clinical trials to check that trials are set up and run efficiently. We provide feedback to sites throughout the year and we discuss site quality and performance at our twice-yearly meeting of site investigators.

The ECFS-CTN training committee organises a yearly training day for research coordinators and investigators.



A project of the EUROPEAN CYSTIC FIBROSIS SOCIETY

CTN activities

Our work

Feasibility services

After a protocol has been approved to run in ECFS-CTN, we help the pharma company identify appropriate sites to participate in the trial.

The clinical trial protocol includes a checklist of which patients should be enrolled.

ECFS-CTN then helps pharmaceutical companies contact sites to see if they can participate in trials. We encourage companies to contact all eligible sites and to give all sites a chance to participate.

In 2019, we coordinated feasibility checks for 11 trials (for 9 sponsors).

Example

A clinical trial needs to enrol girls and boys with CF aged 11-17 with the G551D mutation. Sites must be trained to do a measurement called multiple breath washout (also called LCI).

We shortlist the sites fulfilling some of these criteria and encourage the sponsor to approach all the shortlisted sites.

We send a questionnaire to sites who check the criteria closely and tell us if they want to participate.

CTN activities

Our work

Expert advice to regulators

ECFS-CTN members give expert advice to the regulatory agencies that decide whether or not to license new medicines.

Safety monitoring in trials

In some clinical trials, data is shared with an external committee who independently monitor data as the trial is ongoing. If they notice any safety problems, this committee can stop the trial. Companies can use the ECFS-CTN affiliated “data safety monitoring board”, based in Lyon, France.

Increasing research capacity

A 2016 survey of ECFS-CTN sites found that lack of research staff was a major barrier to participating in clinical trials. The CFF generously offered to partially fund extra research staff at qualifying sites. In total, 19 ECFS-CTN sites were awarded funding to hire research staff.

We are very grateful to the CFF for supporting research capacity in Europe, in the spirit of our shared vision to bring new treatments for CF to patients. Funding continued in 2018, and we surveyed sites to see what impact the funding had. Here’s some of the feedback:

“Thanks to the new person our site can now participate in an early phase study including overnight stays”

“It is easier to participate in many simultaneous studies”

Plain summaries of clinical trial results

In 2019, ECFS-CTN started a new collaboration with Cystic Fibrosis Europe (CFE) to improve plain language summaries of clinical trial results. Twice a year, CFE gathers together companies involved in CF research to discuss a variety of issues facing people with CF. In autumn 2019, we discussed how ECFS-CTN, CFE and the companies can work together to improve plain language summaries of clinical trial results. We decided that a good first step is to create a glossary of terms that are often seen in summaries of CF trials. A poster about this project was presented at the 2019 European Conference on Rare Diseases and Orphan Products (ECRD).

Active clinical trials

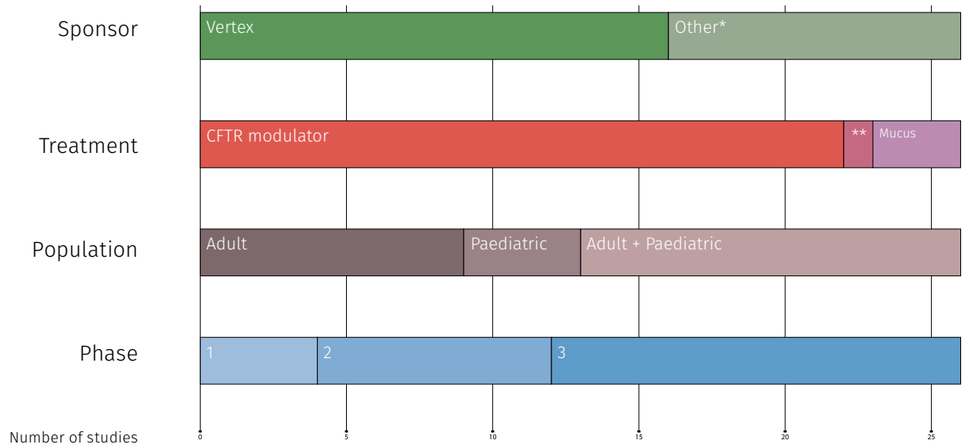
in ECFS-CTN in 2019

In 2019, there were 26 active studies in ECFS-CTN sites.

There was a good mix of trials open to adults and children. Most trials were phase 2 or 3.

Between November 2018 and November 2019, CTN sites enrolled 475 people with CF into trials. Adults represented 69% of new enrolment.

You can find a full list of the studies we supported in the Appendix (p32).



(*) : Proteostasis (2), Corbus (1), Flatley (1), UMC Erasmus (1), Eloxx (1), Boehringer Ingelheim (1), Spyryx (1), Galapagos (1), Abbvie (1)
(**) : Infection

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

European research projects

ECFS-CTN is a partner in several ongoing EU projects

More information is available at this link :

In 2019 we created a new application process and form for consortia who would like CTN to be a partner in European projects. This way we make sure the network has sufficient time to review the proposal before deciding on participation, and to provide input on the content before submission to the funding agency. More information is available at this link.

We have aligned this with CF Europe, who have a similar process in place.

The HIT-CF-Europe trial

In 2019, nearly 500 people with rare forms of CF participated in the first phase of the project, by donating rectal biopsies. These biopsies are grown in the lab to form organoids. In 2020, the teams will assess which organoids respond to medicines in the lab. Clinical trials will be planned throughout 2020, to see if people with CF respond to medicines as their organoid lab tests predicted.

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

In the first half of 2018, CTN reviewed the clinical trial protocol and performed feasibility to help find CF centres to participate in the trial.

The team has received regulatory approvals from Austria, UK, Germany and Ireland, and ethics approvals from Austria and UK. Ethics approvals from Germany and Ireland are expected to follow in 2020 in order to proceed with the clinical study in 2020.

European research projects

ECFS-CTN is a partner in several ongoing EU projects

Collaborative network for European clinical trials for children

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

Our role in this vast project is in the education work package. We surveyed pediatric clinical trial centres throughout Europe about their needs for training in pediatric clinical trials and helped revise some general clinical trials training material to tailor it to pediatric trials.

We are helping create training for the upcoming cASPerCF trial to investigate aspergillus treatment in children with CF. This trial was selected by c4c as part of it's research portfolio and will be performed within the new c4c infrastructure.

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

https://conect4children.org/

European Reference Network-LUNG

We gave a webinar to members of ERN-Lung in November 2018, to share our expertise in setting up and successfully running a clinical trials network. Five members of CTN presented at this webinar, with great feedback received.

You can watch the webinar here:
https://www.youtube.com/watch?v=43hcJnl2PUc

Financial report 2019

Our budget

Reflects book-keeping year 1 Jan – 31 Dec 2019:

CTN - Budget 2019	Euro €
ECFS Support	100,000
National CF associations	113,749
Services to companies	174,019
LCI	37,637
Other income	3,499
Total Income	***428,904***
Travel / Meetings	26,969
Human resources	335,972
Computer & Software/ Office equipment	1,050
Publication	2,103
Telecommunication	345
Training - Research coordinators Support	8,155
Software Development / Maintenance	5,329
Dedicated Server	10,268
IIT - TORPEDO	4,145
Miscelleanous	67
Total Expenditures	***336,566***
*Pre-Finance Leuven Department	90,659
Year Result	**1,679**

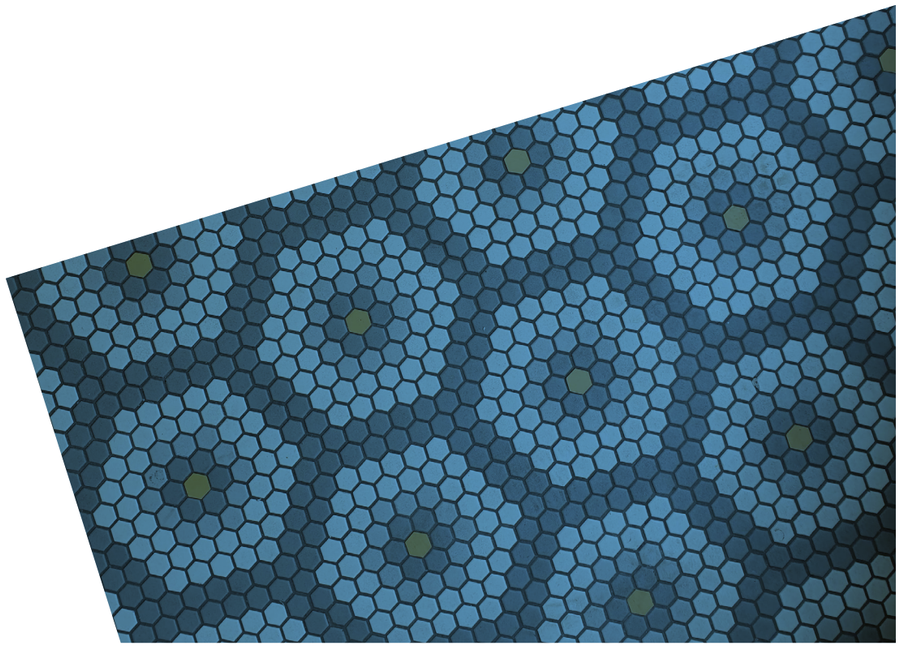
*Refund of HR expenses pertaining to 2018

CFF grant for Additional Research Capacity (“ARC”)

We are grateful to the US Cystic Fibrosis Foundation for the financial support granted to ECFS-CTN for the period 2017-2019 for the following :

1. Partial funding to hire additional research personnel for maximum 22 selected sites
2. Funding of an administrator at the CTN coordinating centre
3. Support to sites for entering data in the Trial Management System (2600€ per year)

In 2019 the maximum amount for this grant was $759,475



Appendix

Studies supported by ECFS-CTN in 2019

RESTORE CFTR FUNCTION

Phase 1b safety and drug behaviour testing of GLPG2451 and GLPG2222 combination treatment with or without GLPG2737 in adults with 1 or 2 ΔF508 mutations (GLPG2737-CL-105)

Phase 1 safety and drug behaviour testing of PTI-801 in healthy volunteers and in adults with CF (PTI-801-01)

Phase 1 safety and drug behaviour testing of PTI 808 in adults with and without CF (PTI-808-01)

Phase 3 testing of VX-659 in combination with ivacaftor and tezacaftor in people aged 12 years and older with the ΔF508 mutation and a minimal function mutation (VX17-659-102)

Phase 3 open-label testing of VX-659 in triple combination with ivacaftor and tezacaftor in people aged 12 years and older with 1 or 2 ΔF508 mutations (VX17-659-105)

Phase 3 open-label extension observation of long-term treatment with tezacaftor in combination with ivacaftor in children aged 6 years and older with 1 or 2 ΔF508 mutations (VX16-661-116; parent studies: VX16-661-113 and VX16-661-115)

Long term rollover testing of VX-661 in combination with ivacaftor in people aged 12 years and older with 1 or 2 ΔF508 mutations (VX14-661-110)

Phase 3 testing of VX-445 in combination with ivacaftor and tezacaftor in people aged 12 years and older with ΔF508 mutation and a minimal function mutation (VX17-445-102)

Phase 3 open-label extension testing of VX-445 in combination with ivacaftor and tezacaftor in people aged 12 years and older with 1 or 2 ΔF508 mutations (VX17-445-105; parent studies: VX17-445-102 and VX17-445-103)

Long term rollover testing of Orkambi (Lumacaftor/Ivacaftor) in people aged 6 years and older with 2 ΔF508 mutations (VX15-809-110)

Phase 2 open-label long-term observation of Orkambi's (Lumacaftor/Ivacaftor) effect on CF progression in children aged 2-5 years with 2 ΔF508 mutations (VX16-809-121)

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

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

New Phase 2 testing of VX-121 in combination with tezacaftor and ivacaftor in adults with CF with one ΔF508 mutation and one minimal function mutation (VX17-121-001; PartD)

New Phase 2 testing of VX-121 in combination with tezacaftor and ivacaftor in adults with CF with one ΔF508 mutation and one minimal function mutation, or two ΔF508 mutations (VX17-121-101)

New Phase 2 study of ELX-02 in people aged 16 years and over with at least one G542X nonsense mutation (EL-004)

New Phase 3 study of elexacaftor (VX-445) in triple combination with tezacaftor and ivacaftor in people with CF aged 12 years and over with one ΔF508 mutation and one gating or residual function mutation (VX18-445-104)

New Phase 3 study of elexacaftor (VX-445) in triple combination with tezacaftor and ivacaftor in people with CF aged 12 years and over with two ΔF508 mutations (VX18-445-109)

New Phase 1 and 2 study of how FDL176 and FDL176 interact and behave in the body in adults with CF who have two ΔF508 mutations (FDL169-2018-10)

New Phase 3 study of long term safety of elexacaftor (VX-445) in triple combination with tezacaftor and ivacaftor in people with CF aged 12 years and over who previously participated in Study VX17-659-105 (VX18-445-113)

New Phase 3 study of elexacaftor (VX-445) in triple combination with tezacaftor and ivacaftor in people with CF aged 6 to 11 years with one ΔF508 mutation and one minimal function mutation, or two ΔF508 mutations (VX18-445-106)

New A phase 2 study of ABBV-3067 alone and in combination with various doses of ABBV-2222 in adults with CF who have two ΔF508 mutations (M19-530)

ANTI-INFLAMMATORY

ANTI-INFECTIVE

Phase 2 testing of lenabasum in in people aged 12 years and older with recent antibiotic treatment for pulmonary exacerbation (JBT101-CF-002)

MUCOCILIARY CLEARANCE

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

Phase 2 testing of inhaled SPX-101 (SPX-101-CF-201)

New Phase 2 study of BI 1265162 to clear mucus in the airway in adults and teenagers with CF (BI 1399-0003)

Clinical Trials Network

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