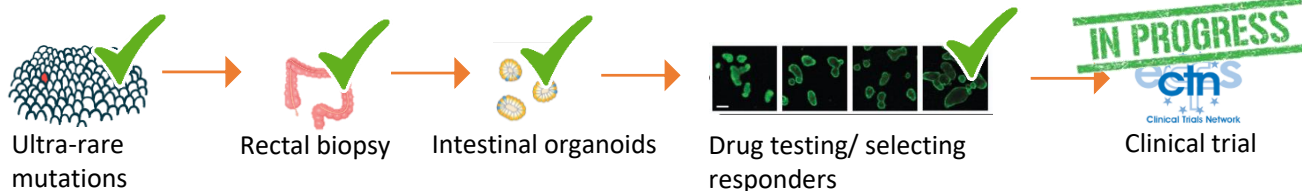


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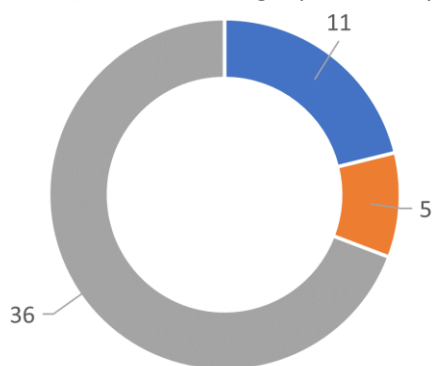


The HIT-CF Europe project aims to provide new treatment options to people with cystic fibrosis (CF) and ultra-rare genetic profiles. The project will evaluate the efficacy and safety of drug candidates provided by collaborating pharmaceutical companies in patients selected through preliminary tests in the laboratory on their mini-intestines – also called organoids.

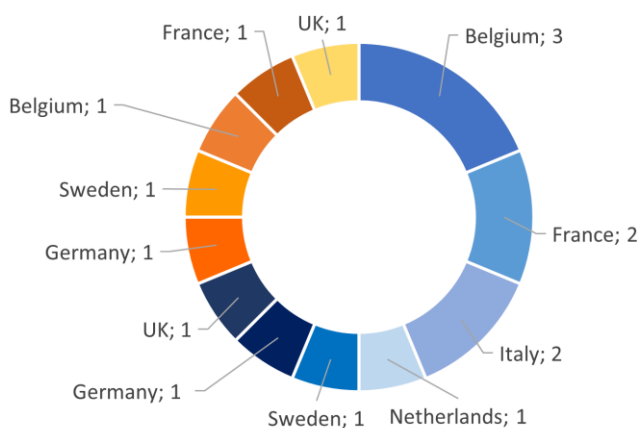


Enrollment in the CHOICES trial is in full swing

We hope you all enjoyed a relaxing summer and were able to spend time with your loved ones. During the summer months, the CHOICES study team and the staff at the local study sites have been hard at work. At this moment, 11 people have been enrolled in CHOICES. Enrolled means that they are taking the active drug or placebo. An additional 5 have been screened. Screened means that all necessary exams have been done and participants are ready to start the trial. The left graph, or “pie” represents all 52 people that need to be enrolled in CHOICES. In blue you see the ones that are already enrolled, in orange the ones that are screened to be enrolled, and in grey the participants that are expected, but not yet screened. CHOICES is currently running in 10 study sites in 7 countries: Belgium, France, Italy, the Netherlands, Germany, Sweden and the UK. On the right “pie” you see how many participants are enrolled (shades of blue) and screened (shades of orange) per country.



■ Enrolled ■ Screened ■ Expected



Attention to all HIT-CF participants: reconsenting to organoid biobanking

At the beginning of the HIT-CF project, you have undergone a rectal biopsy. You have given your consent, or permission, to culture organoids from this biopsy, and to use and store these organoids for the duration of the project. Several drug compounds have been tested on these organoids, which enabled us to start the CHOICES study. Worldwide, there is a growing number of people with CF who can be treated with new medications. However, still an important number of people with CF have no treatment opportunities yet. Therefore, further studies are done worldwide by researchers and pharmaceutical companies. Your organoids can be very important for testing new therapies in the future.

The consent you have given, is only valid for the duration of the HIT-CF project. By the end of 2024, the HIT-CF project in its current form will finish. **This means that we would have to destroy your organoids if no further action is undertaken.**

To learn more about the HIT-CF project, visit www.hitcf.org or send an e-mail to HITCF@umcutrecht.nl



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The HIT-CF Europe project aims to provide new treatment options to people with cystic fibrosis (CF) and ultra-rare genetic profiles. The project will evaluate the efficacy and safety of drug candidates provided by collaborating pharmaceutical companies in patients selected through preliminary tests in the laboratory on their mini-intestines – also called organoids.

Fortunately, we have found a way to keep your organoids available for future studies by storing them in a new European Cystic Fibrosis Stem Cell Biobank. **This does mean that you will need to sign a new informed consent; otherwise, your organoids will still be destroyed.**

How do I re-consent? By simply sending an email to HITCF@umcutrecht.nl with either the message:

- Yes, I am interested in keeping my organoids available, or
- No, I am not interested, please destroy my organoids.

If you indicate you are interested, we will send you a letter with all necessary information, and a new consent form. After we have received your new consent form, we will store your organoids in the new biobank. Otherwise, we will destroy your organoids according to your wishes. If you feel you first need more information to be able to make an informed decision, please write down your questions and send them to HITCF@umcutrecht.nl.

You might have received this information from your CF doctor as well. Please feel free to discuss this with him or her too.

Good news: ReCode mRNA trial is recruiting!

As we mentioned in the February newsletter, HIT-CF participants that were not selected for CHOICES, will have the opportunity to participate in another study. ReCode Therapeutics has developed an investigational inhaled therapy based on mRNA for people with CF with rare mutations, including nonsense/stop mutations. mRNA stands for messenger ribonucleic acid and contains instructions to tell our cells how to make a protein, such as the CFTR channel. mRNA is not able to alter or modify a person's genetic makeup (DNA). In people with CF, the CFTR protein is not functioning well or isn't there at all. By delivering correct copies of CFTR mRNA to the lung cells, this problem can be bypassed, and the cells can once again start making functional CFTR channels.

The innovative **inhaled** mRNA therapy, which is called **RCT2100** for now, is currently being tested in people with CF for the first time. This process is also known as a **phase 1 study**. A phase 1 study focuses primarily on **finding the right dose of the drug and evaluating the safety**. Participants to a phase 1 study may or may not have personal benefits from the treatment, but it is not the primary goal at that point. Moreover, it cannot be guaranteed that participants will automatically be able to take part in later phases of the study that do focus on investigating effectiveness. Nevertheless, this is a very important, if not the most important phase of the clinical research. Without sufficient safety data, the experimental drug cannot progress to the next phase. Therefore, it is very important to find enough participants.

During this study, the researchers want to determine how much RCT2100 can be administered, to find out whether RCT2100 is well tolerated, as well as how the body uses RCT2100 and how RCT2100 affects the body. To do so, the safety of several different doses of RCT2100 will be tested. **Each participant is guaranteed to receive the experimental therapy; in this part of the study, there is no control group receiving a placebo or dummy drug.** This summer, ReCode obtained approval to perform the study in Europe, and they are now looking for participants. Participating in this study means that you will have to visit the study centre about 17 times and requires blood draws, lung function testing and/or other measurements. The study will run in the **Netherlands** (Utrecht), **France** (Paris Necker, Toulouse and Montpellier) and the **UK** (Leeds, London King's College Hospital, Nottingham, Southampton, Cambridge and Birmingham). **If you don't live in one of these countries, you can still participate if you are able and willing to travel to one of the study sites.** For more information, you or your CF doctor can contact the HIT-CF team via HIT-CF@umcutrecht.nl.

To learn more about the HIT-CF project, visit www.hitcf.org or send an e-mail to HITCF@umcutrecht.nl

