

Innovative project matching people with rare CF mutations to medicines hits initial enrolment target

Phase 1 of the breakthrough HIT-CF project ended with the enrolment of 502 people with ultra-rare forms of cystic fibrosis.

***Ex vivo* testing has started and clinical trials are expected to start in Autumn.**

Hitting targets

BRUSSELS, Belgium – February 2020 – The HIT-CF project is a EU-funded programme that aims to provide better treatment to people with cystic fibrosis (CF) and ultra-rare genetic profiles that are not routinely included in clinical trials and therefore cannot benefit from novel therapeutic compounds. Today, CF Europe is proud to announce, on behalf of the HIT-CF consortium, the successful completion of the first phase of the project with the collection of biopsies from 502 people with ultra-rare forms of cystic fibrosis (CF).

"Enrolled individuals are a portion of the approximately 2,300 adults in the European patient registry who are not eligible for any currently approved modulator due to their genotype" said Jacquelin Noordhoek, President of CF Europe and representative of the Netherlands Cystic Fibrosis Society (NCFS). *"The HIT-CF project represents the only option to explore potential benefit of disease modifying drugs in this group. Putting patients with CF first is our highest priority and we are looking forward to continuing our partnerships and providing Europeans with CF the best possible care."*

Since January 2019, the 47 biggest CF centres from 16 countries throughout Europe, all members of the European Cystic Fibrosis Society-Clinical Trial Network (ECFS-CTN), participated in the collection of rectal biopsies from patients with a rare genetic profile. These samples will be used to grow personalised cellular models called "organoids" by the foundation Hubrecht Organoid Technology (HUB, The Netherlands).

"This milestone is a huge achievement for the CF community. Such a broad and close collaboration between patients, caregivers, scientists and pharmaceutical industries has never happened before and illustrates the determination of the community to get a treatment for this group of patients" said Kors van der Ent, paediatric pulmonologist at the University Medical Centre in Utrecht (The Netherlands) and coordinator of the project.

Next steps and perspectives

In the next step, experimental CF medicines provided by several pharmaceutical partners will be tested on these organoids to check for their efficacy in the tissue of each individual donor. Two pharmaceutical companies are involved in the project: Proteostasis Therapeutics Inc. (US, MA) and Eloxx Pharmaceuticals (US, MA). Drugs will be screened on the organoids in partner university laboratories in the Netherlands (Utrecht), Belgium (Leuven) and Portugal (Lisbon).

Based on the response of their organoids, smaller groups of patients can participate in clinical trials from autumn 2020, in order to evaluate the real life benefit of specific drugs. The trials will be organised within the ECFS-CTN and assisted by Julius Clinical; final results are expected in 2021.

In parallel, the pharmaceutical partners are working towards market approval of their drug candidates with indications for larger groups of patients including more genetic profiles.

At the same time, the consortium is working with the European Medicines Agency (EMA) to clear the path towards the validation of the organoids as a predictive model of the clinical response of patients to new drugs.

Treating CF today

The treatment of cystic fibrosis (CF), a rare genetic disease mainly affecting the lungs and pancreas, has seen exciting developments in recent years, with the introduction of a new class of effective medicines that target the underlying biology causing the disease. However, these new drugs have only been tested in people with the most common mutations in the CF-causing gene “*CFTR*”. As a result, these new medicines, known as CFTR modulators, cannot be prescribed to people with rarer CFTR mutations – who account for around 10% of people with CF.

The HIT-CF project

The HIT-CF project is an ambitious European research programme that aims to fill in this gap for people with rare genotypes. The HIT-CF consortium involves partners with various expertise: hospitals and CF centres, pharmaceutical companies, university and not-for-profit organisation laboratories, grant management and research organisations, all working closely with the ECFS-CTN and CF Europe as a representative of the CF patients.

Together, the scientists will investigate if CFTR modulators work on cells grown in the laboratory from patient biopsies, the so-called organoids. A selection of the people with CF who donated biopsies will then take part in clinical trials to see if the medicines work in real life, as well as in the biopsies.

The ultimate goal of this project is to develop a path for access to therapies for patient groups or individuals who show positive response to the therapy in an organoid test. One major outcome will be the innovative methodologies used to acquire marketing authorisation and eventually reimbursement. This will represent a new era in CF care as it implements a new type of personalised medicine based on *ex vivo* testing, by shifting therapeutic trials from patients to the laboratory.

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