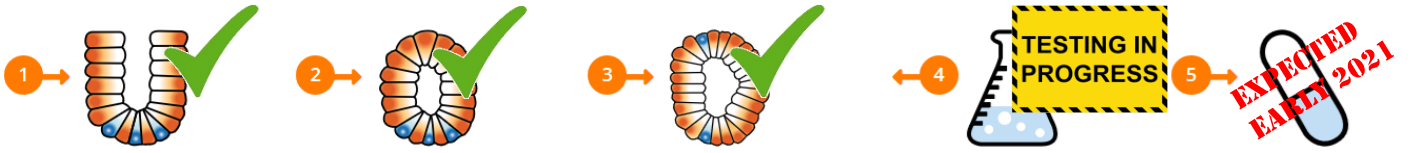
Newsletter HIT-CF Europe

October 2020

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 Eloxx Pharmaceuticals and Proteostasis Therapeutics, Inc. (PTI) in patients selected through preliminary tests in the laboratory on their mini-intestines – also called organoids.



We take some tissue from the intestine | **This tissue is cultured in the lab** | **The result is an organoid** | **On this organoid we test medicines** | **And we bring the correct medicines to the patients**

Message from Professor Kors van der Ent, paediatric CF doctor at UMC Utrecht, the Netherlands, and principal investigator of HIT-CF

Dear Friends

The news about Proteostasis (PTI, one of the pharma companies providing compounds for HIT-CF) merging with Yumanity, and the delays caused by Covid-19 have led to concerns about the progress and execution of HIT-CF, and in particular of the CHOICES trial (= trial with PTI compounds).

Fortunately the organoid-collection part of the project was finalized just before the pandemic. With some minor delays, the labs in the consortium were able to continue the screening. We expect that all organoids will be screened with PTI compounds in November and that we can continue screening with Eloxx compounds from there. Originally, the HIT-CF project had foreseen placebo-controlled 8-weeks cross-over trials with both PTI and Eloxx compounds. Before the pandemic PTI asked us to extend the second period of the cross-over trial with a 16-weeks extension period, to collect in total 24-weeks safety data. We agreed with this approach.

The merge had an impact on PTI and on the support that can be provided at this moment. We had to remove the 16-weeks extension period from the study again and also open label access after the study is not fully assured at this moment. We currently have the agreement with PTI that we will perform HIT-CF in its original form and we see it as our joint responsibility and top priority to make the drugs available for patients in case CHOICES will come up with positive outcomes. We will start with protocol submission to local Institutional Review Boards very soon now and, depending on how the pandemic will evolve, we hope to start patient inclusions some months later.

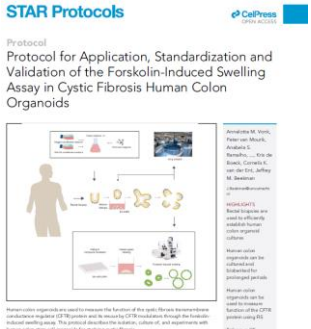
Also, the ongoing clinical program of Eloxx has some delay. The company has to finalize the phase II dose-finding study before we can start with the Eloxx HIT-CF study. The company currently expects this will be in summer 2021.

We all have to deal with these unprecedented times. The consortium is highly motivated to make HIT-CF to a success for patients with rare mutations. If you have specific questions, please don't hesitate to contact us and we will try to answer them the best we can.

Thank you and stay safe, Kors

HIT-CF on the international scientific scene

- ✓ Professor van der Ent had the opportunity to present an overview of the HIT-CF project during the recent North American CF Conference. You can watch his talk here
- ✓ The consortium recently published its protocol for application, standardization and variation of the Forskolin-induced swelling assay in CF human colon organoids. This publication aims to standardize methods to ensure high reproducibility and correct interpretation of results among different laboratories, and will enable other scientists to also perform functional experiments with organoids



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