For those of you who missed our social media posts, or who could not join us for the HIT-CF workshop in Glasgow, we are more than happy to repeat that the CHOICES trial has now finally begun! On June 3rd, in Utrecht, the Netherlands, the first participant was enrolled into CHOICES and started this incredible journey with us. CHOICES is a double-blinded trial, which means that neither the participants nor the investigators know whether the active drug or a placebo is being administered. CHOICES is also a crossover study. This entails that after an initial treatment period of 8 weeks with the active drug or placebo and a consecutive washout period of 8 weeks (to ensure that any longer-term effects of the medication have disappeared), participants are switched to the placebo or active drug, respectively. This means that every participant is guaranteed 8 weeks of active drug, and that every participant can serve as its own control. As a reminder, in CHOICES, we are investigating the safety and efficacy of a triple modulator combination of Fair Therapeutics, called Diponecaftor, consisting of a potentiator, Dirocaftor, a corrector, Posenacaftor, and an amplifier, Nesolicaftor. Disclaimer: we obtained permission from this participant to use her picture for communication purposes.

**Historic CHOICES trial finally kicked off!**

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**CHOICES aims to enrol 52 HIT-CF participants in the next months**

To obtain sufficient information on the safety and efficacy of Diponecaftor, we need 52 people to participate in and complete CHOICES. Those people are selected based on their organoid screening: 26 so-called high-responders, whose organoids responded well to the triple combination, and 26 randomly selected people with a variety of organoid responses. Very importantly, these participants do not know how their organoid responded. CHOICES will be run in the following countries: Belgium, France, Germany, Italy, the Netherlands, Portugal, Spain, Sweden and the UK. So where are we now? 2 people have been enrolled (meaning that they taking the active drug or placebo), 1 person has been screened (meaning that all necessary exams have been done and participants are ready to start the trial) and 49 people are expected for a screening visit. If everything goes well, CHOICES will end by spring 2025.

**Points of attention for people participating in CHOICES**

CHOICES is a first-of-its-kind clinical trial. Its results can be a game changer for the future of CF medicines. Therefore, we want to stress how crucial your participation is. It is of utmost importance to fully complete the trial (both treatment periods) and take all pills (we know there’s a lot of them) every day, even when treatment doesn’t seem to have much effect. If you have any doubts while you are in the trial, please talk to your doctor. Every participant in CHOICES is fundamental to the success of the study; you can truly make a difference and move a stone in the river. Thank you so much.

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