

Which clinical trial is this summary about?

The official title of the trial is ‘A Phase IIb, Multicentre, Randomised, Double-Blind, Placebo-Controlled, Crossover Study to Evaluate the Efficacy and Safety of Dirocaftor/Posenacaftor/Nesolicaftor in Subjects with Cystic Fibrosis Aged 18 Years or Older (CHOICES)’

It is a trial in which the drugs dirocaftor, posenacaftor, and nesolicaftor are tested in people who have a disorder named cystic fibrosis.

The trial is also known as CHOICES, HIT-CF-001, or 2022-500410-26.

Who conducted this trial?

A doctor from the University Medical Center in Utrecht (Heidelberglaan 100, 3584 CX), The Netherlands, led the trial. The company FAIR Therapeutics, B.V., provided the medication dirocaftor, posenacaftor, and nesolicaftor (together called DIR/POS/NES). Doctors and nurses throughout Europe conducted the trial. All these people are called investigators.

Where was the trial conducted?

This trial took place in 15 hospitals. There were participants in Belgium, Germany, Spain, France, the United Kingdom, Italy, The Netherlands, Portugal, and Sweden.

Why was the trial conducted?

Cystic fibrosis is a serious disorder that patients are born with. People with cystic fibrosis get lung disease and may suffer from airway blockage, infections, and inflammations. They may also experience problems with other body parts.

Cystic fibrosis is caused by changes (‘mutations’) in the DNA. It differs between people with cystic fibrosis how the DNA is altered exactly. For people with common mutations in the DNA, there are some treatments available. However, for people who have rare mutations there are no treatments yet.

Before this trial started, a few cells were taken from people with rare types of cystic fibrosis. These cells were grown into mini-organs (called organoids) in a laboratory. Researchers added DIR/POS/NES to these mini-organs to see if this made the mini-organs swell. Then, 2 groups of people were invited to take part in the trial: 1 group of people whose mini-organs swelled the most (named selected participants), and 1 group of people who were invited irrespective of the swelling of their mini-organs (named random participants).

In this trial, the investigators tested whether DIR/POS/NES could indeed be a treatment for people with a rare type of cystic fibrosis. They tested this both for the selected participants and for the random participants.

When was the trial conducted?

The trial was conducted from 27 May 2024 to 20 June 2025. The analysis of the results took until February 2026.

What was the aim of the trial?

The primary goal of the trial was to test in how far lung functioning improved by treatment with DIR/POS/NES.

Secondary goals of the trial were to test if other aspects of cystic fibrosis improved by treatment with DIR/POS/NES. These aspects were the amount of salt in sweat, body weight, and experienced wellbeing.

The investigators tested this both in the selected participants and in the random participants.

The trial also checked if adverse reactions occurred.

Who participated in the trial?

Patients with cystic fibrosis could participate if they were at least 18 years old, if they had a rare mutation, and if their cells had been taken to grow an organoid.

When the trial started, the plan was to enrol 26 selected participants and 26 random participants. However, there were not enough people whose mini-organs swelled well and who were available to find 26 participants for the selected group. In the end, 15 selected participants and 26 random participants were enrolled and received treatment. Almost 60% of the participants (24 out of 41) were female, and the mean age was 36 years.

Which drugs were tested?

Participants received DIR/POS/NES for 8 weeks, and a placebo for 8 weeks. A placebo is a drug that looks like the real drug, but does not contain the substances that makes it work. During the trial, neither the investigators nor the participant knew whether the participant received DIR/POS/NES or the placebo. This way, the investigators tested if a possible change in cystic fibrosis was due to DIR/POS/NES or due to other reasons.

Treatment with DIR/POS/NES consisted of 300 mg dirocaftor, 600 mg posenacaftor, and 10 mg nesolicaftor per day. Both DIR/POS/NES and placebo were given in capsules for swallowing.

Which adverse reactions were seen?

More than a third of the participants experienced that their skin reacted quickly to sunlight or UV rays during DIR/POS/NES treatment. Their skin then became itchy, painful, or got other types of rash.

What were the results of the trial?

Neither in the selected participants nor in the random participants, there was a clear improvement of lung function or other measures of cystic fibrosis. However, it seemed that in the selected participants there were some positive effects of DIR/POS/NES treatment.

How can the results be explained?

We cannot be sure if DIR/POS/NES does or does not help people with rare types of cystic fibrosis. There are some indications that the treatment might help better in those whose organoids swell strongly when DIR/POS/NES is given. However, in this trial there were not so many participants with a strong swelling of their organoids. This might explain why no firm conclusions could be drawn.

What is next?

There is currently no further study planned with DIR/POS/NES.

Where can I find more information?

You can find more details on this trial if you search for 2022-500410-26-01 on [euclinicaltrials.eu](https://www.euclinicaltrials.eu).