



# Cystic Fibrosis Research News

## **Title:**

CLINICAL EFFECTS OF THE THREE CFTR POTENTIATOR TREATMENTS CURCUMIN, GENISTEIN AND IVACAFTOR IN PATIENTS WITH THE CFTR-S1251N GATING MUTATION

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## **What was your research question?**

Our question was if these compounds were also clinically effective when we treated these people with cystic fibrosis with (a combination of) the compounds.

## **Why is this important?**

First of all, we found in the laboratory that a combination of the food supplements curcumin and genistein had a positive effect and also that addition of the food supplements to ivacaftor resulted in a bigger improvement in CFTR function than ivacaftor alone. If these compounds are also effective in the clinical setting this would not only mean that we can improve the effect of ivacaftor but maybe also have a (cheaper) alternative to ivacaftor therapy. Second of all, it is important to know if the addition of a compound in the lab to the intestinal organoids of a patient is a good predictor of what happens when a patient is treated with the same compound. If the responses are comparable this means that the organoid model could be a valuable tool for drug screening in the laboratory.

## **What did you do?**

We performed three clinical trials in which we treated people with an S1251N mutation with different (combinations of the) compounds. These treatments were: curcumin + genistein (study 1), ivacaftor (study 2) and ivacaftor + genistein (study 3). In all three studies people were treated during eight weeks. We evaluated the condition of the lungs, the chloride concentration in the sweat of the patient, the quality of life of the patient and two nutritional parameters.

## **What did you find?**

We found that almost all clinical parameters showed a significant improvement during treatment with ivacaftor. When people were treated with curcumin + genistein or genistein was added to a treatment with ivacaftor we observed no change in most of the clinical parameters. The only exceptions were a small but significant change in the chloride concentration in the sweat and a significant change in the resistance in the lungs, when people were treated with curcumin + genistein. The concentrations of curcumin and genistein that we found in the blood of the people after treatment was very low, especially compared to the concentration that was used in the laboratory.

## **What does this mean and reasons for caution?**

The fact that ivacaftor has a positive effect in the organoids of a patient and also results in a clinical improvement supports that intestinal organoids might be a valuable tool for drug



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screening in the laboratory. The absence of a clear and statistically significant improvement in the clinical parameters when people are treated with the natural food supplements curcumin and genistein is probably caused by the low concentration of these compounds in the blood. This highlights that it is important to take the characteristics of a compound (such as absorption) into account when experiments are performed in the laboratory.

## **What's next?**

Because of the potential of the intestinal organoid model to screen the effect of a large numbers of drugs for an individual patient, more drug screens will be performed in the near future. When these screens are performed the effect of the blood of patient that is using a drug can also be measured, by which the concentration of a drug in the blood can be taken into account when the effect is evaluated.

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