



# Cystic Fibrosis Research News

## **Title:**

Chronic incretin-based therapy in cystic fibrosis-related diabetes: a tale of 3 patients treated with sitagliptin for over 5 years

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

Sitagliptin and similar pills work by increasing levels of natural substances called incretins. Incretins help to control blood sugar by increasing insulin release, particularly after a meal. Will treating patients with cystic fibrosis-related diabetes (CFRD) with sitagliptin over a period of few months control their blood sugars, and continue to do so if taken for several years?

## **Why is this important?**

Nearly half of adult patients with CF (cystic fibrosis) have CFRD. Managing CFRD with insulin injection, the only treatment currently recommended by experts, is often very challenging to patients and caregivers. Some patients are reluctant to take their insulin due to scary experiences they had with low blood sugars. Others refuse insulin treatment because of the inconvenience, while some are extremely afraid of needles. Untreated CFRD will lead to a worse outcome for CF. Finding an effective and safe alternative medication for CFRD that can be given by mouth is clearly needed.

## **What did you do?**

Three patients with CF and pancreatic insufficiency, on enzyme replacement, were found to have CFRD during oral glucose (sugar) tolerance testing with blood sugar measurements, and hemoglobin A1C (A1C) measurement. A sitagliptin pill 100mg daily was prescribed, either because of patient's absolute refusal of insulin treatment or unwillingness to take it regularly due to fear of low blood sugars. Continuous glucose monitoring (CGM) was performed before treatment was started. To see the effect of sitagliptin treatment, CGM was repeated a few months later, as well as blood sugars and A1C which were measured regularly for more than 5 years.

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## What did you find?

The follow-up CGM for each of the patients while on sitagliptin showed improvement in glucose measurements; also, blood sugar and A1C levels improved. The improvement was maintained for 5 years in all the three patients without any incident of a low blood sugar. After 5 years, the treatment was no longer working in one patient who had excess weight as she continued to gain weight and was not following a healthy lifestyle; she frequently missed her medications. The other two patients were able to maintain excellent control of their blood sugars with sitagliptin for 10 years without any bad effects.

## What does this mean and reasons for caution?

Sitagliptin and similar drugs may help with blood sugar control in CFRD during the early stage of the disease, and possibly for many years when patients are not too sick and if their insulin needs are low. Insulin has been proven to be life-saving in CFRD; it helps to gain weight, improve breathing ability and it prolongs life. It is still unknown if the benefits from sitagliptin and similar drugs are more than blood sugar control alone. Possible side effects include joint pain, worsening of sinus symptoms, and very rarely pancreatitis but this is unlikely to occur in patients already with pancreatic insufficiency.

## What's next?

Studies in which the patients are assigned by chance to receive one of different treatments are needed to confirm the findings from this report. There is a need to find out if there are additional benefits to treating CFRD with sitagliptin and similar drugs, that is, beyond blood sugar control.

## Original manuscript citation in PubMed

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