

Cystic Fibrosis Research News

Title:

Effect of Lumacaftor/Ivacaftor on glucose metabolism and insulin secretion in Phe508del homozygous cystic fibrosis patients

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What was your research question?

Our investigation was conducted in patients with cystic fibrosis (CF) who had two copies (i.e. homozygous) of the F508del Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mutation and were starting treatment with the CFTR-modulator Lumacaftor/Ivacaftor (Orkambi®). We looked at the effect of Lumacaftor/Ivacaftor on blood sugar (i.e. glucose) metabolism and insulin secretion in these patients.

Why is this important?

With increasing life expectancy and continuously improving therapies the risk of secondary disease effects of CF will increase further. CF-related diabetes (CFRD) represents one of the most frequent complications of CF. Approximately 20% of adolescents and 40-50% of adults with CF develop CFRD. CFRD is associated with a decrease in lung function, a deterioration in nutritional status and an increased rate of mortality. Recent studies investigated the influence of CFTR on glucose metabolism and insulin secretion in CF, but it is still unclear whether CFTR-modulation therapies such as Lumacaftor/Ivacaftor have a positive impact on how the pancreas (where insulin is produced) works or might even prevent the development of CFRD.

What did you do?

We investigated the effect of Lumacaftor/Ivacaftor treatment on glucose metabolism and acute insulin secretion in five pancreatic-insufficient CF-patients by using an oral glucose tolerance test (OGTT) and an intravenous glucose tolerance test (IVGTT). These tests were

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performed before and after 6-8 weeks of treatment with Lumacaftor/Ivacaftor. We also determined the body mass index (BMI) and sweat chloride before and under treatment.

What did you find?

Following treatment with Lumacaftor/Ivacaftor the 2-hour glucose levels improved in three patients but worsened in two patients in the OGTT. In response to IVGTT, acute insulin secretion improved in two patients and worsened in three patients. All patients showed an increase of body weight (mean: +1,48 kg) and BMI (mean: +2,7 %) under treatment. There was no correlation between the change in BMI and the blood glucose and insulin response. Sweat chloride after 6-8 weeks of treatment showed individual changes with an improvement in 4 out of 5 patients.

What does this mean?

The investigation could not show a consistent effect of treatment with Lumacaftor/Ivacaftor on glucose tolerance and insulin secretion in this small group of patients. The results suggest that the effect of Lumacaftor/Ivacaftor on glucose metabolism might differ between different individuals. Limitations of this investigation include the small number of investigated patients and short duration of follow-up, so larger studies with a longer follow-up period have the potential to generate more comprehensive results and may lead to alternate conclusions.

What's next?

Larger studies examining glucose metabolism are needed to investigate the influence of CFTR-modulators on the glucose metabolism and to test whether new CFTR-modulating treatments could eventually prevent the development of CFRD.

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