

primary studies - published, non RCT

The long-term effects of insulin use in incident cystic fibrosis-related diabetes: a target trial emulated using longitudinal national registry data.

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Study design (if review, criteria of inclusion for studies)

Prospective observational study.

Participants

50 adult patients with CF starting CFTR modulator therapy with elexacaftor/tezacaftor/ivacaftor between May 2020 and June 2021. Cystic fibrosis clinic, Aarhus University Hospital, Denmark.

Interventions

elexacaftor/tezacaftor/ivacaftor

Outcome measures

Quantification of urine bicarbonate excretion after an acute oral sodium bicarbonate challenge before and 6 months after elexacaftor/tezacaftor/ivacaftor treatment.

Main results

At baseline, challenged urine bicarbonate excretion was associated with several CF disease characteristics. Bicarbonate excretion was higher in patients with residual function mutations. A higher bicarbonate excretion was associated with better lung function, pancreatic sufficiency, and lower relative risk for chronic pseudomonas infections. Elexacaftor/tezacaftor/ivacaftor treatment increased bicarbonate excretion by 3.9 mmol/3 h (95% CI, 1.6 to 6.1 mmol/3 h), reaching about 70% of that seen in healthy control participants. In healthy control participants, individual bicarbonate excretion at each visit correlated with the individual mean bicarbonate excretion. The median coefficient of variation was 31%.

Authors' conclusions

Although further studies are needed to address the performance and sensitivity of this approach, this early-stage evaluation shows that challenged urine bicarbonate excretion may offer a new, simple, and safe quantification of CFTR function and the extent of its pharmacologic improvement. Elexacaftor/tezacaftor/ivacaftor partially restores renal CFTR function in patients with CF, likely resulting in decreased risk for electrolyte disorders and metabolic alkalosis.

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See also

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Keywords

Adult; Aged; CFTR Modulators; Genetic Predisposition to Disease; pharmacological_intervention; placebo; VX-770; VX-661; ivacaftor; Aminophenols; tezacaftor; VX-445; elexacaftor; non pharmacological intervention - diagn; Trikafta;