primary studies - published RCT

VX-445-Tezacaftor-Ivacaftor in Patients with Cystic Fibrosis and One or Two Phe508del Alleles.

Code: PM30334692 **Year:** 2018 **Date:** 2018 **Author:** Keating D

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

Randomized, placebo-controlled, double-blind, dose-ranging, phase 2 trial

Participants

Patients heterozygous for the Phe508del CFTR mutation and a minimal-function mutation (Phe508del-MF) and patients homozygous for the Phe508del CFTR mutation (Phe508del-Phe508del)

Interventions

VX-445, a next-generation cystic fibrosis transmembrane conductance regulator (CFTR) corrector vs placebo

Outcome measures

Primary end points were safety and absolute change in percentage of predicted forced expiratory volume in 1 second (FEV1) from baseline.

Main results

In vitro, VX-445-tezacaftor-ivacaftor significantly improved Phe508del CFTR protein processing, trafficking, and chloride transport to a greater extent than any two of these agents in dual combination. In patients with cystic fibrosis, VX-445-tezacaftor-ivacaftor had an acceptable safety and side-effect profile. Most adverse events were mild or moderate. The treatment also resulted in an increased percentage of predicted FEV1 of up to 13.8 points in the Phe508del-MF group (P

Authors' conclusions

The use of VX-445-tezacaftor-ivacaftor to target Phe508del CFTR protein resulted in increased CFTR function in vitro and translated to improvements in patients with cystic fibrosis with one or two Phe508del alleles. This approach has the potential to treat the underlying cause of cystic fibrosis in approximately 90% of patients.

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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;