primary studies - published RCT

Triple Therapy for Cystic Fibrosis Phe508del-Gating and -Residual Function Genotypes.

Code: PM34437784 **Year:** 2021 **Date:** 2021 **Author:** Barry PJ

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

Phase 3, double-blind, randomized, active-controlled trial

Participants

Patients 12 years of age or older with cystic fibrosis and Phe508del-gating or Phe508del-residual function genotypes.

Interventions

After the run-in period, 132 patients received elexacaftor-tezacaftor-ivacaftor and 126 received active control.

Outcome measures

Elexacaftor-tezacaftor-ivacaftor resulted in a percentage of predicted FEV(1) that was higher by 3.7 percentage points (95% confidence interval [CI], 2.8 to 4.6) relative to baseline and higher by 3.5 percentage points (95% CI, 2.2 to 4.7) relative to active control and a sweat chloride concentration that was lower by 22.3 mmol per liter (95% CI, 20.2 to 24.5) relative to baseline and lower by 23.1 mmol per liter (95% CI, 20.1 to 26.1) relative to active control (P

Main results

Elexacaftor-tezacaftor-ivacaftor was efficacious and safe in patients with Phe508del-gating or Phe508del-residual function genotypes and conferred additional benefit relative to previous CFTR modulators.

Authors' conclusions

AB - BACKGROUND: Elexacaftor-tezacaftor-ivacaftor is a small-molecule cystic fibrosis transmembrane conductance regulator (CFTR) modulator regimen shown to be efficacious in patients with at least one Phe508del allele, which indicates that this combination can modulate a single Phe508del allele. In patients whose other CFTR allele contains a gating or residual function mutation that is already effectively treated with previous CFTR modulators (ivacaftor or tezacaftor-ivacaftor), the potential for additional benefit from restoring Phe508del CFTR protein function is unclear. METHODS: We conducted a phase 3, double-blind, randomized, active-controlled trial involving patients 12 years of age or older with cystic fibrosis and Phe508del-gating or Phe508del-residual function genotypes. After a 4-week run-in period with ivacaftor or tezacaftor-ivacaftor, patients were randomly assigned to receive elexacaftor-tezacaftor-ivacaftor or active control for 8 weeks. The primary end point was the absolute change in the percentage of predicted forced expiratory volume in 1 second (FEV(1)) from baseline through week 8 in the elexacaftor-tezacaftor-ivacaftor group. RESULTS: After the run-in period, 132 patients received elexacaftor-tezacaftor-ivacaftor and 126 received active control. Elexacaftor-tezacaftor-ivacaftor resulted in a percentage of predicted FEV(1) that was higher by 3.7 percentage points (95% confidence interval [CI], 2.8 to 4.6) relative to baseline and higher by 3.5 percentage points (95% CI, 2.2 to 4.7) relative to active control and a sweat chloride concentration that was lower by 22.3 mmol per liter (95% CI, 20.2 to 24.5) relative to baseline and lower by 23.1 mmol per liter (95% CI, 20.1 to 26.1) relative to active control (P

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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; Trikafta;