primary studies - published RCT

Elexacaftor/tezacaftor/ivacaftor for cystic fibrosis and rare CFTR variants: in vitro translation to a phase 3, double-blind, randomized, placebo-controlled trial, and real-world study.

Code: PM41738096 **Year:** 2026 **Date:** **Author:** Castellani C

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

Randomized, placebo-controlled, Phase 3 trial

Participants

Authors engineered Fischer rat thyroid (FRT) cells each of which express 1 of 620 rare exonic CFTR variants present in public databases and evaluated their in vitro response to elexacaftor/tezacaftor/ivacaftor; and evaluated efficacy and safety of elexacaftor/tezacaftor/ivacaftor in a 24-week randomized, placebo-controlled, Phase 3 trial (445-124) in participants with 1 of 18 rare variants and no F508del and in a real-world study (CFD-016) in people carrying 82 rare variants and no F508del.

Interventions

Elexacaftor/tezacaftor/ivacaftor

Outcome measures

Efficacy and safety; primary endpoint: percent predicted FEV1; secondary endpoints: sweat chloride and CFQ-R RD

Main results

In FRT cells, 518 of 620 (84%) rare variants responded to elexacaftor/tezacaftor/ivacaftor. In 445-124, mean improvements were seen in the primary endpoint of percent predicted FEV1 (9.2 percentage points [95% CI: 7.2, 11.3; Pâ€‰

Authors' conclusions

In vitro, clinical, and real-world data support elexacaftor/tezacaftor/ivacaftor treatment in people carrying a range of CFTR variants and no F508del. The response of 84% of rare CFTR variants that produce protein to protein-stabilizing therapy suggests variants in many regions of the protein causes disease via protein destabilization.

http://dx.doi.org/10.1093/ajrccm/aamaf001

See also

Am J Respir Crit Care Med. 2026 Feb 1;212(2):327-337. doi: 10.1093/ajrccm/aamaf001.

Keywords

CFTR Modulators; Genetic Predisposition to Disease; pharmacological_intervention; placebo; VX-770; VX-661; ivacaftor; Aminophenols; tezacaftor; VX-445; elexacaftor; Trikafta; Child; kaftrio;