primary studies - published RCT

Efficacy and safety of elexacaftor plus tezacaftor plus ivacaftor versus tezacaftor plus ivacaftor in people with cystic fibrosis homozygous for F508del-CFTR: a 24-week, multicentre, randomised, double-blind, active-controlled, phase 3b trial.

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

Multicentre, randomised, double-blind, active-controlled, phase 3b trial

Participants

People with cystic fibrosis homozygous for the F508del-CFTR mutation.

Interventions

Elexacaftor plus tezacaftor plus ivacaftor. After a 4-week run-in period, in which participants received tezacaftor 100 mg orally once daily and ivacaftor 150 mg orally every 12 h, participants were randomly assigned (1:1) to receive 24 weeks of either elexacaftor 200 mg orally once daily plus tezacaftor 100 mg orally once daily plus ivacaftor 150 mg orally every 12 h (elexacaftor plus tezacaftor plus ivacaftor group) or tezacaftor 100 mg orally once daily plus ivacaftor 150 mg orally every 12 h (tezacaftor plus ivacaftor group).

Outcome measures

The primary endpoint was the absolute change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score from baseline (ie, at the end of the tezacaftor plus ivacaftor run-in period) up to and including week 24. The key secondary endpoint was the absolute change from baseline in percent predicted FEV(1) up to and including week 24; other secondary endpoints were the absolute change from baseline in sweat chloride concentrations up to and including week 24, and safety and tolerability. All endpoints were assessed in all randomised patients who had received at least one dose of their assigned regimen.

Main results

Between Oct 3, 2019, and July 24, 2020, 176 participants were enrolled. Following the 4-week tezacaftor plus ivacaftor run-in period, 175 participants were randomly assigned (87 to the elexacaftor plus tezacaftor plus ivacaftor group and 88 to the tezacaftor plus ivacaftor group) and dosed in the treatment period. From baseline up to and including week 24, the mean CFQ-R respiratory domain score increased by 17·1 points (95% CI 14·1 to 20·1) in the elexacaftor plus tezacaftor plus ivacaftor group and by 1·2 points (-1·7 to 4·2) in the tezacaftor plus ivacaftor group (least squares mean treatment difference 15·9 points [95% CI 11·7 to 20·1], p

Authors' conclusions

The elexacaftor plus tezacaftor plus ivacaftor regimen was safe and well tolerated, and led to significant and clinically meaningful improvements in respiratory-related quality of life and lung function, as well as improved CFTR function, changes that were durable over 24 weeks and superior to those seen with tezacaftor plus ivacaftor in this patient population.

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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; kaftrio;