primary studies - published RCT

Sweat chloride as a biomarker of CFTR activity: Proof of concept and ivacaftor clinical trial data.

Code: PM24660233 **Year:** 2014 **Date:** 2019 **Author:** Accurso FJ

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

Phase 3, multicentre, randomised, double-blind, active-controlled trial

Participants

Eligible participants were those with cystic fibrosis homozygous for the F508del mutation, aged 12 years or older with stable disease, and with a percentage predicted forced expiratory volume in 1 s (ppFEV1) of 40-90%, inclusive.

Interventions

After a 4-week tezacaftor plus ivacaftor run-in period, participants were randomly assigned (1:1) to 4 weeks of elexacaftor 200 mg orally once daily plus tezacaftor 100 mg orally once daily plus ivacaftor 150 mg orally every 12 h versus tezacaftor 100 mg orally once daily plus ivacaftor 150 mg orally every 12 h alone.

Outcome measures

The primary outcome was the absolute change from baseline (measured at the end of the tezacaftor plus ivacaftor run-in) in ppFEV1 at week 4. Key secondary outcomes were absolute change in sweat chloride and Cystic Fibrosis Questionnaire-Revised respiratory domain (CFQ-R RD) score.

Main results

Between Aug 3 and Dec 28, 2018, 113 participants were enrolled. Following the run-in, 107 participants were randomly assigned (55 in the elexacaftor plus tezacaftor plus ivacaftor group and 52 in the tezacaftor plus ivacaftor group) and completed the 4-week treatment period. The elexacaftor plus tezacaftor plus ivacaftor group had improvements in the primary outcome of ppFEV1 (least squares mean [LSM] treatment difference of 10.0 percentage points [95% CI 7.4 to 12.6], p

Authors' conclusions

Elexacaftor plus tezacaftor plus ivacaftor provided clinically robust benefit compared with tezacaftor plus ivacaftor alone, with a favourable safety profile, and shows the potential to lead to transformative improvements in the lives of people with cystic fibrosis who are homozygous for the F508del mutation.

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/403/CN-00978403/frame.html

See also

J Cyst Fibros. 2014 Mar;13(2):139-47.

Keywords

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