primary studies - published RCT

Ivacaftor in People With Cystic Fibrosis and a 3849+10kb C â†’T or D1152H Residual Function Mutation.

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

Placebo-controlled randomized crossover study

Participants

People with cystic fibrosis aged â‰¥6 years with 3849+10kb Câ†’T or D1152H residual function mutations. N = 38

Interventions

Ivacaftor; each treatment sequence included two 8-week treatments with an 8-week washout period.

Outcome measures

The primary endpoint was absolute change in lung clearance index2.5 from baseline through Week 8. Additional endpoints included lung function, patient-reported outcomes, and in vitro intestinal organoid-based measurements of ivacaftor-induced cystic fibrosis transmembrane conductance regulator function.

Main results

Of 38 participants, 37 completed the study. The primary endpoint was met; the Bayesian posterior probability of improvement in lung clearance index2.5 with ivacaftor vs placebo was >99%. Additional endpoints improved with ivacaftor. Safety findings were consistent with ivacaftor's known safety profile. Dose-dependent swelling was observed in 23/25 viable organoid cultures with ivacaftor treatment. Correlations between ivacaftor-induced organoid swelling and clinical endpoints were negligible to low.

Authors' conclusions

In people with cystic fibrosis aged â‰¥6 years with a 3849+10kb C â†’T or D1152H mutation, ivacaftor treatment improved clinical endpoints vs placebo; however, there was no correlation between organoid swelling and change in clinical endpoints. The organoid assay may assist in identification of ivacaftor-responsive mutations but in this study did not predict magnitude of clinical benefit for individual people with cystic fibrosis with these two mutations.

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See also

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Keywords

Aminophenols; CFTR Modulators; Genetic Predisposition to Disease; pharmacological_intervention; VX-770; ivacaftor;