primary studies - published RCT

A CFTR corrector (lumacaftor) and a CFTR potentiator (ivacaftor) for treatment of patients with cystic fibrosis who have a phe508del CFTR mutation: a phase 2 randomised controlled trial.

Code: PM24973281 **Year:** 2014 **Date:** 2014 **Author:** Boyle MP

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

Phase 2 clinical trial, recruitment from 24 cystic fibrosis centres in Australia, Belgium, Germany, New Zealand, and the USA.

Participants

Eligibility criteria were: confirmed diagnosis of cystic fibrosis, age at least 18 years, and a forced expiratory volume in 1 s (FEV1) of 40% or more than predicted. Cohort 1 included phe508del CFTR homozygous patients. Cohort 1 included phe508del CFTR homozygous patients. Together, cohorts 2 and 3 included phe508del CFTR homozygous and heterozygous patients.

Interventions

Cohort 1 included phe508del CFTR homozygous patients randomly assigned to either lumacaftor 200 mg once per day for 14 days followed by addition of ivacaftor 150 mg or 250 mg every 12 h for 7 days, or 21 days of placebo. Together, cohorts 2 and 3 included phe508del CFTR homozygous and heterozygous patients, randomly assigned to either 56 days of lumacaftor (cohort 2: 200 mg, 400 mg, or 600 mg once per day, cohort 3: 400 mg every 12 h) with ivacaftor 250 mg every 12 h added after 28 days, or 56 days of placebo.

Outcome measures

The primary outcomes for all cohorts were change in sweat chloride concentration during the combination treatment period in the intention-to-treat population and safety (laboratory measurements and adverse events).

Main results

Cohort 1 included 64 participants. Cohort 2 and 3 combined contained 96 phe508del CFTR homozygous patients and 28 compound heterozygotes. Treatment with lumacaftor 200 mg once daily and ivacaftor 250 mg every 12 h decreased mean sweat chloride concentration by 9.1 mmol/L (p

Authors' conclusions

Combination of lumacaftor and ivacaftor improves FEV1 for patients with cystic fibrosis who are homozygous for phe508del CFTR, with a modest effect on sweat chloride concentration. These results support the further exploration of combination lumacaftor and ivacaftor as a treatment in this setting.

http://dx.doi.org/10.1016/S2213-2600(14)70132-8

See also

Lancet Respir Med. 2014 Jun 24. pii: S2213-2600(14)70132-8. doi: 10.1016/S2213-2600(14)70132-8.

Keywords

Child; Adult; Adolescent; Aminophenols; CFTR Modulators; Genetic Predisposition to Disease; Orkambi; pharmacological_intervention; VX-770; ivacaftor; lumacaftor; VX-809;