primary studies - published RCT

Results of a phase IIa study of VX-809, an investigational CFTR corrector compound, in subjects with cystic fibrosis homozygous for the F508del-CFTR mutation.

Code: PM21825083 **Year:** 2012 **Date:** 2012 **Author:** Clancy JP

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

randomised, double-blind, placebo-controlled study

Participants

adult patients with cystic fibrosis (n=89) who were homozygous for the F508del-CFTR mutation

Interventions

Subjects were randomised to one of four VX-809 28 day dose groups (25, 50, 100 and 200 mg) or matching placebo

Outcome measures

The type and incidence of adverse events. Respiratory events. CFTR function: sweat chloride, function in the nasal epithelium as measured by nasal potential difference, changes in lung function or patient-reported outcomes.

Main results

The type and incidence of adverse events were similar among VX-809- and placebo-treated subjects. Respiratory events were the most commonly reported and led to discontinuation by one subject in each active treatment arm. Pharmacokinetic data supported a once-daily oral dosing regimen. Pharmacodynamic data suggested that VX-809 improved CFTR function in at least one organ (sweat gland). VX-809 reduced elevated sweat chloride values in a dose-dependent manner (p=0.0013) that was statistically significant in the 100 and 200 mg dose groups. There was no statistically significant improvement in CFTR function in the nasal epithelium as measured by nasal potential difference, nor were there statistically significant changes in lung function or patient-reported outcomes. No maturation of immature F508del-CFTR was detected in the subgroup that provided rectal biopsy specimens.

Authors' conclusions

In this study, VX-809 had a similar adverse event profile to placebo for 28 days in F508del-CFTR homozygous patients, and demonstrated biological activity with positive impact on CFTR function in the sweat gland. Additional data are needed to determine how improvements detected in CFTR function secondary to VX-809 in the sweat gland relate to those measurable in the respiratory tract and to long-term measures of clinical benefit.

http://dx.doi.org/10.1136/thoraxjnl-2011-200393

See also

Thorax. 2012 Jan;67(1):12-8. Epub 2011 Aug 8.

Keywords

Adult; Aged; CFTR Modulators; placebo; VX-809; pharmacological_intervention; lumacaftor;