primary studies - published, non RCT

Effect of elexacaftor-tezacaftor-ivacaftor on bronchial dilatations in adolescents with cystic fibrosis: a multicentre prospective observational study.

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

Prospective observational study i

Participants

33 paediatric cystic fibrosis reference centres in France. Adolescent cohort of individuals with cystic fibrosis (aged 12-18 years) from the Modul-CF study who initiated treatment with ETI as part of routine care. These individuals were either homozygous for F508del and previously treated with lumacaftor-ivacaftor (LI), or F508del homozygous or compound heterozygous for F508del with a minimal function or residual function variant and naive to CFTR modulator treatment.

Interventions

Elexacaftor-tezacaftor-ivacaftor (ETI)

Outcome measures

The primary outcome measure was chest CT to investigate the effect of CFTR restoration on the natural history of cystic fibrosis lung disease. Secondary outcomes were sweat chloride, weight and height Z scores, quality of life, pulmonary function tests, lung clearance index at 2Â·5% of starting concentration (LCI(2Â·5)) from nitrogen multiple breath washout, and proinflammatory biomarkers in sputum (calprotectin, neutrophil elastase, IL-1Î², IL-6, IL-8, and TNF-Î±) and blood (C-reactive protein and polymorphonuclear neutrophils). Outcome data were collected from baseline (in the 4 weeks before commencement of ETI [denoted month 0]) up to 1 year of ETI treatment (denoted month 12), with low-dose inspiratory-controlled chest CT done at month 0 and month 12. Changes in outcome measures from month 0 to month 12 were assessed with non-parametric Wilcoxon tests. Modul-CF was registered with ClinicalTrials.gov, NCT04301856, and is ongoing and open to recruitment. The data cutoff for the present analysis was July 28, 2023.

Main results

Between March 22, 2021, and May 25, 2022, a total of 330 adolescents with cystic fibrosis were enrolled in the study, of whom 320 were treated with ETI for 12 months and included in analyses (mean age at ETI initiation 14Â·1 years [SD 1Â·5]; 162 [51%] female and 158 [49%] male participants). Of the 320 participants, 112 (35%) were switched from LI to ETI, and 208 (65%) were CFTR modulator-naive. In the overall population, improvement in percent predicted FEV(1) (ppFEV(1)) was observed from the first month of ETI treatment and was sustained at 12 months (mean absolute ppFEV(1) change from month 0 to month 12, 14Â·0% [95% CI 12Â·4-15Â·7], p

Authors' conclusions

Bronchial dilatations can reverse in adolescents with cystic fibrosis treated with ETI. The correlation with reduced airway inflammation provides insight into the effect of ETI on cystic fibrosis lung disease. FUNDING: Vaincre La Mucoviscidose, Mucoviscidose ABCF2, and the Cystic Fibrosis Foundation.

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See also

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Keywords

CFTR Modulators; Genetic Predisposition to Disease; pharmacological_intervention; placebo; VX-770; VX-661; ivacaftor;

Aminophenols; tezacaftor; VX-445; elexacaftor; Trikafta;