*primary studies - published RCT*

# Withdrawal of dornase alfa increases ventilation inhomogeneity in children with cystic fibrosis.

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

Phase 3, open-label, single-arm extension study

### Participants

Patients with F508del-minimal function genotypes (from 24-week parent study 445-102 [n = 399]) or with the F508del-F508del genotype (from 4-week parent study 445-103 [n = 107])

### Interventions

Participants received ELX/TEZ/IVA (ELX 200 mg once daily, TEZ 100 mg once daily, and IVA 150 mg every 12 hours) over 192 weeks.

### Outcome measures

Primary endpoint was safety and tolerability. Mean exposure to ELX/TEZ/IVA was 172.6 weeks.

### Main results

Most participants had adverse events classified as mild (12.8%) or moderate (60.7%) in severity. Eighteen participants (3.6%) had adverse events that led to treatment discontinuation. After starting ELX/TEZ/IVA, participants had consistent increases in percent predicted FEV(1) (ppFEV(1)), Cystic Fibrosis Questionnaire-Revised respiratory domain score, and body mass index, with decreases in sweat chloride concentration and pulmonary exacerbations rates; these improvements were maintained through 192 weeks. The mean annualized rate of change in ppFEV(1) was 0.02 percentage points (95% CI, -0.14 to 0.19) after initiation of ELX/TEZ/IVA.

### Authors' conclusions

During this 192-week open label extension study, the longest clinical study of a CFTR modulator to date, ELX/TEZ/IVA remained generally safe and well-tolerated. Participants had sustained improvements in lung function, respiratory symptoms, CFTR function, pulmonary exacerbation rates, and nutritional status. The estimated annualized rate of change in ppFEV(1) suggests no evidence of pulmonary function loss across the study population over the 4-year treatment period. These results confirm the favorable long-term safety profile and durable disease-modifying clinical benefits of ELX/TEZ/IVA in adolescents and adults with CF.

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### See also

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### Keywords

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