*primary studies - published RCT*

# Ataluren for the treatment of nonsense-mutation cystic fibrosis: a randomised, double-blind, placebo-controlled phase 3 trial.

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

Randomised, double-blind, placebo-controlled, phase 3 study

### Participants

Patients with nonsense-mutation cystic fibrosis from 36 sites in 11 countries in North America and Europe (aged >/=6 years; abnormal nasal potential difference; sweat chloride >40 mmol/L; forced expiratory volume in 1 s [FEV1] >/=40% and

### Interventions

Patients were randomly assigned by interactive response technology to receive oral ataluren (10 mg/kg in morning, 10 mg/kg midday, and 20 mg/kg in evening) or matching placebo for 48 weeks. Randomisation used a block size of four, stratified by age, chronic inhaled antibiotic use, and percent-predicted FEV1.

### Outcome measures

The primary endpoint was relative change in percent-predicted FEV1 from baseline to week 48, analysed in all patients with a post-baseline spirometry measurement.

### Main results

Between Sept 8, 2009, and Nov 30, 2010, 238 patients were randomly assigned, of whom 116 in each treatment group had a valid post-baseline spirometry measurement. Relative change from baseline in percent-predicted FEV1 did not differ significantly between ataluren and placebo at week 48 (-2.5% vs -5.5%; difference 3.0% [95% CI -0.8 to 6.3]; p=0.12). The number of pulmonary exacerbations did not differ significantly between treatment groups (rate ratio 0.77 [95% CI 0.57-1.05]; p=0.0992). However, post-hoc analysis of the subgroup of patients not using chronic inhaled tobramycin showed a 5.7% difference (95% CI 1.5-10.1) in relative change from baseline in percent-predicted FEV1 between the ataluren and placebo groups at week 48 (-0.7% [-4.0 to 2.1] vs -6.4% [-9.8 to -3.7]; nominal p=0.0082), and fewer pulmonary exacerbations in the ataluern group (1.42 events [0.9-1.9] vs 2.18 events [1.6-2.7]; rate ratio 0.60 [0.42-0.86]; nominal p=0.0061). Safety profiles were generally similar for ataluren and placebo, except for the occurrence of increased creatinine concentrations (ie, acute kidney injury), which occurred in 18 (15%) of 118 patients in the ataluren group compared with one (

### Authors' conclusions

INTERPRETATION: Although ataluren did not improve lung function in the overall population of nonsense-mutation cystic fibrosis patients who received this treatment, it might be beneficial for patients not taking chronic inhaled tobramycin. FUNDING: PTC Therapeutics, Cystic Fibrosis Foundation, US Food and Drug Administration's Office of Orphan Products Development, and the National Institutes of Health.

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### See also

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### Keywords

PTC124; Ataluren; CFTR Modulators; pharmacological_intervention;