primary studies - published RCT

Safety and tolerability of denufosol tetrasodium inhalation solution, a novel P2Y2 receptor agonist: results of a phase 1/phase 2 multicenter study in mild to moderate cystic fibrosis.

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

double-blind, placebo-controlled, multicenter trial

Participants

37 adult (18 years of age or older) and 24 pediatric (5-17 years of age) subjects with CF were evaluated in five cohorts.

Interventions

ascending single doses of denufosol (10, 20, 40, and 60 mg, administered by inhalation via the Pari LC Star nebulizer) vs. placebo (normal saline), followed by twice-daily administration of the maximum tolerated dose (MTD) of denufosol or placebo for 5 days. Subjects were randomized in a 3:1 ratio to receive either denufosol or placebo within each cohort.

Outcome measures

adverse events, FEV1.

Main results

The percent of subjects experiencing adverse events was similar between the denufosol and placebo groups. The most common adverse event in subjects receiving denufosol was chest tightness in adult subjects (39%) and cough in pediatric subjects (56%). Three (7%) subjects receiving denufosol and one (7%) subject receiving placebo experienced a serious adverse event. Forced expiratory volume in 1 sec (FEV(1)) profiles following dosing were similar across treatment groups, with some acute, reversible decline seen in both groups, most notably in subjects with lower lung function at baseline.

Authors' conclusions

Doses up to 60 mg of denufosol inhalation solution were well-tolerated in most subjects. Some intolerability was noted among subjects with lower baseline lung function. Based on the results of this phase 1/phase 2 study, the Therapeutics Development Network (TDN) of the Cystic Fibrosis Foundation (CFF) and Inspire Pharmaceuticals, Inc., recently completed a multicenter, 28-day, phase 2 safety and efficacy clinical trial of denufosol inhalation solution in CF subjects with mild lung disease.

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See also

Pediatr Pulmonol. 2005 Apr;39(4):339-48.

Keywords

Adolescent; Child; Other drugs; denufosol; Inhalation OR nebulised; pharmacological_intervention;