primary studies - published RCT

Inhaled dry powder mannitol in children with cystic fibrosis: A randomised efficacy and safety trial.

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

Randomized controlled trial (crossover design)

Participants

CF Patients aged â‰¥12 years with A455E-CFTR mutation

Interventions

Participants were randomized to 1 of 2 treatment sequences (LUM/IVAâ†'placebo or placeboâ†'LUM/IVA) with an 8-week washout period between.

Outcome measures

Primary endpoint was absolute change in ppFEV(1) from study baseline through 8 weeks. Additional endpoints were change in sweat chloride concentration (SwCl) and CFQ-R respiratory domain score. Correlations between organoid-based measurements and clinical endpoints were investigated.

Main results

Twenty participants were randomized at 2 sites in the Netherlands. Mean absolute change in ppFEV(1) from study baseline through Week 8 showed a treatment difference of 0.1 percentage points (95% CI, -2.5 to 2.7; P = 0.928) between LUM/IVA (within-group mean change, 2.7) and placebo (within-group mean change, 2.6). The mean absolute change in SwCl concentration from study baseline through Week 8 showed a treatment difference of -7.8 mmol/L between LUM/IVA and placebo (P = 0.004), while the absolute change in CFQ-R respiratory domain score showed a treatment difference of 3.5 between LUM/IVA and placebo (P = 0.469). The in vitro organoid-based assay demonstrated a concentration-dependent swelling increase with LUM/IVA. Exploratory correlation analyses between organoid swelling and ppFEV(1) and SwCl outcomes showed correlation coefficients of 0.49 and -0.11, respectively.

Authors' conclusions

In this exploratory study, LUM/IVA elicited an in vitro response in organoid swelling and in vivo response in SwCl in participants with CF and â‰¥1 A455E-CFTR mutation. The primary endpoint (ppFEV(1)) did not show a statistically significant difference between LUM/IVA and placebo; correlations between in vitro and in vivo responses were not established

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See also

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Keywords

Adult; Aminophenols; Anti-Bacterial Agents; CFTR Modulators; Genetic Predisposition to Disease; pharmacological_intervention; Quinolones; GLPG2737; ivacaftor+lumacaftor; Orkambi;