Randomised trial of the $P2X_3$ receptor antagonist sivopixant for refractory chronic cough

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Shareable abstract (@ERSpublications)
This study shows the efficacy of a highly selective $P2X_3$ receptor antagonist to reduce cough frequency, with low incidence of taste disturbance. Sivopixant may be a promising therapeutic option for refractory or unexplained chronic cough. https://bit.ly/3awojQH

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Abstract

Background The purinoceptor subtype $P2X_3$ has been shown to have significant involvement in the cough reflex; the heterotrimer version of the purinoceptor ($P2X_{2/3}$) has been implicated in taste disturbance. The most advanced clinical candidate antagonist gefapixant has low selectivity among $P2X_3$ receptors and induced taste disturbance, whereas newly developed sivopixant has high selectivity towards $P2X_3$ *versus* $P2X_{2/3}$.

Methods In a phase 2a, randomised, double-blind, placebo-controlled, crossover, multicentre study, adult patients with refractory or unexplained chronic cough received oral sivopixant 150 mg or placebo once daily for 2 weeks, followed by a 2–3-week washout period, and then crossed over to placebo or sivopixant for 2 weeks. Efficacy and safety of sivopixant were evaluated.

Results Of 31 randomised patients, 15 in the sivopixant-first group and 15 in the placebo-first group completed the study. After 2 weeks of treatment, the placebo-adjusted ratios of the average hourly number of coughs to baseline during daytime (primary end-point) and over 24 h (secondary end-point) were −31.6% (p=0.0546) and −30.9% (p=0.0386), respectively. Sivopixant also improved health-related quality of life. Treatment-related adverse events occurred in 12.9% and 3.2% of patients during sivopixant and placebo administration, respectively. Mild taste disturbance occurred in two patients (6.5%) during sivopixant administration.

Conclusions Sivopixant reduced objective cough frequency and improved health-related quality of life, with a low incidence of taste disturbance, among patients with refractory or unexplained chronic cough.