'The drugs do work!’ – New treatments in cough

A PHASE 3B TRIAL OF GEFAPIXANT, A P2X3-RECEPTOR ANTAGONIST, IN WOMEN WITH CHRONIC COUGH AND STRESS URINARY INCONTINENCE

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Introduction and Objectives The majority of women with chronic cough experience cough-induced stress urinary incontinence (cSUI), or involuntary loss of urine on coughing; however, this complication of cough is underappreciated. This multicenter, randomized, placebo-controlled phase 3b trial (NCT04193176) investigated gefapixant in women with refractory or unexplained chronic cough (RCC/UCC) and cSUI.

Methods Adult women with RCC/UCC for ≥12 months and pure/predominant SUI for ≥3 months were enrolled. Additional inclusion criteria were ≥40-mm cough severity visual analog scale score (100-mm scale) at screening and placebo run-in, ≥2 cSUI episodes/day before placebo run-in and randomization, and positive cough stress test for SUI at screening. After screening and a 2-week, single-blind, placebo run-in, participants were randomized to gefapixant 45 mg twice daily (BID) or placebo for 12 weeks. Change in frequency of self-reported cSUI episodes from baseline to Week 12 (measured as a 7-day daily average using the Incontinence Diary) was the primary endpoint. An exploratory endpoint was change in Cough Severity Diary (CSD) scores from baseline to Week 12. Safety and tolerability were also evaluated.

Results Of 375 women, 190 and 185 were randomized to gefapixant 45 mg BID or placebo, respectively. Mean age (~56–57 years), cough duration (~5.1–5.2 years), SUI duration (~3.6–4.5 years), and number of daily cSUI episodes (~4.7 episodes/day) were similar between groups at baseline. At Week 12, treatment with gefapixant 45 mg BID resulted in greater model-based mean (95% confidence interval [CI]) reductions in daily cSUI episodes (52.76% [47.09, 58.44%]) compared with placebo (41.09% [35.45, 46.74%]; figure 1), with an estimated treatment difference (95% CI) of −11.67% (−19.67, −3.67; P=0.004). Mean weekly CSD scores at Week 12 were also reduced compared with placebo, with an estimated treatment difference (95% CI) of −0.85 (−0.85, −0.03). Adverse events were reported in 69.7% and 37.4% of women in the gefapixant and placebo groups, respectively, with no serious treatment-related adverse events.

Conclusions After 12 weeks of treatment, gefapixant was superior to placebo in reducing mean daily cSUI episodes and improving cough severity in women with RCC/UCC and cSUI, with a safety profile similar to previous studies.

REFERENCE

Please refer to page A282 for declarations of interest related to this abstract.

PACIFY COUGH: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, TWO-WAY CROSSOVER TRIAL OF MST FOR THE TREATMENT OF COUGH IN IDIOPATHIC PULMONARY FIBROSIS

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Introduction Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic lung disease. The majority of patients with IPF report cough which is associated with significant negative physical, social and psychological consequences. At present there are no approved treatments for IPF-related cough. We evaluated the effect of low dose controlled-release morphine sulfate (MST) as an antitussive therapy in individuals with IPF.

Design PulmonArty Fibrosis (PaciFy) Cough was a randomised, double-blind, placebo-controlled, two-way crossover trial of MST in subjects with IPF. Patients were randomised (1:1) to either placebo twice daily or MST 5 mg twice daily for 14 days. Patients then underwent crossover after a 7-day washout period. The primary endpoint was percent change in objective awake cough frequency at day 14 of treatment. The primary endpoint was percent change in objective awake cough frequency at day 14 of treatment in the intention-to-treat population. Secondary endpoints included change from baseline in patient reported outcomes (cough VAS, Leicester Cough Questionnaire [LCQ], Dyspnoea 12, Living with IPF [L-IPF] questionnaires). This study was registered at ClinicalTrials.gov, NCT04429516.
Results Among the 44 patients who were randomized (mean age 71 years; 70% men), 43 completed the morphine arm and 41 completed the placebo arm. In the ITT analysis, MST reduced awake cough frequency by 39.4% compared to placebo (95% CI, -54.4 to -19.4; P < 0.001). The proportion of responders was greater in the MST arm (25/43) compared to placebo (odds ratio 2.48, [95% CI 1.01 to 5.9]). Furthermore, MST treatment led to improvements in cough VAS (-16.1mm, P < 0.001), LCQ (1.8 points, P < 0.001), L-IPF impacts (-5.2, P = 0.033) and L-IPF cough domain (-10.8, P < 0.001). The main side effects reported were nausea (14%) and constipation (21%). One serious adverse event (death) occurred during the placebo arm, the cause of which was not related to trial drug.

Conclusion MST is an effective antitussive in patients with IPF. Given the established safety profile of morphine in IPF these findings are rapidly translatable into clinical practice.

S3
GEFAPIXANT EFFICACY AND SAFETY IN PARTICIPANTS WITH HISTORY OF REFRACTORY OR UNEXPLAINED CHRONIC COUGH FOR ≥1 VS <1 YEAR

Introduction and Objectives The efficacy, safety, and tolerability of gefapixant were previously studied in two phase 3 trials of individuals with refractory or unexplained chronic cough (RCC/UCC) for ≥1 year and in a phase 3b trial of individuals with cough history >8 weeks and RCC/UCC for <1 year. This analysis compared baseline characteristics and efficacy and safety profiles of gefapixant 45 mg twice daily (BID) after 12 weeks of treatment in these trial populations to assess how these variables compare in individuals with RCC/UCC for ≥1 vs <1 year.

Methods Participants with RCC/UCC for ≥1 year in the phase 3 trials (NCT03449134 [COUGH-1], NCT03449147 [COUGH-2]; pooled) and with RCC/UCC for <1 year in the phase 3b trial (NCT04193202) who received gefapixant 45 mg BID or placebo were analyzed. Change from baseline in patient-reported outcomes, including Leicester Cough Questionnaire (primary endpoint for <1-year trial), cough severity visual analog scale, and Cough Severity Diary, were evaluated at Week 12. Safety was also evaluated at Week 12.

Results Demographics and baseline cough characteristics were similar across trials (≥1 year: gefapixant 45 mg BID, n=682; placebo, n=678; <1 year: gefapixant 45 mg BID, n=206; placebo, n=209), with the exception of cough duration (mean [standard deviation]: 11 [9] years vs 7 [3] months; median [range]: 8 [2–65] years vs 8 [1–12] months). Compared with placebo, the efficacy of gefapixant 45 mg BID in improving patient-reported outcomes was similar, regardless of RCC/UCC duration (figure 1). Adverse event (AE) incidences for gefapixant 45 mg BID were 80% (≥1 year) and 64% (<1 year); taste-related AEs occurred in 64% (≥1 year) and 54% (<1 year) of participants, and >95% of AEs were mild or moderate in both data sets.

Conclusions Results from this analysis suggest a similar and favorable response to gefapixant 45 mg BID regardless of RCC/UCC duration. Please refer to page A282 for declarations of interest related to this abstract.