



SHAREABLE PDF

# Gefapixant in two randomised dose-escalation studies in chronic cough

Jaclyn A. Smith <sup>1</sup>, Michael M. Kitt<sup>2</sup>, Peter Butera<sup>2</sup>, Steven A. Smith<sup>2</sup>, Yuping Li<sup>3</sup>, Zhi Jin Xu<sup>2</sup>, Kimberley Holt<sup>1</sup>, Shilpi Sen<sup>1</sup>, Mandel R. Sher<sup>4</sup> and Anthony P. Ford<sup>2</sup>

**Affiliations:** <sup>1</sup>University of Manchester and Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Manchester, UK. <sup>2</sup>Merck & Co., Inc., Kenilworth, NJ, USA. <sup>3</sup>GetStat Solutions, LLC, Palo Alto, CA, USA. <sup>4</sup>Center for Cough, Largo, FL, USA.

**Correspondence:** Jaclyn A. Smith, Division of Infection, Immunity and Respiratory Medicine, University of Manchester, Manchester University NHS Foundation Trust, Level 2, Education and Research Centre, Wythenshawe Hospital, Manchester M23 9LT, UK. E-mail: [jacky.smith@manchester.ac.uk](mailto:jacky.smith@manchester.ac.uk)



@ERSpublications

**Patients with refractory chronic cough had significant reductions in coughing with lower doses of gefapixant than previously evaluated demonstrating efficacy and improved tolerability** <http://bit.ly/2Rg3q2t>

**Cite this article as:** Smith JA, Kitt MM, Butera P, *et al.* Gefapixant in two randomised dose-escalation studies in chronic cough. *Eur Respir J* 2020; 55: 1901615 [<https://doi.org/10.1183/13993003.01615-2019>].

This single-page version can be shared freely online.

## ABSTRACT

**Background and objectives:** Gefapixant has previously demonstrated efficacy in the treatment of refractory chronic cough at a high daily dose. The current investigations explore efficacy and tolerability of gefapixant, a P2X3 receptor antagonist, for the treatment of chronic cough using a dose-escalation approach.

**Materials and methods:** Two randomised, double-blind, placebo-controlled, crossover, dose-escalation studies recruited participants with refractory chronic cough. Patients were assigned to receive ascending doses of gefapixant (study 1: 50–200 mg, study 2: 7.5–50 mg) or placebo for 16 days, then crossed-over after washout. The primary end-point was awake cough frequency assessed using a 24-h ambulatory cough monitor at baseline and on day 4 of each dose. Patient-reported outcomes included a cough severity visual analogue scale and the cough severity diary.

**Results:** In clinical studies, gefapixant doses  $\geq 30$  mg produced maximal improvements in cough frequency compared with placebo ( $p < 0.05$ ); reported cough severity measures improved at similar doses. Taste disturbance exhibited a different relationship with dose, apparently maximal at doses  $\geq 150$  mg.

**Conclusions:** P2X3 antagonism with gefapixant demonstrates anti-tussive efficacy and improved tolerability at lower doses than previously investigated. Studies of longer duration are warranted.