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The effect of exacerbation history on outcomes in the IMPACT trial

David M.G. Halpin¹, Mark T. Dransfield², MeiLan K. Han³, C. Elaine Jones⁴, Sally Kilbride⁵, Peter Lange^{6,7}, David A. Lipson^{8,9}, David A. Lomas¹⁰, Fernando J. Martinez¹¹, Steve Pascoe^{8,12}, Dave Singh¹³, Robert Wise¹⁴ and Gerard J. Criner¹⁵

Affiliations: ¹University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, UK. ²Division of Pulmonary, Allergy, and Critical Care Medicine, Lung Health Center, University of Alabama at Birmingham, Birmingham, AL, USA. ³University of Michigan, Pulmonary & Critical Care, Ann Arbor, MI, USA. ⁴GlaxoSmithKline, Research Triangle Park, NC, USA. ⁵GlaxoSmithKline, Stockley Park, UK. ⁶Medical Dept, Herlev and Gentofte Hospital, Herlev, Denmark. ⁷University of Copenhagen, Copenhagen, Denmark. ⁸GlaxoSmithKline, Collegeville, PA, USA. ⁹Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. ¹⁰UCL Respiratory, University College London, London, UK. ¹¹New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY, USA. ¹²Sanofi, Philadelphia, PA, USA. ¹³University of Manchester, NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Hospitals Trust, Manchester, UK. ¹⁴Division of Pulmonary and Critical Care Medicine, Johns Hopkins Medicine, Baltimore, MD, USA. ¹⁵Lewis Katz School of Medicine at Temple University, Philadelphia, PA, USA.

Correspondence: David M.G. Halpin, University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, EX1 2LU, UK. E-mail: d.halpin@nhs.net



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FF/UMEC/VI shows benefits vs FF/VI and UMEC/VI across multiple endpoints irrespective of exacerbation history. Exacerbation history and eosinophils influenced the comparison between UMEC/VI and FF/VI, and eosinophils that between FF/UMEC/VI and UMEC/VI. <http://bit.ly/2SHu2ey>

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ABSTRACT IMPACT, a 52-week, randomised, double-blind trial, assessed the efficacy and safety of fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) triple therapy *versus* FF/VI or UMEC/VI in patients with symptomatic COPD and a history of exacerbations.

Subgroup analyses assessed whether the efficacy of FF/UMEC/VI *versus* FF/VI or UMEC/VI and UMEC/VI *versus* FF/VI varies according to prior exacerbation history, and the combined effects of exacerbation history and blood eosinophil counts. Three subgroups were defined: single moderate (1 moderate/no severe; n=3056 (30%)), frequent moderate (≥ 2 moderate/no severe; n=4628 (45%)) and severe (≥ 1 severe/any moderate; n=2671 (26%)). End-points included annual on-treatment moderate/severe exacerbation rate (pre-specified), lung function and health status (both post-hoc).

Moderate/severe exacerbation rates (reduction % (95% CI)) were reduced in the FF/UMEC/VI group *versus* FF/VI (single moderate 20% (10–29), frequent moderate 11% (2–19), severe 17% (7–26)) and *versus* UMEC/VI (single moderate 18% (5–29), frequent moderate 29% (21–37), severe 26% (14–35)). Moderate/severe exacerbation rates were reduced in the FF/VI group *versus* UMEC/VI in the frequent moderate subgroup; a numerical reduction was observed in the severe subgroup (single moderate 2% (–12–18), frequent moderate 21% (11–29), severe 11% (–3–22)). Moderate/severe exacerbation rates were lower in the FF/VI group compared with UMEC/VI in patients with higher eosinophil counts. FF/UMEC/VI improved lung function and health status *versus* both dual therapies irrespective of exacerbation subgroup. UMEC/VI improved lung function *versus* FF/VI in all subgroups.

Triple therapy was more effective than dual regardless of exacerbation history, consistent with results in the intent-to-treat population. Comparisons between dual therapies were influenced by prior exacerbation history and eosinophil counts.