Clinical Research Results Abstract

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Lung function Improvement and Asthma Exacerbation Reduction with Indacaterol/Glycopyrronium/Mometasone Furoate in Uncontrolled Asthma: IRIDIUM Study

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Aim: A novel once-daily (o.d.) fixed-dose combination of indacaterol (IND, long-acting β_2-agonist [LABA]), glycopyrronium (GLY, long-acting muscarinic antagonist) and mometasone furoate (MF, inhaled corticosteroid [ICS]) is under development for maintenance treatment of asthma. As a part of a pre-specified and post-hoc analysis, the IRIDIUM study (NCT02571777) evaluated the efficacy of IND/GLY/MF medium-dose o.d. (via Breezhaler®) on lung function (trough forced expiratory volume in one second [FEV_1]) and asthma exacerbations compared with salmeterol/fluticasone (Sal/Flu) twice daily (b.i.d.) (via Diskus®) and IND/MF o.d. (via Breezhaler®) in patients with uncontrolled asthma.

Methods: This was a Phase-III, multicentre, 52-week, randomised, double-blind, parallel-group, double-dummy, active-controlled study. Patients aged ≥18 – ≤75 years with asthma, pre-bronchodilator FEV_1% predicted <80%, an Asthma Control Questionnaire (ACQ-7) score ≥1.5, who experienced ≥1 severe asthma exacerbation requiring systemic corticosteroids in the previous year, and symptomatic at screening despite treatment with medium-/high-dose LABA/ICS were included. Data for patients randomised to receive IND/GLY/MF medium-dose (150/50/80 µg) o.d. or IND/MF high-dose (150/320 µg) o.d. or Sal/Flu high-dose (50/500 µg) b.i.d. for 52-weeks are presented. Trough FEV_1 (Weeks 26 and 52) and the rate of asthma exacerbations (moderate/severe, severe, and all [mild, moderate and severe]) over 52-weeks with IND/GLY/MF versus Sal/Flu and IND/MF were evaluated. Safety was also assessed.

Results: Significant improvements in trough FEV_1 at Weeks 26 and 52 were observed with IND/GLY/MF medium-dose o.d. versus Sal/Flu high-dose b.i.d. ($p<0.001$) (**Figure 1a**). Over 52 weeks, IND/GLY/MF medium-dose o.d. showed greater reductions in the rates of moderate/severe (19%; $p=0.041$), and all exacerbations (30%; $p<0.001$) compared with Sal/Flu high-dose b.i.d., while there was a non-significant reduction in severe exacerbations (16%, $p=0.117$) (**Figure 1b**). At Week 26, trough FEV_1 significantly improved with IND/GLY/MF medium-dose o.d. versus IND/MF high-dose o.d. with a mean treatment difference of 44 mL (95% CI: 10 to 79, $p=0.012$) and at Week 52, the two treatments were comparable with a mean treatment difference of 27 mL (95% CI: −8 to 62, $p=0.128$). Over 52 weeks, the rates of moderate/severe, severe and all exacerbations were comparable between IND/GLY/MF medium-dose o.d. and IND/MF high-dose o.d. (all $p>0.05$). All treatments were well tolerated with favourable safety profiles.

Conclusions: Once-daily IND/GLY/MF medium-dose resulted in a significant improvement in lung function and a reduction in moderate/severe and all exacerbations versus twice-daily Sal/Flu high-dose, while reducing the steroid load. Once-daily IND/GLY/MF medium dose also improved lung function versus once-daily IND/MF high-dose in patients with uncontrolled asthma.

Declaration of Interest: Study funded by Novartis Pharma AG. Alberto Papi reports personal fees for board membership, consultancy and lectures, grants for research, and travel expenses reimbursement from Chiesi, AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Mundipharma and TEVA, personal fees for lectures and travel expenses reimbursement from Menarini, Novartis and Zambon, personal fees for board membership and consultancy from Sanofi/Regeneron. Marc Humbert has relationships with drug companies including AstraZeneca, GlaxoSmithKline, Novartis, Roche, Sanofi/Regeneron and TEVA. In addition to being an investigator in trials involving these companies, relationships include consultancy services and membership of scientific advisory boards. Konstantinos Kostikas has received honoraria for presentations and/or consulting services from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GlaxoSmithKline, Menarini, and Novartis. Christian Domingo reports personal fees for lectures and advisory board participation from MSD, AstraZeneca, ALK and Sanofi-Aventis, personal fees for lectures, advisory board participation and non-financial support (study collaboration) from Novartis and TEVA, personal fees for meeting attendance from Allergy Therapeutics, Immunotek, Esteve and Menarini, personal fees from Chiesi, personal fees for lectures from Ferrer, non-financial support (study collaboration) from GlaxoSmithKline, outside the submitted work. Jorge F. Máspero reports personal fees and grants from Novartis during the conduct of the study, personal fees from AstraZeneca, grants and

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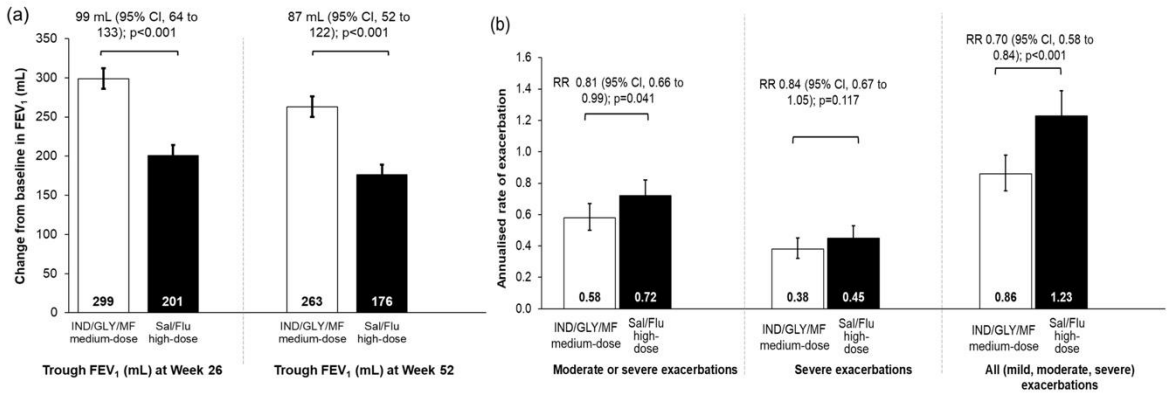
References and Clinical Trial Registry Information: Clinicaltrials.gov:NCT02571777

Figure 1. Indacaterol/glycopyrronium/mometasone furoate medium-dose (a) improved lung function and decreased (b) decreased exacerbation rates versus salmeterol/fluticasone high-dose in uncontrolled asthma



CI, confidence intervals; FEV_1, forced expiratory volume in 1 second; IND/GLY/MF, indacaterol/glycopyrronium/mometasone furoate; IND/GLY/MF medium-dose, 150/50/80 µg; IND/MF high-dose, 150/320 µg; RR, rate ratio; Sal/Flu, salmeterol/fluticasone; Sal/Flu high-dose, 50/500 µg

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