Clinical Research Results Abstract

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Efficacy and Safety of Indacaterol/Glycopyrronium/Mometasone Furoate in Patients with Uncontrolled Asthma: The Phase III IRIDIUM Study

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Aim: The IRIDIUM study (NCT02571777) assessed the efficacy and safety of indacaterol/glycopyrronium/mometasone furoate (IND/GLY/MF), a once-daily (o.d.) fixed-dose combination of a long-acting β_2-agonist/long-acting muscarinic antagonist/inhaled corticosteroid (LABA/LAMA/ICS), versus LABA/ICS in patients with uncontrolled asthma.

Methods: IRIDIUM was a Phase III, multicentre, 52-week, randomised, double-blind, double-dummy, parallel-group, active-control study that included patients (≥18–≤75 years) who were symptomatic (Asthma Control Questionnaire [ACQ-7] ≥1.5) at screening, had ≥1 severe exacerbation in previous year and forced expiratory volume in 1 second (FEV_1) <80%. Patients were randomised (1:1:1:1:1) to receive IND/GLY/MF medium-dose (150/50/80 µg), IND/GLY/MF high-dose (150/50/160 µg), or IND/MF medium-dose (150/160 µg), IND/MF high-dose (150/320 µg) o.d., all via Breezhaler®, or salmeterol/fluticasone high-dose (Sal/Flu; 50/500 µg) twice-daily (b.i.d.), via Diskus®. Primary endpoint was superiority in trough FEV_1 with IND/GLY/MF versus IND/MF at Week 26. Key secondary endpoint was improvement in ACQ-7 score after 26 weeks; other secondary endpoint was reduction in annualised rate of asthma exacerbations over 52 weeks.

Results: In total, 3092 patients were randomised. At Week 26, the primary endpoint was met with both IND/GLY/MF medium- and high-dose demonstrating superiority in improvement in trough FEV_1 versus the respective IND/MF doses (both $p<0.001$; **Figure 1**). Both IND/GLY/MF medium- and high-dose also demonstrated significant improvement in trough FEV_1 versus Sal/Flu ($p<0.001$). These improvements were sustained through Week 52. Clinically meaningful improvements in ACQ-7 score from baseline were observed across all treatment arms (IND/GLY/MF medium-dose: −0.97; IND/GLY/MF high-dose: −0.99; IND/MF medium-dose: −0.90; IND/MF high-dose: −0.99; Sal/Flu: −0.89). The difference between doses of IND/GLY/MF and the respective IND/MF doses at Week 26 for ACQ-7 score however did not achieve statistical significance. IND/GLY/MF medium-dose reduced annualised rates of moderate/severe and severe asthma exacerbations by 13% (95% CI, 0.71–1.06; non-significant [ns]) and 7% (95% CI, 0.74–1.17; ns), respectively, versus IND/MF medium-dose. IND/GLY/MF high-dose reduced annualised rates of moderate/severe and severe asthma exacerbations by 15% (95% CI, 0.68–1.04; ns) and 22% (95% CI, 0.61–1.00; ns), respectively, versus IND/MF high-dose, and by 36% (95% CI, 0.52–0.78; $p<0.001$) and 42% (95% CI, 0.45–0.73; $p<0.001$), respectively, versus Sal/Flu. Safety was comparable across treatment arms and no new safety signals were observed.

Conclusions: The combination inhaled therapy of once-daily IND/GLY/MF medium-dose and high-dose significantly improved lung function versus the comparators, demonstrated comparable improvements in asthma control from baseline versus the respective once-daily IND/MF doses and twice-daily Sal/Flu high-dose, and reduced asthma exacerbations versus this standard-of-care in patients with uncontrolled asthma.

Declaration of Interest: Study funded by Novartis Pharma AG. Huib A. M. Kerstjens reports grants and consultancy/advisory board participation from/for Novartis during the conduct of the study, grants and consultancy/advisory board participation from/for GlaxoSmithKline, and Boehringer Ingelheim, and a grant from Chiesi outside the submitted work. All were paid to his institution. Jorge F. Maspero reports personal fees and grants from Novartis during the conduct of the study, personal fees from AstraZeneca, grants and personal fees from Sanofi, personal fees from ImmunoTek. Kenneth R. Chapman reports grants and personal fees from AstraZeneca, grants and personal fees from Boehringer Ingelheim, personal fees from CSL Behring, grants and personal fees from GlaxoSmithKline, personal fees from Inhibrx, grants and personal fees from Grifols, personal fees from Kamada, grants and personal fees from Sanofi, grants and personal fees from Regeneron, grants and personal fees from Novartis, grants and personal fees from Takeda, grants from Vertex, outside the submitted work. Richard van Zyl-Smit reports personal fees from Aspen/ GlaxoSmithKline, personal fees from Pfizer, personal fees from Roche, personal fees from MSD, personal fees from AstraZeneca, personal fees from Novartis, personal fees from Cipla, outside of the submitted work. Karen Mezzi, Ivan Nikolaev, Motoi Hosoe and Ana-Maria Tanase are employees of Novartis Pharma AG. Catherine

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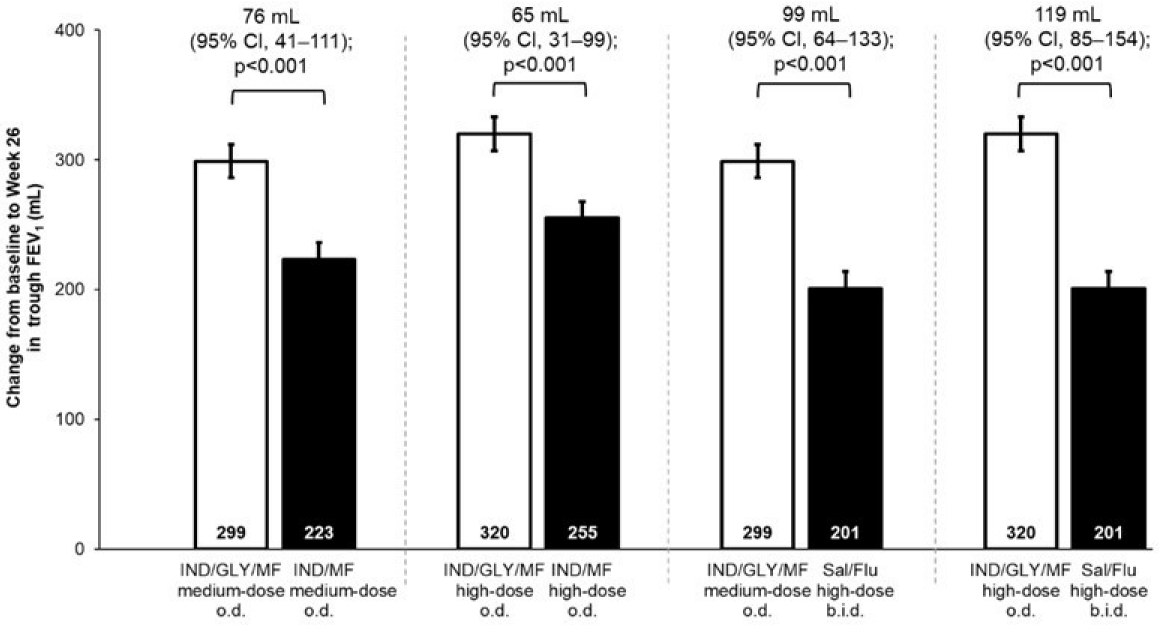
References and Clinical Trial Registry Information: Clinicaltrials.gov:NCT02571777

Figure 1. Improvements in trough FEV_1 with IND/GLY/MF o.d. versus IND/MF o.d. and Sal/Flu b.i.d. at Week 26 in patients with uncontrolled asthma



Data represented as LS mean ± SE change from baseline; treatment differences represent LS mean change from baseline

b.i.d., twice daily; CI, confidence interval; FEV_1, forced expiratory value in 1 second; IND/GLY/MF high-dose, indacaterol/glycopyrronium/mometasone furoate 150/50/160 µg; IND/GLY/MF medium-dose, indacaterol/glycopyrronium/mometasone furoate 150/50/80 µg; IND/MF high-dose, indacaterol/mometasone furoate 150/320 µg; IND/MF medium-dose, indacaterol/mometasone furoate 150/160 µg; LS, least-squares; o.d., once daily; Sal/Flu high-dose, salmeterol/fluticasone 50/500 µg