Abstract Presentations

4. Huib Kerstjens, Netherlands

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

Presented by:

Huib A. M. Kerstjens

University of Groningen, and University Medical Center Groningen, Groningen, the Netherlands

Email id: h.a.m.kerstjens@umcg.nl

Co- authored by:

Jorge F. Maspero, Kenneth R. Chapman, Richard van Zyl-Smit, Karen Mezzi, Ivan Nikolaev, Motoi Hosoe, Ana-Maria Tanase, Catherine Lavecchia, Abhijit Pethe, Xu Shu, Peter D'Andrea

Breathing and feeling well through universal access to right care

Introduction

- GINA 2019:
  - medium-dose ICS with LABA the preferred controller for patients with asthma at GINA step 4[1]
  - high-dose ICS with LABA for GINA step 5[1]
  - in patients inadequately controlled, add-on treatment with a LAMA can provide further benefit in these patients[1,2]

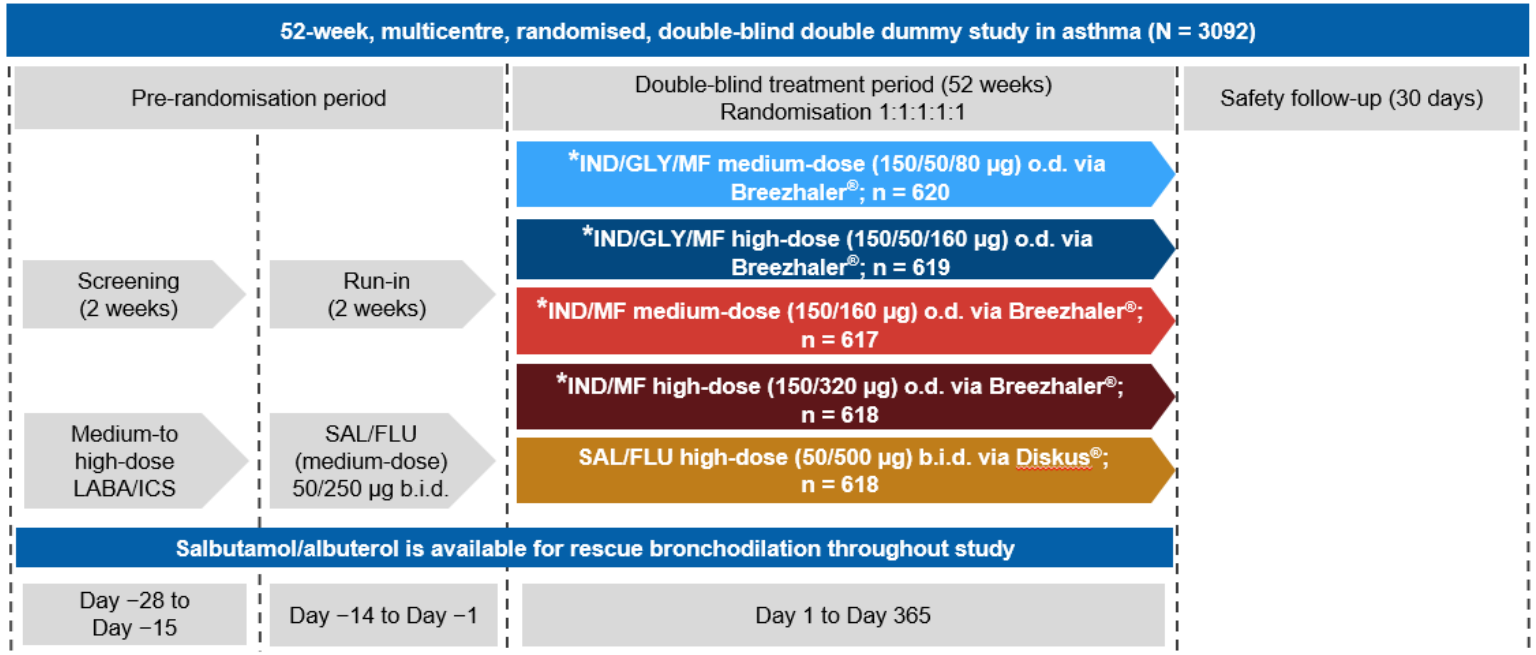
- A novel once daily LABA/LAMA/ICS combination of IND/GLY/MF, delivered via the Breezhaler® device, is under development for maintenance treatment of asthma

- We present results from the Phase III IRIDIUM study
  - evaluated the efficacy and safety of IND/GLY/MF medium- (150/50/80 µg) and high-dose (150/50/160 µg) o.d.
  - versus IND/MF medium- (150/160 µg) and high-dose (150/320 µg) o.d., respectively
  - and versus salmeterol/fluticasone (SAL/FLU) high-dose (50/500 µg) b.i.d. in adult patients with inadequately controlled asthma

b.i.d, twice-daily; GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA; long-acting muscarinic antagonist; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; o.d., once-daily

1. Global strategy for asthma management and prevention, Global Initiative for Asthma (GINA) 2019. Available from: http://www.ginasthma.org/; 2. Munoz-Cano R, et al. Eur Respir J 2017; 49:1501885

Study design and key inclusion and exclusion criteria



ClinicalTrials.gov number: NCT02571777

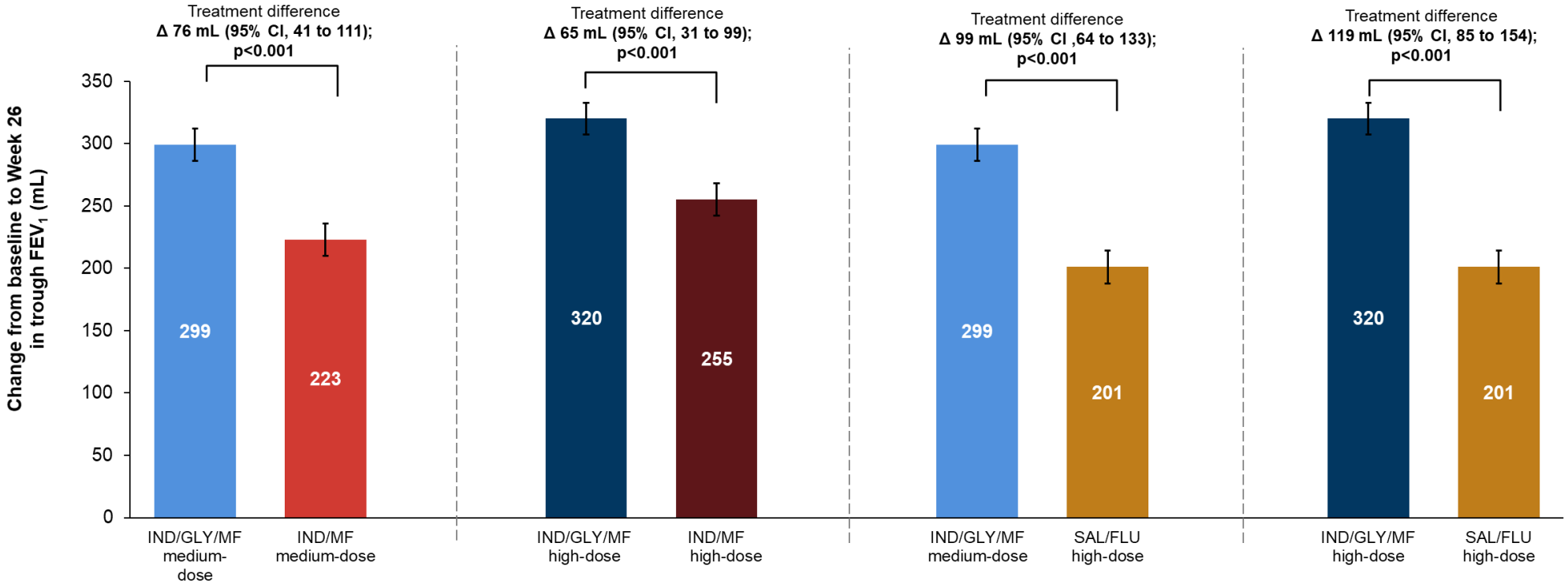
- Aged ≥18 and ≤75 years
- On LABA/ICS medium- or high-dose for ≥3 months and at a stable dose for ≥1 month prior to screening
- Pre-bronchodilator FEV_1 <80% predicted and increase in FEV_1 of ≥12% and 200 mL after salbutamol/albuterol
- ACQ-7 score ≥1.5 at run-in visit
- History of ≥1 asthma exacerbation 12 months prior to screening

- Inhaled tobacco products in 6 months before screening or >10 pack-year smoking history
- History of chronic lung disease
- An asthma exacerbation requiring SC or hospitalisation or ER visit within 6 weeks of screening
- Patients with an RTI or asthma worsening within 4 weeks prior to screening, or during the run-in period
- Clinically significant comorbidities

*treatments were administered in the evening *SFC 50/250µg b.i.d.
ACQ, asthma control questionnaire; b.i.d., twice daily; ER, emergency room; FEV_1, forced expiratory volume in 1 second; GLY, glycopyrronium bromide; ICS, inhaled corticosteroid; IND, indacaterol acetate; LABA, long-acting β_2-agonist; MF, mometasone furoate; o.d., once daily; RTI, respiratory tract infection; SC, systemic corticosteroids SAL/FLU salmeterol /fluticasone

Trough FEV_1 at Week 26 (primary endpoint)

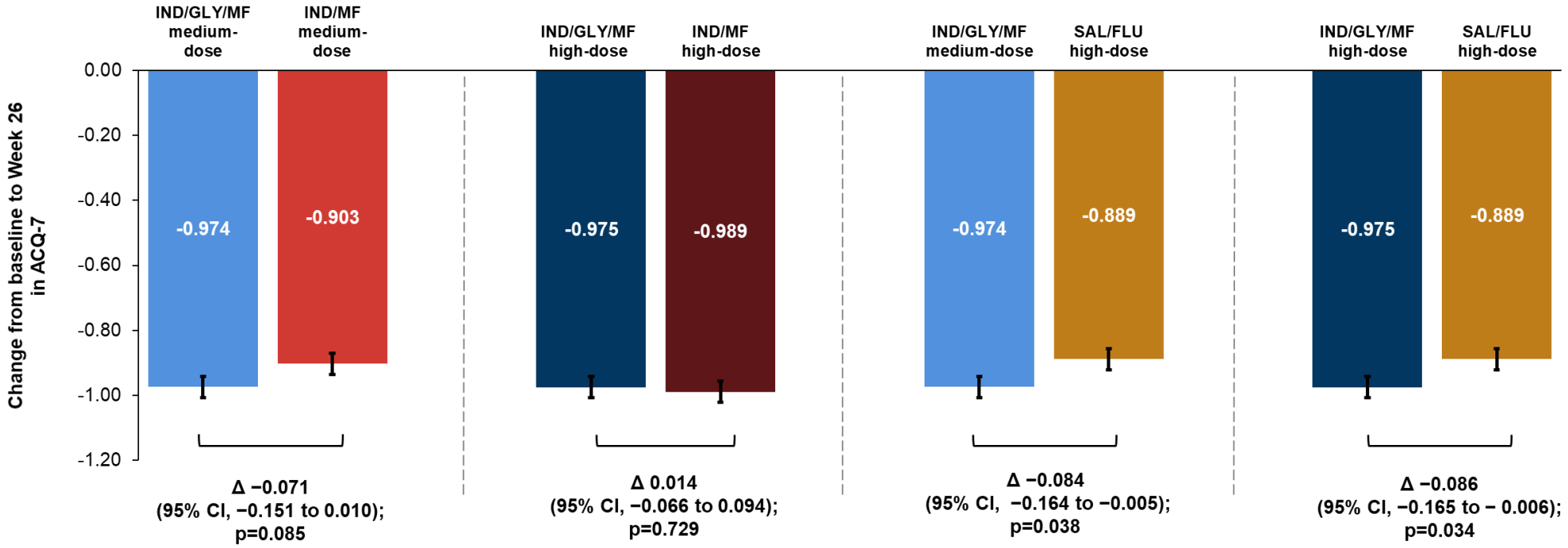
- Primary objective met: IND/GLY/MF medium- and high-dose demonstrated significantly greater improvement in trough FEV_1 versus IND/MF medium- and high-dose o.d., respectively at Week 26;
  - Greater improvements were also observed versus SAL/FLU high-dose b.i.d.
  - Similar improvements in trough FEV_1 were seen across all comparisons at Week 52



Data presented as LS mean ± SE, error bars represent SE values.
IND/GLY/MF high-dose, IND/GLY/MF, 150/50/160 µg; IND/GLY/MF medium-dose, IND/GLY/MF, 150/50/80 µg, ND/MF high-dose, IND/MF 150/320 µg; IND/MF medium-dose, IND/MF 150/160 µg; SAL/FLU high-dose, SAL/FLU 50/500 µg
FEV_1, forced expiratory volume in 1 second; IND/MF, indacaterol/mometasone furoate; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; o.d., once daily; SAL/FLU, salmeterol/fluticasone

ACQ-7 at Week 26 (Key secondary endpoint)

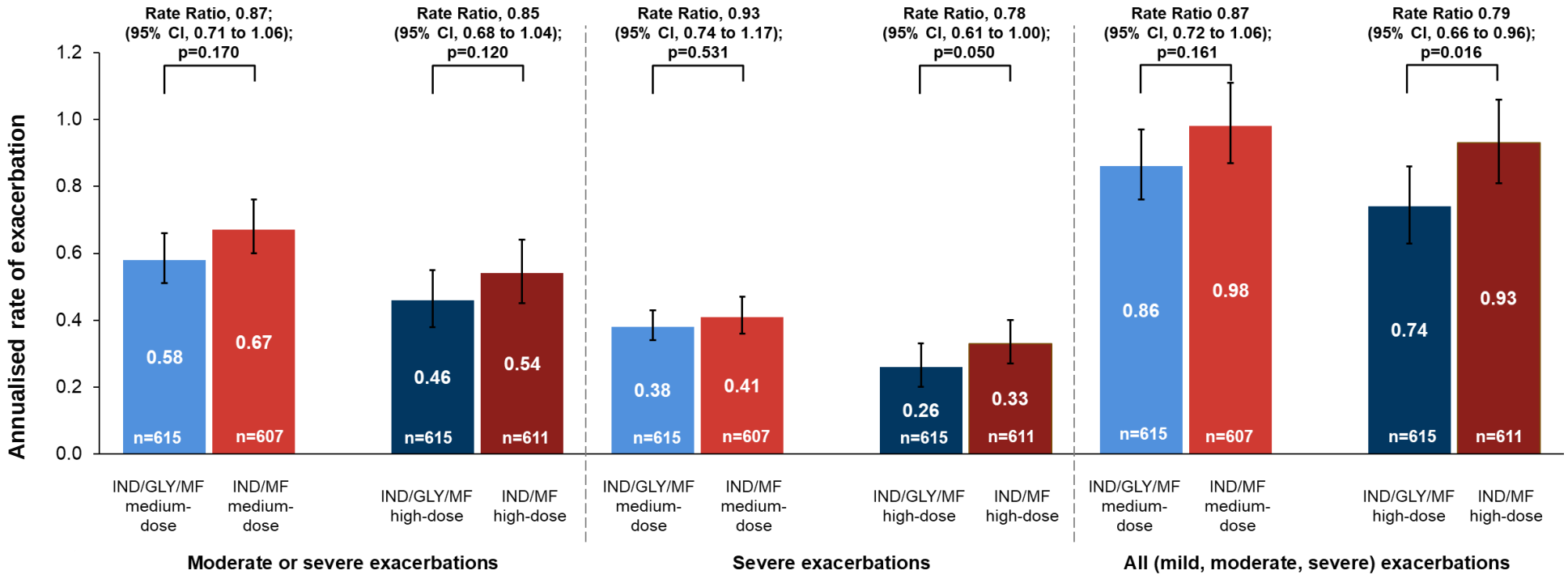
- All treatment arms showed comparable and clinically meaningful improvements in ACQ-7 score from baseline at Week 26
- Key secondary objective not met; no significant differences in change from baseline in ACQ-7 score were observed with either doses of IND/GLY/MF vs IND/MF at Week 26
  - However greater improvements with IND/GLY/MF vs SAL/FLU at Week 26



Data presented as LS mean ± SE, error bars represent SE values.
IND/GLY/MF high-dose, IND/GLY/MF, 150/50/160 µg; IND/GLY/MF medium-dose, IND/GLY/MF, 150/50/80 µg; IND/MF high-dose, IND/MF 150/320 µg; IND/MF medium-dose, IND/MF 150/160 µg; SAL/FLU high-dose, SAL/FLU 50/500 µg
ACQ-7; asthma control questionnaire; IND/MF, indacaterol/mometasone furoate; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; SAL/FLU, salmeterol/fluticasone

Annualised rate of exacerbations over 52 weeks (Secondary endpoint)

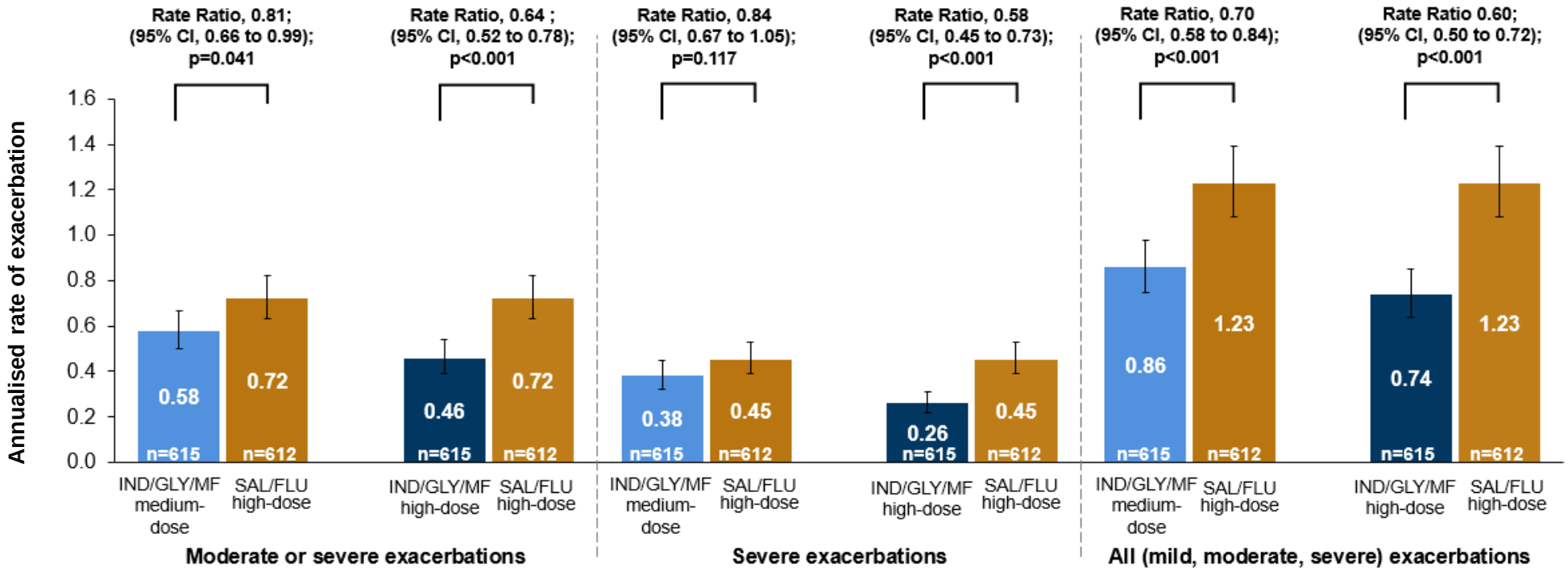
- IND/GLY/MF high-dose reduced the annualised rate of moderate or severe exacerbations by 15%, severe exacerbations by 22%, and all exacerbations by 21% versus IND/MF medium- and high-dose, respectively, over 52 weeks
  - IND/GLY/MF medium-dose versus IND/MF medium-dose: 13%, 7% and 13% reduction in rate of exacerbations, respectively



Data presented as annualised rate (95% CI); error bars represented as CI values
IND/GLY/MF high-dose, IND/GLY/MF, 150/50/160 µg; IND/GLY/MF medium-dose, IND/GLY/MF, 150/50/80 µg; IND/MF high-dose, IND/MF 150/320 µg; IND/MF medium-dose, IND/MF 150/160 µg; SAL/FLU high-dose, SAL/FLU 50/500 µg
IND/MF, indacaterol/mometasone furoate; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; SAL/FLU, salmeterol/fluticasone

Annualised rate of exacerbations over 52 weeks (vs SAL/FLU)

- Greater reductions in the annualised rate of exacerbations observed with IND/GLY/MF high-dose versus SAL/FLU high-dose: 36% reduction in moderate or severe exacerbations, 42% in severe exacerbations, and 40% in all exacerbations, respectively
  - IND/GLY/MF medium-dose versus SAL/FLU high-dose: 19%, 16% and 30% reduction in rate of exacerbations, respectively



Data presented as annualised rate (95% CI); error bars represented as CI values
IND/GLY/MF high-dose, IND/GLY/MF, 150/50/160 µg; IND/GLY/MF medium-dose, IND/GLY/MF, 150/50/80 µg; IND/MF high-dose, IND/MF 150/320 µg; IND/MF medium-dose, IND/MF 150/160 µg; SAL/FLU high-dose, SAL/FLU 50/500 µg
IND/MF, indacaterol/mometasone furoate; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; SAL/FLU, salmeterol/fluticasone

Safety

- Safety was comparable across treatment arms

	IND/GLY/MF medium-dose (n=617) exp. = 575.9 years	IND/GLY/MF high-dose (n=616) exp. = 583.8 years	IND/MF medium-dose (n=608) exp. = 573.2 years	IND/MF high-dose (n=613) exp. = 578.9 years	SAL/FLU high-dose (n=618) exp. = 575.6 years
Patients with at least one AE, n (IR)	460 (174.2)	458 (163.3)	453 (163·8)	454 (169.0)	487 (193.9)
Most frequently observed AE - Asthma	248 (57.4)	247 (56.1)	268 (65·0)	256 (60.1)	309 (79.4)
Patient with at least one AE suspected to be study drug-related, n (IR)	46 (8.4)	51 (9.2)	42 (7·6)	38 (6.9)	51 (9.3)
Patient with at least one SAE, n (IR)	49 (8.8)	46 (8.2)	38 (6.8)	52 (9.3)	39 (7.0)
Total deaths*	7				
aortic dissection	1	1	-	-	-
sudden death	-	1	-	1	-
Train accident	-	-	-	1	-
Lymphoma	-	-	-	1	-
Sudden death in a patient with multiple, severe cardiovascular comorbidities	-	-	-	1	-

***None of the deaths were related with the study drug**
IND/GLY/MF high-dose, IND/GLY/MF, 150/50/160 µg; IND/GLY/MF medium-dose, IND/GLY/MF, 150/50/80 µg; IND/MF high-dose, IND/MF 150/320 µg; IND/MF medium-dose, IND/MF 150/160 µg; SAL/FLU high-dose, SAL/FLU 50/500 µg,
IND/MF, indacaterol/mometasone furoate; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; SAL/FLU, salmeterol/fluticasone

Conclusion

In patients with inadequately controlled asthma

- Lung Function: with IND/GLY/MF medium- and high-dose
  - significantly superior improvements versus respective IND/MF o.d. doses
  - and greater improvements versus SAL/FLU high dose b.i.d.
- Asthma control: with IND/GLY/MF medium- and high-dose
  - comparable improvements versus respective IND/MF o.d. doses
  - and greater improvements versus SAL/FLU high-dose b.i.d.
- Annualised rate of exacerbations: with IND/GLY/MF medium- and high-dose
  - nominally lower versus respective IND/MF o.d. doses
  - substantial reduction versus SAL/FLU high-dose b.i.d.
- Both doses of IND/GLY/MF were well tolerated, and safety was comparable across treatment arms and no new safety signals were observed

IND/GLY/MF high-dose, IND/GLY/MF, 150/50/160 µg; IND/GLY/MF medium-dose, IND/GLY/MF, 150/50/80 µg; IND/MF high-dose, IND/MF 150/320 µg; IND/MF medium-dose, IND/MF 150/160 µg; SAL/FLU high-dose, SAL/FLU 50/500 µg
ICS, inhaled corticosteroid; LABA, LABA, long-acting β2-agonist; IND/MF, indacaterol/mometasone furoate; IND/GLY/MF; indacaterol/glycopyrronium/mometasone furoate; SAL/FLU, salmeterol/fluticasone