Abstract Presentations

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Efficacy And Safety of Indacaterol/Glycopyrronium/Mometasone Furoate Versus Salmeterol/Fluticasone Plus Tiotropium in Uncontrolled Asthma: The ARGON Study

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Breathing and feeling well through universal access to right care

Presenter disclosures

- Richard van Zyl-Smit has received honoraria for academic talks and advisory boards from Novartis, GlaxoSmithKline, Cipla, MSD, Pfizer, Roche, AstraZeneca

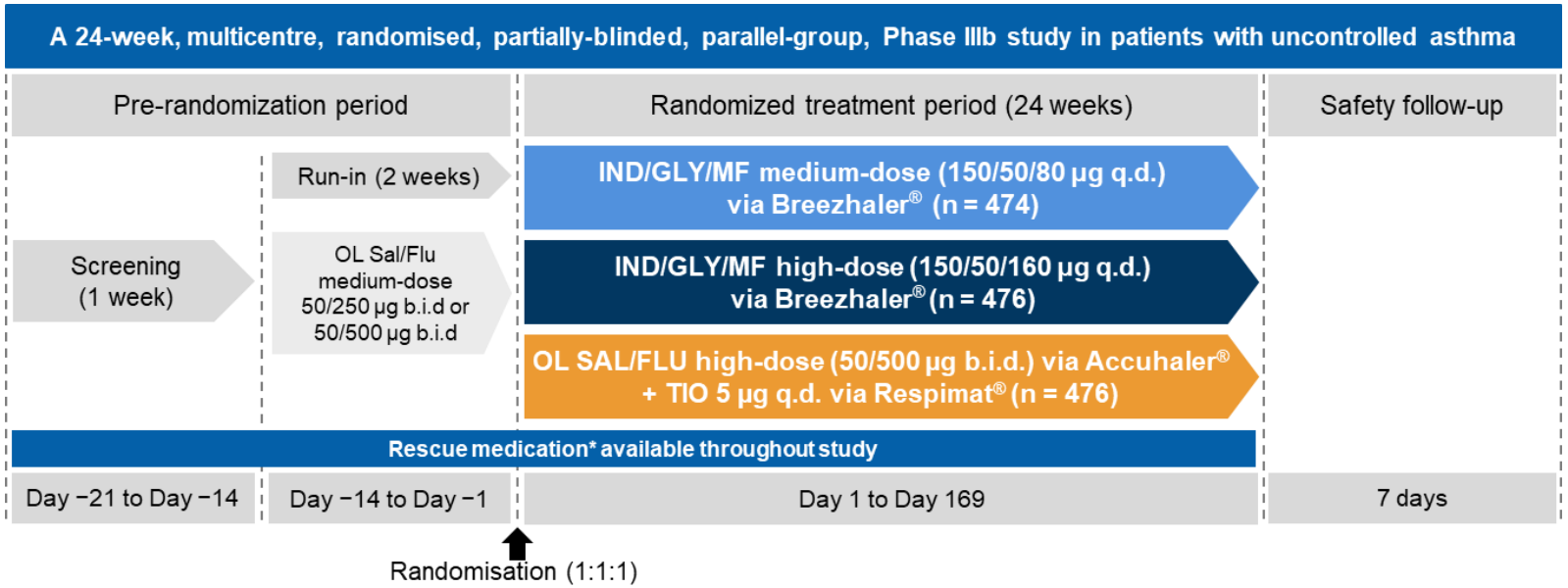
Introduction

- GINA 2020 recommends medium-dose ICS/LABA at GINA Step 4 and high-dose ICS/LABA at step 5, as preferred controller treatment for patients with asthma[1]
  - The addition of a LAMA can improve lung function and decrease exacerbations in patients with inadequate control on ICS/LABA therapy[2-4]
- Indacaterol/ glycopyrronium/ mometasone furoate (IND/GLY/MF) fixed-dose combination is being developed as a once-daily (o.d.) maintenance treatment in asthma
- The availability of a fixed dose combination in a single inhaler may offer advantages and convenience over the loose combinations of a LABA/ICS + LAMA[5,6]
- Here we present the results from the ARGON study, which evaluated the efficacy and safety of:
  - IND/GLY/MF high- (150/50/160µg) and medium-dose (150/50/80µg) o.d. via Breezhaler® versus salmeterol/fluticasone (SAL/FLU) high-dose (50/500µg) twice daily via Accuhaler® + tiotropium (TIO) 5µg o.d. via Respimat® in patients with uncontrolled asthma

FDC, fixed-dose combination; GINA, global initiative for asthma; GLY, glycopyrronium bromide; ICS, inhaled corticosteroid; IND, indacaterol acetate; LABA, long-acting β_2- agonist; LAMA, long-acting muscarinic antagonist; MF, mometasone furoate; q.d., once daily; SAL, salmeterol; TIO, tiotropium

1. Global strategy for asthma management and prevention, Global Initiative for Asthma (GINA) 2020. Available from: http://www.ginasthma.org/; 2. Kerstjens HA. Allergy Clin Immunol 2011;128:308–314;
3. Kerstjens HA, et al. N Engl J Med 2012;367:1198–1207; 4. Kew KM, Dahri K. Cochrane Database Syst Rev 2016: CD011721; 5. Virchow JC, et al. Lancet 2019;394:1727–1749;
6. Stoloff SW, et al. Allergy Clin Immunol 2004;113:245–251

ARGON study design



- Total number of patients randomised : 1426

*Salbutamol/albuterol
IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg o.d.; IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg o.d.; SAL/FLU high-dose, SAL/FLU 50/500 µg b.i.d.; TIO, TIO 5 µg o.d

ACQ, Asthma Control Questionnaire; b.i.d., twice daily; FEV1, forced expiratory volume in one second; FLU, fluticasone propionate; GLY, glycopyrronium bromide; ICS, inhaled corticosteroid; IND, indacaterol acetate; LABA, long-acting β_2-agonist; LAMA, long acting muscarinic agonist; MF, mometasone furoate; OL, open label; o.d., once daily; SAL, salmeterol; TIO, tiotropium

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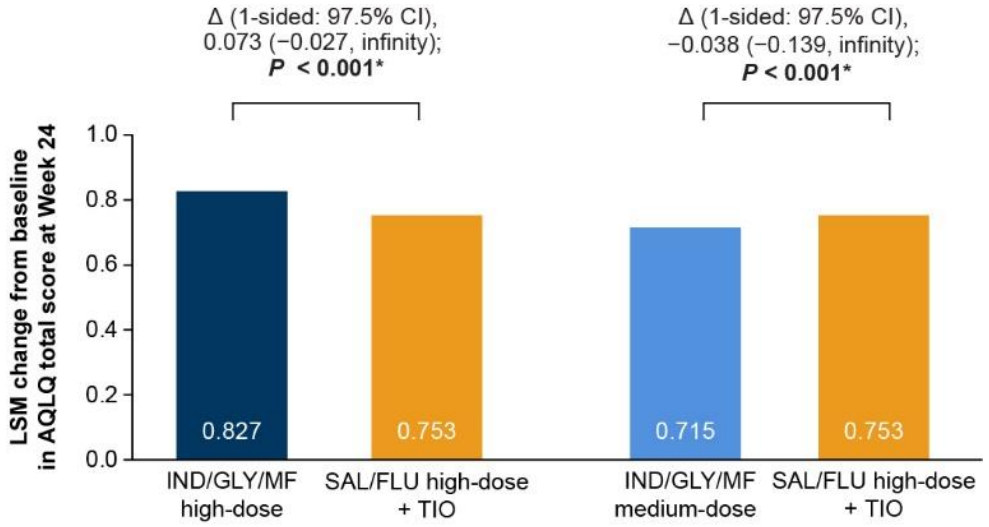
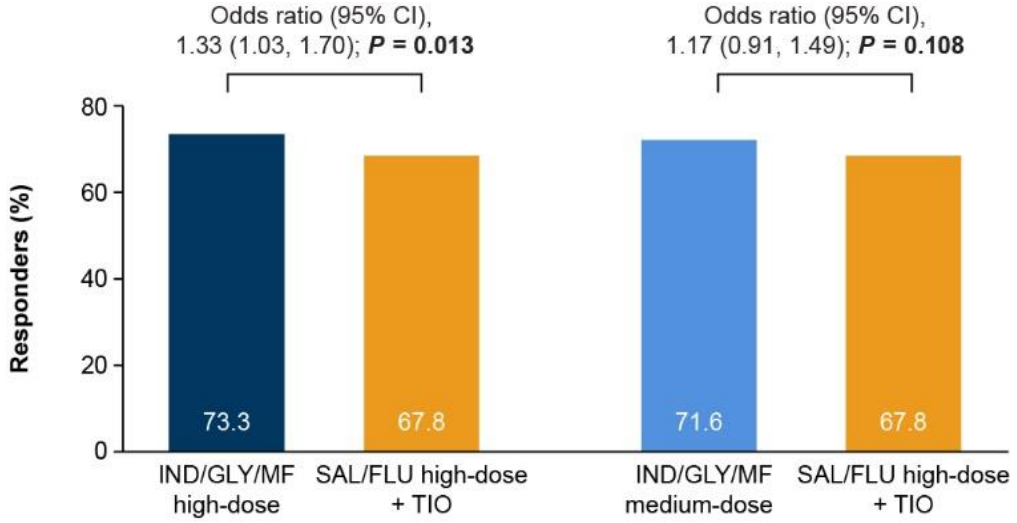
- Men and women (aged ≥18 years) diagnosed with asthma for ≥6 months
- Inadequately controlled on medium- or high-dose of LABA/ICS
- History of ≥1 severe asthma exacerbation in the past 12 months
- Asthma Control Questionnaire 7 (ACQ-7) score ≥1.5
- Pre-bronchodilator FEV_1 <85% of predicted normal and reversibility in FEV_1 of ≥12% and 200 mL after salbutamol/albuterol

- Smoking history of >20 pack-years
- Diagnosis of chronic obstructive pulmonary disease or other chronic respiratory diseases
- History of long QT syndrome, or prolonged QTc interval
- Patients treated with a LAMA for asthma within 3 months prior to screening

Primary endpoint: AQLQ total score at Week 24

- The primary endpoint: **Non-inferiority in change from baseline in AQLQ total score** with IND/GLY/MF high- and medium-dose versus SAL/FLU high-dose + TIO at Week 24 was met
- IND/GLY/MF high-dose demonstrated a **greater percentage of AQLQ responders** versus SAL/FLU high-dose + TIO
- IND/GLY/MF medium-dose and SAL/FLU high-dose + TIO AQLQ responders were similar





*One sided non-inferiority *P*-value for both the comparisons

IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg o.d.; IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg o.d.; SAL/FLU high-dose, SAL/FLU 50/500 µg b.i.d; TIO, TIO 5 µg o.d.

Δ, least squares mean treatment difference; AQLQ, Asthma Quality of Life Questionnaire; b.i.d., twice daily; FLU, fluticasone propionate; GLY, glycopyrronium bromide; IND, indacaterol acetate; LSM, least squares mean; MF, mometasone furoate; o.d., once daily; SAL, salmeterol; TIO, tiotropium

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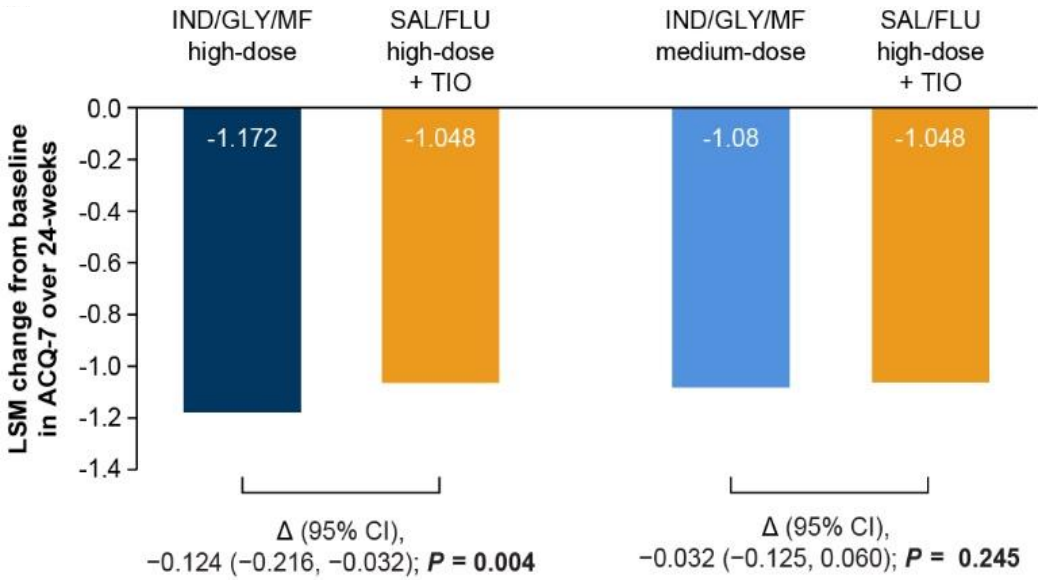
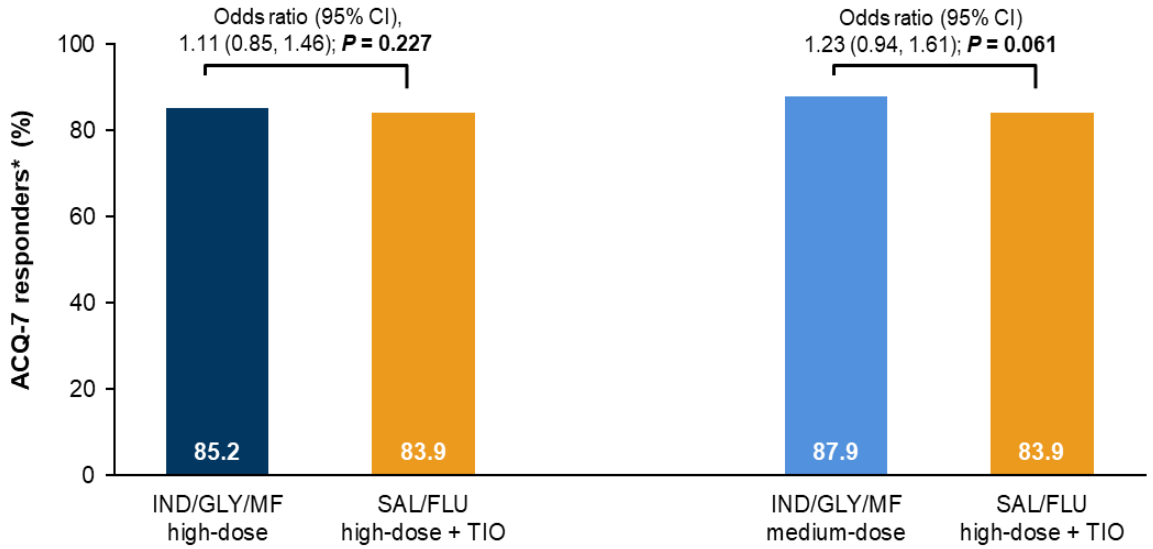
Secondary endpoint: ACQ-7 at Week 24

- Change from baseline in **ACQ-7 total score at Week 24 was greater for IND/GLY/MF high-dose** versus SAL/FLU high-dose + TIO and comparable for IND/GLY/MF medium-dose o.d. versus SAL/FLU high-dose + TIO
- The percentage of ACQ-7 responders for IND/GLY/MF high- and medium-dose were comparable with SAL/FLU high-dose + TIO at Week 24





IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg o.d.; IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg o.d.; SAL/FLU high-dose, SAL/FLU 50/500 µg b.i.d; TIO, TIO 5 µg o.d.

Δ, least squares mean treatment difference; ACQ, Asthma Control Questionnaire; b.i.d., twice daily; FLU, fluticasone propionate; GLY, glycopyrronium bromide; IND, indacaterol acetate; LSM, least squares mean; MF, mometasone furoate; o.d., once daily; SAL, salmeterol; TIO, tiotropium

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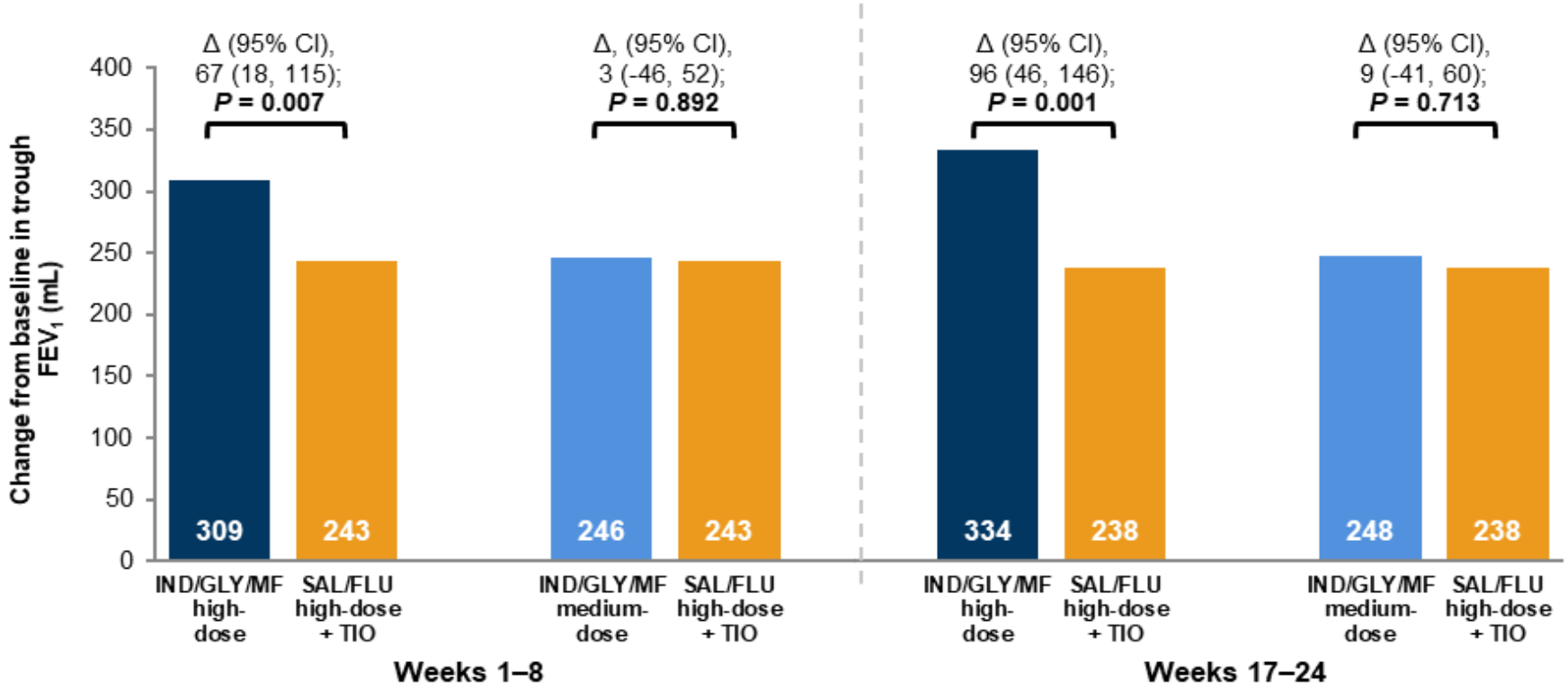
Secondary endpoint: Trough FEV_1 at Week 24

- IND/GLY/MF high-dose showed greater improvements in trough FEV_1 versus SAL/FLU high-dose + TIO at Week 24
- IND/GLY/MF medium-dose improvements in trough FEV_1 were comparable with SAL/FLU high-dose + TIO at Week 24



IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg o.d.; IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg o.d.; SAL/FLU high-dose, SAL/FLU 50/500 µg b.i.d; TIO, TIO 5 µg o.d.

Δ, least squares mean treatment difference; b.i.d., twice daily; FLU, fluticasone propionate; FEV_1, forced expiratory volume in 1 second; GLY, glycopyrronium bromide; IND, indacaterol acetate; LSM, least squares mean; MF, mometasone furoate; o.d., once daily; SAL, salmeterol; TIO, tiotropium

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Conclusions

- IND/GLY/MF high- and medium-dose o.d. via a single inhaler **was non-inferior in quality of life (AQLQ) improvement** versus SAL/FLU high-dose b.i.d. + TIO o.d. via separate inhalers
- **Clinically meaningful improvements in AQLQ occurred in a greater percentage** of patients treated with IND/GLY/MF high-dose versus SAL/FLU high-dose + TIO
- IND/GLY/MF high-dose o.d. demonstrated **greater improvements in asthma control and lung function** versus SAL/FLU high-dose b.i.d. + TIO o.d.
- IND/GLY/MF medium-dose o.d. demonstrated **comparable improvements in asthma control and lung function** versus SAL/FLU high-dose b.i.d. + TIO o.d. but with a **reduced steroid exposure**
- Both IND/GLY/MF doses were well tolerated, and adverse events were generally comparable across treatments

IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg o.d.; IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg o.d.; SAL/FLU high-dose, SAL/FLU 50/500 µg b.i.d; TIO, TIO 5 µg o.d.

b.i.d., twice daily; FLU, fluticasone propionate; GLY, glycopyrronium bromide; IND, indacaterol acetate; LSM, least squares mean; MF, mometasone furoate; o.d., once daily; SAL, salmeterol; TIO, tiotropium