

# Efficacy of one time per day, single-inhaler indacaterol/glycopyrronium/mometasone in patients with inadequately controlled asthma: post hoc analysis of IRIDIUM study in Asian population

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## ABSTRACT

**Background and objective** The 52-week IRIDIUM study demonstrated the efficacy of indacaterol acetate/glycopyrronium bromide/mometasone furoate (IND/GLY/MF) versus IND/MF and salmeterol xinafoate/fluticasone propionate (SAL/FLU) in patients with symptomatic asthma, despite long-acting  $\beta_2$ -agonist/inhaled corticosteroids (LABA/ICS) medium-dose or high-dose, predicted forced expiratory volume in 1 s (FEV<sub>1</sub>) <80% and at least one exacerbation in the previous year. Here, we present data from a post hoc analysis of the IRIDIUM study in the Asian subpopulation.

**Methods** This post hoc analysis evaluated improvements in lung function, asthma control and reduction in asthma exacerbations with IND/GLY/MF medium- (150/50/80  $\mu$ g) and high-dose (150/50/160  $\mu$ g) versus IND/MF medium- (150/160  $\mu$ g) and high-dose (150/320  $\mu$ g), all one time per day and SAL/FLU high-dose (50/500  $\mu$ g) two times per day, in Asian patients from the IRIDIUM study.

**Results** In total, 258 patients (IND/GLY/MF medium-dose, 52; IND/GLY/MF high-dose, 52; IND/MF medium-dose, 51; IND/MF high-dose, 51; SAL/FLU high-dose, 52) were included. IND/GLY/MF medium- and high-dose showed greater improvement in trough FEV<sub>1</sub> at week 26 versus respective doses of IND/MF ( $\Delta$ , 100 mL and 101 mL; both  $p < 0.05$ , respectively), and SAL/FLU high-dose ( $\Delta$ , 125 mL;  $p = 0.0189$ , and 136 mL;  $p = 0.0118$ , respectively), which were maintained over 52 weeks. Both doses of IND/GLY/MF showed greater improvement in morning and evening peak expiratory flow versus respective doses of IND/MF and SAL/FLU high-dose at week 52. The changes in Asthma Control Questionnaire-7 scores from baseline were comparable in all treatment groups. IND/GLY/MF medium- and high-dose showed greater reductions in severe (34%, 69%), moderate or severe (18%, 54%) and all exacerbations (21%, 34%) compared with SAL/FLU high-dose over 52 weeks.

**Conclusion** One time per day, single-inhaler IND/GLY/MF improved lung function, reduced asthma exacerbations and provided comparable asthma control versus IND/MF and SAL/FLU in Asian patients with inadequately controlled asthma despite LABA/ICS. The results of this analysis were consistent with the overall population in the IRIDIUM study.

## Key messages

### What is the key question?

- How beneficial is indacaterol acetate/glycopyrronium bromide/mometasone furoate (IND/GLY/MF) compared with IND/MF and salmeterol xinafoate/fluticasone propionate (SAL/FLU) in Asian patients with inadequately controlled asthma?

### What is the bottom line?

- IND/GLY/MF provides greater or comparable improvements in terms of efficacy versus IND/MF and SAL/FLU in Asian patients with inadequately controlled asthma.

### Why read on?

- In this post hoc analysis from the IRIDIUM study, IND/GLY/MF improved lung function, reduced asthma exacerbations and provided comparable improvements in asthma control versus IND/MF and SAL/FLU in Asian patients with inadequately controlled asthma, and these results were in line with overall study population.

## INTRODUCTION

Asthma is a major chronic respiratory disease, affecting approximately 358 million people worldwide.<sup>1</sup> The burden of asthma is substantial in Asia; the disease remains underdiagnosed and undertreated, leading to inadequate asthma control.<sup>2–4</sup> Inhaled corticosteroids (ICS) are the mainstay of treatment for asthma. Both global<sup>5</sup> and Asian guidelines (Japan, Korea and China)<sup>6–8</sup> recommend ICS as initial therapy for patients with asthma. In patients with uncontrolled asthma on ICS monotherapy or a low-dose ICS and long-acting  $\beta_2$ -agonist (LABA) combination, the combination of LABA with medium-dose

or high-dose ICS is widely considered the preferred controller treatment option.<sup>5–8</sup>

However, despite available therapeutic options for asthma, a significant number of patients receiving LABA/ICS treatment continue to experience poor disease control, increased emergency or hospital-based medical care and reduced quality of life and work productivity.<sup>9,10</sup> Similar to the Global Initiative for Asthma report,<sup>5</sup> the Japanese asthma guidelines<sup>6</sup> and Korean asthma guidelines<sup>7</sup> also recommend treatment with add-on long-acting muscarinic antagonist (LAMA, tiotropium) in patients with uncontrolled asthma with LABA/ICS therapy. The addition of LAMA to LABA/ICS has demonstrated improvement in lung function, asthma control and exacerbation reduction, with fewer non-serious adverse events, overall,<sup>11–14</sup> as well as in the Asian population<sup>15</sup> with uncontrolled asthma.

In the IRIDIUM study<sup>14</sup> particularly, one time per day fixed-dose combination of indacaterol acetate/glycopyrronium bromide/mometasone furoate (IND/GLY/MF) demonstrated improvements in lung function and reductions in asthma exacerbations with comparable asthma control versus IND/MF one time per day and salmeterol xinafoate/fluticasone propionate (SAL/FLU) two times per day in patients with asthma inadequately controlled with LABA/ICS medium- and high-dose. In a study including healthy subjects, there were no ethnic differences (Asian vs Caucasian patients) found in the pharmacokinetics of IND, GLY and MF.<sup>16</sup> However, racial and ethnic differences in asthma epidemiology, biology and medical care have been discussed previously,<sup>17,18</sup> and therefore, it is important to evaluate whether these may result in different response of Asian patients to inhaled asthma treatments compared with patients from other regions.

Here, we report a post hoc analysis of the IRIDIUM study to evaluate the efficacy of IND/GLY/MF medium- and high-dose versus respective doses of IND/MF and SAL/FLU high-dose in the Asian subpopulation and to understand whether there is an ethnic difference with the overall study population.

## METHODS

### Study design

This is a post hoc analysis of data from the IRIDIUM study<sup>14</sup> in patients from Asian countries (Japan, China, Philippines, Vietnam and Thailand). IRIDIUM was a 52-week, randomised, double-blind, double-dummy, parallel-group, active-controlled study (ClinicalTrials.gov no. NCT02571777) in patients with inadequately controlled asthma. Patients were randomised (1:1:1:1:1) to IND/GLY/MF medium-dose (150/50/80 µg); IND/GLY/MF high-dose (150/50/160 µg); IND/MF medium-dose (150/160 µg); IND/MF high-dose (150/320 µg); all one time per day or SAL/FLU high-dose (50/500 µg) two times per day. Both IND/GLY/MF and IND/MF were delivered via Breezhaler in the evening, and SAL/

FLU was delivered via Diskus in the morning and the evening. Details of the study design and methodology of the IRIDIUM study are described in the original manuscript.<sup>14</sup>

### Patient and public involvement

Patients were not involved in the design, conduct or interpretation of this post hoc analysis.

### Study population

The study population comprised of patients with inadequately controlled asthma despite treatment with LABA/ICS medium- or high- stable dose, Asthma Control Questionnaire-7 (ACQ-7) score  $\geq 1.5$ , and history of at least one asthma exacerbation requiring systemic corticosteroid (SCS), emergency room (ER) visit or hospitalisation within 12 months prior to screening. Eligible patients also had prebronchodilator forced expiratory volume in 1 s ( $FEV_1$ )  $< 80\%$  of the predicted normal and an increase in  $FEV_1$  of  $\geq 12\%$  and 200 mL after administration of salbutamol/albuterol.

Patients were excluded if they had a smoking history of more than 10 pack-years, a history of chronic lung diseases other than asthma and an asthma exacerbation requiring SCS or ER visit/hospitalisation within 6 weeks of screening. Detailed information on the eligibility criteria is available in the IRIDIUM manuscript.<sup>14</sup>

### Assessments

We evaluated the efficacy of IND/GLY/MF medium- and high-dose versus respective doses of IND/MF and SAL/FLU high-dose in terms of lung function, asthma control and exacerbations. Lung function was evaluated in terms of change from baseline in trough  $FEV_1$  at weeks 26 and 52, post-dose  $FEV_1$  at different time intervals on day 1, and morning and evening peak expiratory flow (PEF) over 52 weeks of treatment. For asthma control, change from baseline in ACQ-7 score<sup>19,20</sup> and proportion of patients achieving improvement of  $\geq 0.5$  units in ACQ-7 score from baseline (ACQ-7 responders)<sup>21,22</sup> were evaluated at weeks 26 and 52. The reduction in annualised rate of asthma exacerbations (moderate or severe, severe, all exacerbations) over 52 weeks of treatment was evaluated. The definitions of asthma exacerbations are available in the published IRIDIUM manuscript.<sup>14</sup>

### Statistical analysis

Trough  $FEV_1$  and ACQ-7 score at week 26 were analysed in the full analysis set (FAS) population using a mixed model for repeated measures. The FAS included all patients who were assigned a randomisation number and received at least one dose of study medication for all analyses. This model contained treatment, visit and treatment-by-visit interaction as fixed effects, with baseline  $FEV_1$ /ACQ-7 measurement, baseline-by-visit interaction,  $FEV_1$  prior to inhalation and  $FEV_1$  within 15–30 min post-inhalation of salbutamol/

**Table 1** Baseline demographics and clinical characteristics (randomised set)

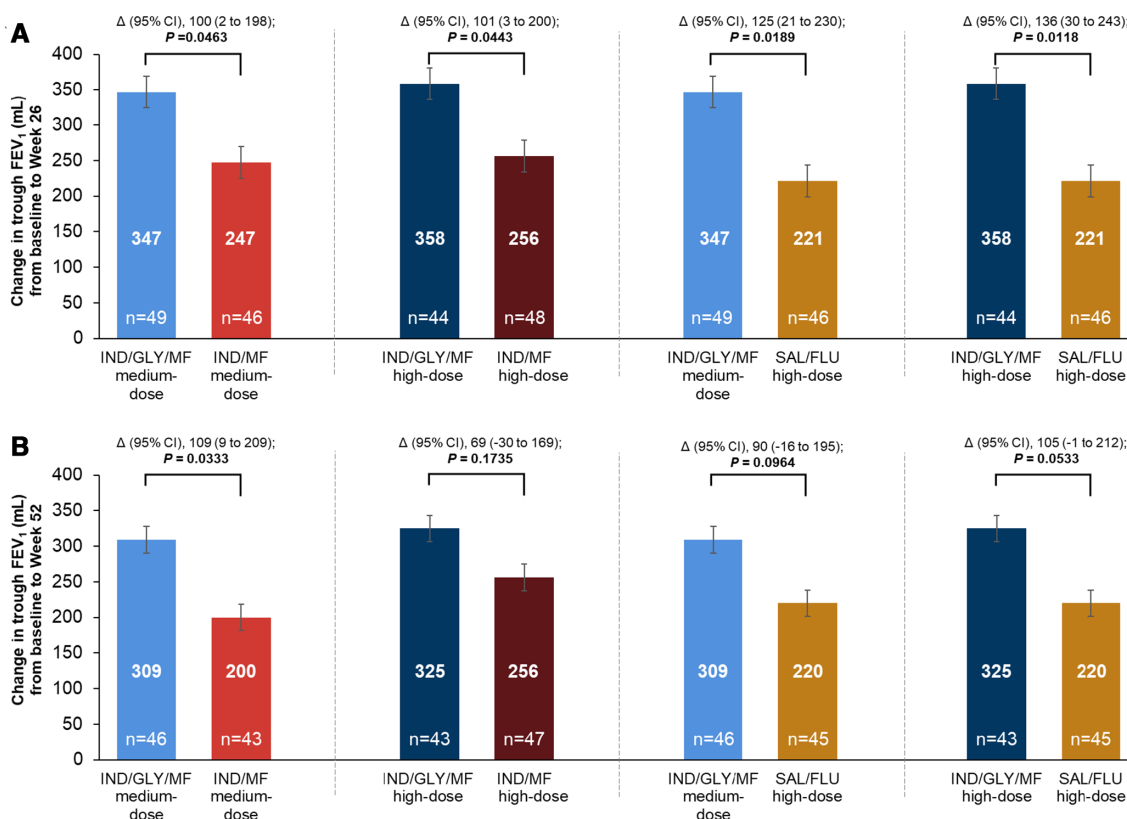
	IND/GLY/MF medium-dose N=52	IND/GLY/MF high-dose N=52	IND/MF medium-dose N=51	IND/MF high- dose N=51	SAL/FLU high-dose N=52	Total N=258
Age, years	52.4±11.57	49.4±11.72	50.9±12.50	52.4±10.52	51.9±12.30	51.4±11.71
Women, n (%)	28 (53.8)	37 (71.2)	37 (72.5)	34 (66.7)	36 (69.2)	172 (66.7)
Number of asthma exacerbations that required treatment in the 12 months prior to start of study, n (%)						
1	39 (75.0)	41 (78.8)	34 (66.7)	31 (60.8)	41 (78.8)	186 (72.1)
2	10 (19.2)	10 (19.2)	16 (31.4)	12 (23.5)	8 (15.4)	56 (21.7)
3	3 (5.8)	0	0	3 (5.9)	0	6 (2.3)
≥4	0	1 (1.9)	1 (2.0)	5 (9.8)	3 (5.8)	10 (3.9)
Never smoked, n (%)	44 (84.6)	48 (92.3)	47 (92.2)	45 (88.2)	45 (86.5)	229 (88.8)
Baseline ACQ-7 score*	2.2±0.46	2.3±0.67	2.3±0.45	2.4±0.52	2.3±0.40	2.3±0.51
Pre-bronchodilator FEV <sub>1</sub> , % predicted	55.6±14.80	57.1±13.65	56.4±11.50	53.6±14.33	54.3±13.59	55.4±13.58
FEV <sub>1</sub> reversibility after salbutamol inhalation, % increase†	26.0±15.13	28.2±12.23	27.0±13.26	29.2±13.59	26.7±13.44	27.4±13.50
Prior asthma treatment, n (%)						
LABA/ICS medium-dose	32 (61.5)	32 (61.5)	35 (68.6)	36 (70.6)	29 (55.8)	164 (63.6)
LABA/ICS high-dose	19 (36.5)	19 (36.5)	15 (29.4)	15 (29.4)	23 (44.2)	91 (35.3)

IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg one time per day; IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg one time per day; IND/MF medium-dose, IND/MF 150/160 µg one time per day; IND/MF high-dose, IND/MF 150/320 µg one time per day; SAL/FLU high-dose, SAL/FLU 50/500 µg two times per day. Data presented as mean±SD, unless otherwise specified.

\*The baseline ACQ-7 score was reported at screening, or if missing, at the last visit from run-in.

†FEV<sub>1</sub> reversibility was calculated as increase of FEV<sub>1</sub> value after inhalation of bronchodilator (400 µg salbutamol/360 µg albuterol, or equivalent dose) relative to FEV<sub>1</sub> value before inhalation of bronchodilator.

ACQ, Asthma Control Questionnaire; eCRF, electronic case report form; FEV<sub>1</sub>, forced expiratory volume in 1 s; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; IND/MF, indacaterol acetate/mometasone furoate; LABA/ICS, long-acting β<sub>2</sub>-agonist/inhaled corticosteroid; SAL/FLU, salmeterol xinafoate/fluticasone propionate.



**Figure 1** Change from baseline in trough FEV<sub>1</sub> with IND/GLY/MF versus IND/MF and SAL/FLU at (A) week 26 and (B) week 52 (full analysis set). IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg one time per day; IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg one time per day; IND/MF medium-dose, IND/MF 150/160 µg one time per day; IND/MF high-dose, IND/MF 150/320 µg one time per day; SAL/FLU high-dose, SAL/FLU 50/500 µg two times per day. Data presented as LS mean±SE, error bars represent SE values. Δ, LS mean treatment difference; FEV<sub>1</sub>, forced expiratory volume in 1 s; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; IND/MF, indacaterol acetate/mometasone furoate; LS, least squares; SAL/FLU, salmeterol xinafoate/fluticasone propionate.

albuterol (components of short-acting β<sub>2</sub>-agonist reversibility) as covariates and centre as a random effect. Mean morning and evening PEF was analysed using an analysis of covariance (ANCOVA) model. The annualised rates of asthma exacerbations were analysed using a generalised linear model assuming the negative binomial distribution. All analyses were performed using SAS V.9.4. Due to the post hoc nature of the analysis, all treatment comparisons assessed in this analysis were descriptive and not powered to claim significance. All p values are nominal.

## RESULTS

### Baseline demographics and clinical characteristics

This post hoc analysis of Asian population included 258 randomised patients, 8.3% of overall randomised population of IRIDIUM study (IND/GLY/MF medium-dose one time per day, n=52; IND/GLY/MF high-dose one time per day, n=52; IND/MF medium-dose one time per day, n=51; IND/MF high-dose one time per day, n=51; SAL/FLU high-dose two times per day, n=52). Baseline demographics and clinical characteristics were comparable across the treatment groups (table 1) and in line with the overall population of the IRIDIUM study.<sup>14</sup>

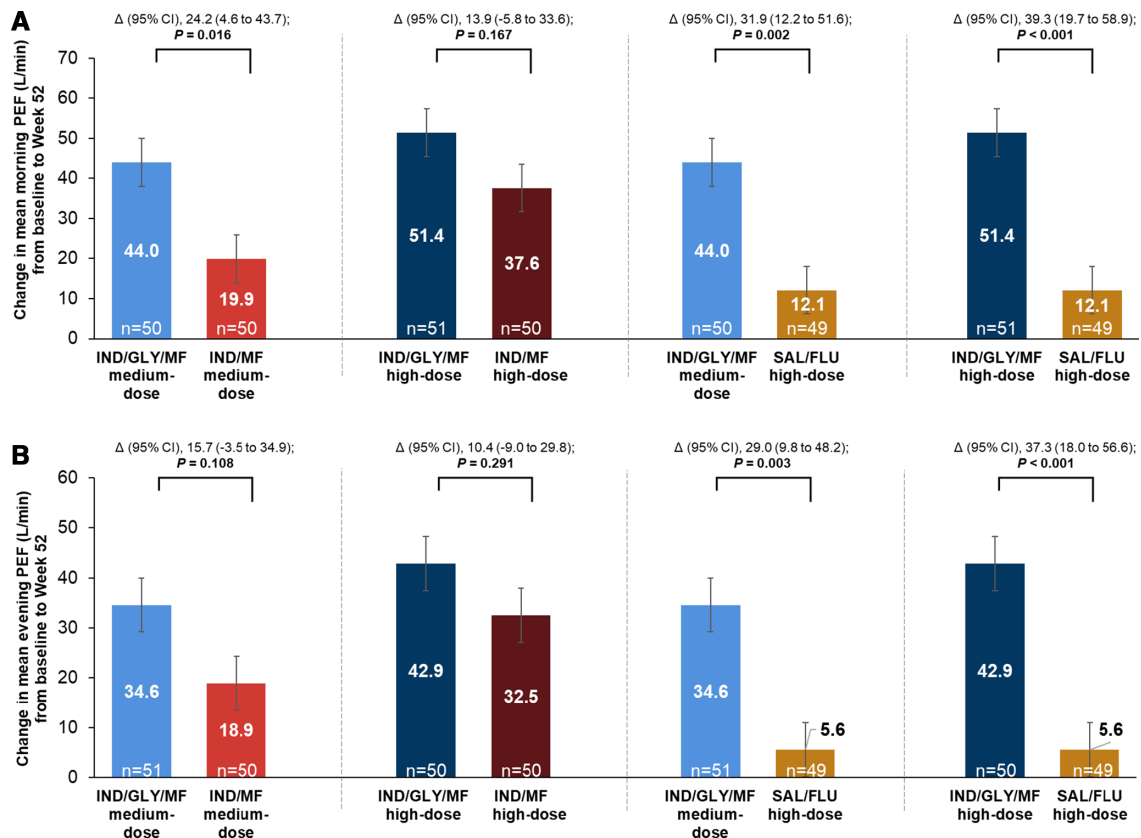
### Lung function

IND/GLY/MF medium- and high-dose one time per day showed greater improvements in trough FEV<sub>1</sub> at week 26 versus respective IND/MF medium-dose one time per day (least squares mean treatment difference (Δ), 100 mL; 95% CI 2 to 198 mL; p=0.0463) and IND/MF high-dose one time per day (Δ, 101 mL; 95% CI 3 to 200 mL; p=0.0443) (figure 1A). The improvement in trough FEV<sub>1</sub> was greater with IND/GLY/MF medium- and high-dose versus SAL/FLU high-dose two times per day at week 26 (Δ, 125 mL; 95% CI 21 to 230 mL; p=0.0189 and Δ, 136 mL; 95% CI 30 to 243 mL; p=0.0118, respectively) (figure 1A). These improvements in trough FEV<sub>1</sub> with IND/GLY/MF versus IND/MF and SAL/FLU were sustained up to week 52 (figure 1B).

IND/GLY/MF medium- and high-dose showed greater improvements in post-dose FEV<sub>1</sub> compared with respective doses of IND/MF and SAL/FLU high-dose as early as 5 min after the study drug administration and up to 1 hour on day 1 (online supplemental material, figure S1).

Both doses of IND/GLY/MF showed greater improvement in morning and evening PEF from baseline to week 52 compared with respective doses of IND/MF and SAL/FLU high-dose (figure 2).





**Figure 2** Change from baseline in (A) morning and (B) evening PEF with IND/GLY/MF, IND/MF and SAL/FLU from baseline to week 52 (full analysis set). IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg one time per day; IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg one time per day; IND/MF medium-dose, IND/MF 150/160 µg one time per day; IND/MF high-dose, IND/MF 150/320 µg one time per day; SAL/FLU high-dose, SAL/FLU 50/500 µg two times per day. Data presented as LS mean±SE, error bars represent SE values. Δ, LS mean treatment difference; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; IND/MF, indacaterol acetate/mometasone furoate; LS, least squares; SAL/FLU, salmeterol xinafoate/fluticasone propionate.

### Asthma control

At week 26, the improvements in ACQ-7 scores were comparable for IND/GLY/MF medium- and high-dose versus the respective doses of IND/MF and SAL/FLU high-dose, such that there were no notable differences observed between the treatment groups in terms of change of ACQ-7 scores from baseline (figure 3A). A similar trend was observed in the changes in ACQ-7 score with all treatments from baseline to week 52 (online supplemental material, figure S2). Approximately 69%–78% of patients across all treatment arms achieved the minimum clinically important difference (MCID ≥0.5 decrease in ACQ-7 score) change from baseline at week 26 (figure 3B). Similarly, 70.2% of patients in IND/GLY/MF medium-dose, 88.6% of patients in IND/GLY/MF high-dose, 81.4% and 89.1% of patients, respectively, for IND/MF medium- and high-dose and 83.3% of patients in SAL/FLU high-dose achieved MCID in ACQ-7 score at week 52.

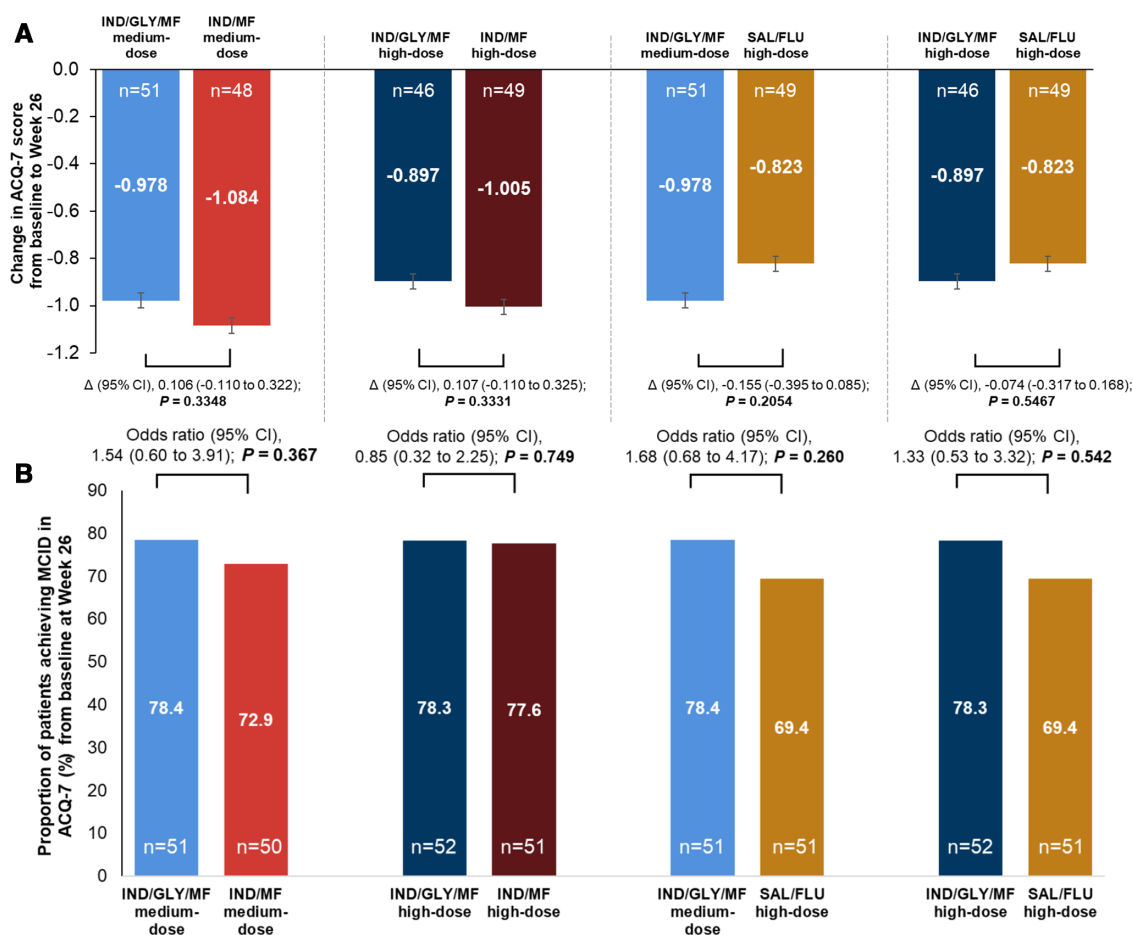
### Asthma exacerbations

Over 52 weeks, IND/GLY/MF medium- and high-dose reduced the rate of severe exacerbations by 32% and 36%

versus respective doses of IND/MF. Comparable reductions in moderate or severe, and all exacerbations, were observed between IND/GLY/MF medium- and high-dose versus respective doses of IND/MF (figure 4A). IND/GLY/MF medium- and high-dose showed reductions of 34% and 69% in the rate of severe exacerbations versus SAL/FLU high-dose, respectively. The reduction in the rate of moderate or severe exacerbations was 18% with IND/GLY/MF medium-dose and 54% with IND/GLY/MF high-dose versus SAL/FLU high-dose. IND/GLY/MF medium- and high-dose showed 21% reductions and 34% reductions in the rate of all exacerbations versus SAL/FLU high-dose, respectively (figure 4B).

### DISCUSSION

This post hoc analysis of the IRIDIUM study assessed lung function, asthma control and asthma exacerbations with IND/GLY/MF medium- (150/50/80 µg) and high-dose (150/50/160 µg) compared with respective doses of IND/MF (150/160 µg and 150/320 µg) and SAL/FLU high-dose (50/500 µg) in Asian patients with inadequately controlled asthma despite LABA/ICS medium-dose or high-dose therapy. The results showed greater



**Figure 3** (A) Change from baseline in ACQ-7 score with IND/GLY/MF versus IND/MF and SAL/FLU at week 26 and (B) proportion of patients achieving MCID in ACQ-7 score with IND/GLY/MF versus IND/MF and SAL/FLU at week 26 (full analysis set). IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg one time per day; IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg one time per day; IND/MF medium-dose, IND/MF 150/160 µg one time per day; IND/MF high-dose, IND/MF 150/320 µg one time per day; SAL/FLU high-dose, SAL/FLU 50/500 µg two times per day. Data presented as LS mean±SE, error bars represent SE values. Δ, LS mean treatment difference; ACQ, Asthma Control Questionnaire; IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; IND/MF, indacaterol acetate/mometasone furoate; LS, least squares; SAL/FLU, salmeterol xinafoate/fluticasone propionate.

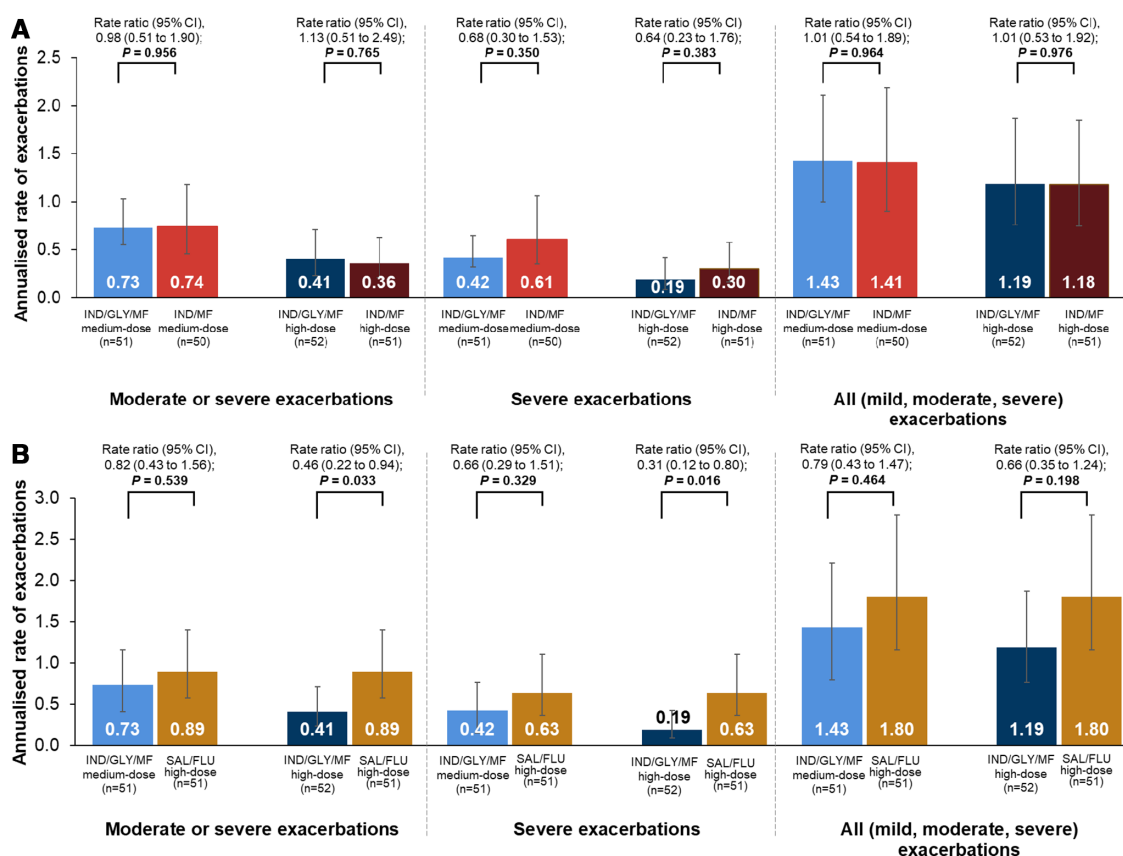
improvements in lung function and exacerbation reduction and comparable asthma control with IND/GLY/MF versus IND/MF and SAL/FLU over 52 weeks of treatment.

Baseline and clinical characteristics were comparable between the Asian patients included in this post hoc analysis and the overall population in the IRIDIUM study.<sup>14</sup> In this analysis, there were more female patients than male patients, similar to that observed in the overall population. In the Asian subgroup, 14.3% patients were aged ≥65 years versus 18.4% in the overall population; those with one asthma exacerbation during the previous year were 72.1% versus 80.3%. Patients who had prior treatment with LABA/ICS medium-dose and high-dose in Asian subgroup were 63.6% and 35.3%, compared with 62.4% and 37%, respectively, in the overall population in the IRIDIUM study.<sup>14</sup>

One time per day, single-inhaler IND/GLY/MF medium- and high-dose showed greater improvement in trough FEV<sub>1</sub> at week 26 compared with respective IND/

MF medium- and high-dose (100 mL and 101 mL) and SAL/FLU high-dose (125 mL and 136 mL). A slightly greater improvement in trough FEV<sub>1</sub> was observed in the Asian population when compared with the results of the IRIDIUM study for the overall population. IND/GLY/MF medium- and high-dose achieved numerically greater improvement in FEV<sub>1</sub> versus the respective doses of IND/MF (76 mL and 65 mL at week 26, both p<0.001), and SAL/FLU high-dose (99 mL and 119 mL at week 26, both p<0.001) in the overall population.<sup>14</sup> A faster onset of action with IND/GLY/MF medium- and high-dose was observed compared with the respective doses of IND/MF and SAL/FLU high-dose on day 1, which was maintained up to week 52. This is in line with the overall population.<sup>14</sup>

IND/GLY/MF medium- and high-dose revealed considerable improvements in terms of morning and evening PEF over 52 weeks, compared with the respective doses of IND/MF (10.4–24.2 L/min) and SAL/FLU high-dose (29.0–39.3 L/min). The PEF results of this analysis can be considered clinically relevant based on the clinically



**Figure 4** Annualised rate of exacerbations with IND/GLY/MF versus (A) IND/MF and (B) SAL/FLU at week 52 in patients with inadequately controlled asthma (full analysis set). IND/GLY/MF medium-dose, IND/GLY/MF 150/50/80 µg one time per day; IND/GLY/MF high-dose, IND/GLY/MF 150/50/160 µg one time per day; IND/MF medium-dose, IND/MF 150/160 µg one time per day; IND/MF high-dose, IND/MF 150/320 µg one time per day; SAL/FLU high-dose, SAL/FLU 50/500 µg two times per day. Data presented as annualised rate (95% CI); error bars represent CI values. IND/GLY/MF, indacaterol acetate/glycopyrronium bromide/mometasone furoate; IND/MF, indacaterol acetate/mometasone furoate; SAL/FLU, salmeterol xinafoate/fluticasone propionate.

important differences reported in the previous publications.<sup>23 24</sup> Compared with the PEF results in the overall population in the IRIDIUM<sup>14</sup> study, both doses of IND/GLY/MF showed slightly greater improvements in PEF versus SAL/FLU high-dose. Overall, in Asian patients with inadequately controlled asthma, IND/GLY/MF medium- and high-dose showed greater lung function benefits (improvement in trough FEV<sub>1</sub>, fast onset of action in post-dose FEV<sub>1</sub> and increase in PEF) compared with respective doses of IND/MF and SAL/FLU high-dose. This was in line with improvements observed with IND/GLY/MF medium- and high-dose in the overall population of the IRIDIUM trial.<sup>14</sup>

IND/GLY/MF medium- and high-dose provided comparable change from baseline to week 26 in ACQ-7 score versus the respective dose of IND/MF and SAL/FLU high-dose in Asian patients. More than 70% of patients in all treatment groups achieved the MCID at the end of study. In this post hoc analysis, more patients receiving IND/GLY/MF high-dose achieved MCID in ACQ-7 score compared with SAL/FLU high-dose at week 26. The proportion of patients achieving MCID in ACQ-7 score with IND/GLY/MF, IND/MF and SAL/FLU in this

analysis was comparable with the overall population in the IRIDIUM study at week 26.<sup>14</sup>

There were no differences among any treatment groups regarding change from baseline in ACQ-7 scores, which is consistent with outcomes in the overall population in the IRIDIUM study.<sup>14</sup> The validity of ACQ-7 scores has been assessed in placebo-controlled trials with milder or treatment-naïve patients. Studies evaluating the add-on treatment of bronchodilators to an established effective regimen in patients with severe asthma showed lack of treatment difference in ACQ-7 scores.<sup>25</sup>

In this post hoc analysis, IND/GLY/MF medium- and high-dose showed greater reductions in severe exacerbations (>30%) and similar reductions in moderate or severe and all exacerbations versus respective IND/MF doses over 52 weeks. On the other hand, greater reductions in asthma exacerbations (moderate or severe, from 18% to 54%; severe, from 34% to 69%; all, from 21% to 34%) were observed with both doses of IND/GLY/MF versus SAL/FLU high-dose in Asian patients. These results are in alignment with the results of the IRIDIUM study in the overall population<sup>14</sup> and revealed that the reductions in asthma exacerbations with both doses of



IND/GLY/MF versus SAL/FLU high-dose in the Asian populations are slightly better than the overall population in the IRIDIUM study. In the overall population, IND/GLY/MF medium- and high-dose resulted in a 7%–22% reduction in annualised rate of exacerbations (severe, moderate or severe and all) versus respective doses of IND/MF and 16%–42% reduction versus SAL/FLU highdose over 52 weeks of treatment.<sup>14</sup>

This analysis of the Asian subpopulation in the IRIDIUM study has the commonly recognised limitations of a post hoc analysis of a subpopulation from a larger study. This analysis included a small number of patients and did not conform to the population or the randomisation model of statistical inference. Due to its post hoc nature, all treatment comparisons assessed in this analysis were descriptive and not powered to claim significance.

## CONCLUSION

In Asian patients with inadequately controlled asthma, single-inhaler, one time per day IND/GLY/MF showed greater improvements in lung function and reduction in exacerbations, compared with respective doses of IND/MF and SAL/FLU, a standard-of-care. The change in ACQ-7 score from baseline was comparable with all treatments. The improvements in lung function, asthma control and exacerbation outcomes observed with IND/GLY/MF in the Asian population are consistent with the results in the overall population of the IRIDIUM study.

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