Cureus
Part of SPRINGER NATURE

Open Access Original Article

A Phase 3 Randomized Controlled Trial of Fixed-Dose Vilanterol/Umeclidinium/Fluticasone Furoate Versus Indacaterol/Glycopyrronium/Mometasone Furoate Dry Powder Inhalers in Indian Adults With Asthma

Review began 10/13/2026
Review ended 11/07/2026
Published 11/12/2026

© **Copyright** 2026
Vyas et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.119573

Pankaj Vyas [1], Mitul Kumar Chaudhari [2], Jaydip Deb [3], Amit Bhate [4], Manish K. Jain [5], Akash Balki [6], Ram Kaulgud [7], Abhay Javia [8], Deven Parmar [9], Kevin Kansagra [9], Hardik Pathak [10]

1. Tuberculosis and Chest Diseases, Namostute Hospital, Gandhinagar, IND 2. Pulmonary Medicine, JK Orthopaedic Hospital, Himmatnagar, IND 3. Respiratory Medicine, Nil Ratan Sircar Medical College, Kolkata, IND 4. General Medicine, Bhate Hospital, Belagavi, IND 5. Pulmonology, Maharaja Agrasen Super Specialty Hospital, Jaipur, IND 6. Critical Care Medicine, Shree Hospital and Critical Care Centre, Nagpur, IND 7. General Medicine, Karnataka Medical College and Research Institute, Hubballi, IND 8. Tuberculosis and Respiratory Disease, Sterling Hospitals, Rajkot, IND 9. Clinical Research and Development, Zydus Research Centre, Ahmedabad, IND 10. Pulmonary Medicine, Zydus Research Centre, Ahmedabad, IND

Corresponding author: Hardik Pathak, drhardiklpathak@gmail.com

Abstract

Background and objective

A novel fixed-dose combination (FDC) of vilanterol 25 µg, umeclidinium 62.5 µg, and fluticasone furoate 200 µg (VIL-UME-FF) in a dry powder inhaler (DPI) formulation has been developed by Zydus Healthcare Limited (Ahmedabad, India) for the management of persistent asthma. This trial aimed to compare its efficacy and safety with those of an approved triple-combination DPI formulation.

Methods

In this phase 3, multicenter, parallel-group, open-label trial, patients with persistent asthma were randomized (1:1) to receive either the test VIL-UME-FF DPI or the reference DPI containing indacaterol 150 µg, glycopyrronium 50 µg, and mometasone furoate 160 µg (IND-GLY-MF), which was approved by the Drugs Controller General of India. Both treatments were administered once daily for 12 weeks. The primary endpoint was the change from baseline in trough forced expiratory volume in one second (FEV1) at week 12, which was analyzed using analysis of covariance in the per-protocol population (non-inferiority margin, −150 mL). Secondary endpoints included trough forced vital capacity (FVC), post-bronchodilator FEV1 and FVC, Asthma Control Test score, rescue medication-free days, and asthma exacerbations.

Results

Of 258 randomized patients aged 18-65 years (test: 129; reference: 129), 257 (test: 129; reference: 128) were included in the per-protocol population. The least squares mean (standard error) change from baseline in trough FEV1 at week 12 was 342.9 (21.27) mL in the test group and 327.6 (21.35) mL in the reference group (difference: 15.2 mL; 95% confidence interval (CI): −44.19 to 74.64 mL; p = 0.6141). The lower limit of the 95% CI was well above the prespecified non-inferiority margin of −150 mL. No statistically significant between-group differences were observed in the secondary efficacy endpoints. Additionally, there were no deaths or serious treatment-emergent adverse events in either group.

Conclusions

VIL-UME-FF DPI was non-inferior to IND-GLY-MF DPI in improving trough FEV1, demonstrated no statistically significant differences in secondary efficacy endpoints, and was well tolerated in Indian patients with persistent asthma.

Categories: Pulmonology, Internal Medicine, Allergy/Immunology
Keywords: asthma, dry powder inhaler, fluticasone furoate, non-inferiority, phase 3, randomized, umeclidinium, vilanterol

Introduction

Asthma is a chronic inflammatory disease of the airways in which the bronchi become inflamed and narrowed, making it difficult to exhale [1]. It typically presents with intermittent breathlessness, cough, and

wheezing. The World Health Organization estimated that asthma affected approximately 262 million people worldwide in 2019 and caused more than 450,000 deaths [2]. In India, asthma is common across all age groups, with an estimated prevalence exceeding 2% [3,4].

Although asthma cannot be cured, it can be controlled by identifying and avoiding triggers, taking regular maintenance therapy, and using reliever medication during acute episodes. Nevertheless, progressive, poorly controlled asthma with exacerbations can be fatal if not treated promptly. The Global Initiative for Asthma (GINA) provides recommendations for the stepwise management of asthma. The 2024 GINA report recommends low-dose inhaled corticosteroid (ICS) combined with a long-acting β2-agonist (LABA) as Step 3 treatment for persistent asthma to reduce the risk of severe exacerbations, and medium- to high-dose ICS-LABA as Step 4 treatment [1]. Approximately 40% of patients with persistent asthma remain symptomatic despite GINA Step 4 treatment. These patients have poorer quality of life, reduced work productivity, and a greater need for emergency and hospital-based care [5]. In such patients, adding an inhaled long-acting muscarinic antagonist (LAMA) has been shown to further improve lung function and reduce asthma exacerbations [6,7].

Single-inhaler fixed-dose combinations (FDCs) of ICS, LABA, and LAMA have been approved for clinical use in several countries to improve adherence and disease control in patients who remain symptomatic on medium- to high-dose ICS-LABA. These include once-daily mometasone furoate-indacaterol-glycopyrronium, once-daily fluticasone furoate (FF)-umeclidinium (UME)-vilanterol, and twice-daily beclomethasone-formoterol-glycopyrronium. In India, two triple-combination dry powder inhaler (DPI) formulations are approved for asthma: indacaterol 150 µg, glycopyrronium 50 µg, and mometasone furoate 160 µg (IND-GLY-MF), approved in November 2022, and vilanterol 25 µg, glycopyrronium 50 µg, and FF 200 µg (VIL-GLY-FF), approved in March 2025 [8-11].

Zydus Healthcare Limited (Ahmedabad, India) has developed a DPI FDC of vilanterol 25 µg, UME 62.5 µg, and FF 200 µg (VIL-UME-FF). This phase 3, randomized, non-inferiority trial compared the efficacy and safety of VIL-UME-FF with those of IND-GLY-MF in Indian patients with persistent asthma.

Materials And Methods

Study design and participants

This prospective, randomized, parallel-group, active-controlled, open-label, multicenter, phase 3 trial was conducted between May 15, 2025, and September 30, 2025, at eight sites in different regions of India. Literate men and women aged 18-65 years with a diagnosis of asthma for at least 12 months before screening were eligible if they met all of the following criteria: (1) a pre-bronchodilator forced expiratory volume in one second (FEV1) of 40%-80% of the predicted normal value at screening spirometry, with bronchodilator reversibility (an increase in FEV1 of ⩾12% and ⩾200 mL after salbutamol inhalation); (2) use of an ICS-LABA combination for ⩾3 months, at a stable medium or high dose for ⩾ 4 weeks before screening; (3) an Asthma Control Test (ACT) score of ⩽ 15 at screening; and (4) at least one severe asthma exacerbation in the 12 months before screening, but none within the six weeks before screening.

Patients were excluded if they met any of the following criteria: (1) known hypersensitivity to any β2-agonist, sympathomimetic drug, antimuscarinic agent, or any inhaled, intranasal, or systemic corticosteroid; (2) a history of life-threatening asthma within the five years before screening; (3) asthma exacerbation requiring systemic corticosteroids or resulting in hospitalization or an emergency department visit within six weeks before screening; (4) treatment with a long-acting muscarinic antagonist (LAMA) within three months before screening; (5) a known diagnosis of narrow-angle glaucoma, prostatic hyperplasia, bladder-neck obstruction, or urinary retention; (6) suspected or confirmed bacterial or viral infection of the upper or lower respiratory tract, sinus, or middle ear within four weeks before screening; (7) a concurrent respiratory disorder other than asthma, including but not limited to pneumonia, pulmonary tuberculosis, chronic bronchitis, chronic obstructive pulmonary disease, pneumothorax, atelectasis, bronchopulmonary dysplasia, interstitial lung disease, or cystic fibrosis; (8) clinical evidence of oropharyngeal candidiasis at screening; (9) clinically significant, uncontrolled systemic disease, including cardiovascular, renal, neurological, psychiatric, endocrine, immunological, or hematological disorders, or malignancy; (10) hepatic dysfunction (serum transaminases ⩾3 × the upper limit of normal) or renal dysfunction (serum creatinine ⩾2.5 mg/dL) at screening; (11) use of any prohibited medication (listed below); (12) pregnancy or lactation, or unwillingness to use effective contraception among female patients of childbearing potential; (13) current smoking, smoking cessation within six months before screening, or a smoking history of at least 10 pack-years; (14) an current or past alcohol and/or drug abuse; (15) participation in another clinical trial within three months before screening; or (16) any other reason the investigator considered sufficient to preclude participation.

Patients with inadequately controlled asthma despite medium- to high-dose ICS-LABA therapy were screened (visit 1) up to three days before enrollment. At the baseline visit (visit 2, day 0), eligible patients were enrolled and randomized to the test group (VIL-UME-FF DPI) or the reference group (IND-GLY-MF DPI). After randomization, patients were followed up on an outpatient basis at week 4 (visit 3), week 8 (visit 4), and week 12 (visit 5; end of study).

Patients in the test and reference groups inhaled the contents of one VIL-UME-FF capsule or one IND-GLY-MF capsule, respectively, once daily (preferably in the morning) using a Respihaler device. Both study medications were supplied as hard capsules containing dry powder for inhalation and were administered using the same capsule-based Respihaler device, which was provided to patients at visit 2 along with instructions for its use. The ICS component of each product corresponded to a high daily ICS dose: fluticasone furoate 200 µg once daily is classified as a high dose in the GINA report [1], and mometasone furoate 160 µg is the high-dose strength of the IND-GLY-MF combination [6].

Before screening spirometry, patients withheld their ICS-LABA maintenance therapy for 24 hours (twice-daily LABA) or 36 hours (once-daily LABA). Their previous ICS-LABA therapy was not resumed; instead, patients initiated the study medication at randomization (visit 2), which occurred up to three days after screening. Salbutamol pressurized metered-dose inhaler (100 µg/puff; one to two puffs as needed, maximum eight puffs/day) was provided as rescue medication. Oral methylxanthines, leukotriene receptor antagonists, and mast cell stabilizers were permitted if the dose had been stable for at least four weeks before screening; no other changes to asthma medication were allowed.

Prohibited medications were systemic corticosteroids (from six weeks before screening); monoclonal antibodies and immunosuppressants (from 12 weeks before screening); inhaled LABAs (from 24 or 36 hours before screening) and inhaled short-acting β2-agonists other than rescue salbutamol (from six hours before screening); inhaled muscarinic antagonists, oral β2-agonists, and non-selective β-blockers (from one week before screening); potent cytochrome P450 3A4 inhibitors and drugs known to prolong the QTc interval (from four weeks before screening); and any other medication that, in the investigator's judgment, could affect the course of asthma or interact with the study drugs. Short courses of inhaled short-acting β2-agonists or muscarinic antagonists or systemic corticosteroids were permitted only for the treatment of an asthma exacerbation. Treatment compliance was assessed at visits 3, 4, and 5 based on study medication entries in the diary cards and counts of the unused capsules returned by patients; inhaler technique was not formally reassessed at follow-up visits.

The protocol was approved by the Drugs Controller General of India (DCGI) and by the institutional/independent ethics committee of each participating site. The trial was conducted in accordance with the Declaration of Helsinki, the International Council for Harmonisation Good Clinical Practice guidelines, the New Drugs and Clinical Trials Rules, 2019, of the Central Drugs Standard Control Organisation (CDSCO), and the Indian Council of Medical Research ethical guidelines for biomedical and health research involving human participants. The trial was registered with the Clinical Trials Registry-India (CTRI/2025/04/085959) before the first patient was enrolled. All patients provided written informed consent before any study-related procedure.

Randomization, allocation concealment, and blinding

A single, central, computer-generated randomization schedule with a 1:1 allocation ratio (test: reference) was prepared using R software, in accordance with the standard operating procedures. The schedule was generated using the randomizeR package (version 3.0.2) in R (version 4.4.3) as a single, unstratified list of 258 randomization numbers with equal allocation (129 per group); randomization was not stratified by site or any other factor. The number of patients randomized per site ranged from 9 to 50 (Appendix Table *10*).

Patients who provided informed consent were assigned a screening number. Patients confirmed to be eligible at the baseline visit (visit 2) were assigned the next sequential four-digit randomization number, and the investigational product kit linked to that number was dispensed by the site team through an interactive web response system (IWRS). Patients who withdrew consent or failed screening retained their screening number but did not receive a randomization number, and randomization numbers of patients who discontinued were not reassigned. The two study medications differed in physical characteristics; therefore, blinding of patients and investigators was not feasible, and the study was conducted in an open-label manner.

Objectives and endpoints

The primary objective was to demonstrate the non-inferiority of VIL-UME-FF DPI to IND-GLY-MF DPI with respect to the change from baseline in trough FEV1 at week 12, using a non-inferiority margin of −150 mL, in patients with persistent asthma inadequately controlled on medium- or high-dose ICS-LABA therapy. The secondary objectives were to compare the two treatments with respect to other lung function parameters, asthma control, rescue medication use, asthma exacerbations, and the patient-reported global impression of change. The safety objective was to compare the safety and tolerability of the two treatments.

The primary endpoint was the change from baseline in trough FEV1 at week 12 (end of study). The secondary efficacy endpoints were the change from baseline in trough FEV1 at week 4; in trough forced vital capacity (FVC) at weeks 4 and 12; in post-bronchodilator FEV1 and FVC at weeks 4 and 12; and in ACT score at weeks 4, 8, and 12; the proportion of rescue medication-free days during the treatment period; asthma exacerbations during the study; and the patient-reported global impression of change (GIC) in disease condition at the end of the study. The safety endpoints were treatment-emergent adverse events (TEAEs),

serious TEAEs, and the investigator-rated overall tolerability of the study medication at the end of the study.

At screening, bronchodilator reversibility was assessed by spirometry performed before and 15 (±5) minutes after inhalation of salbutamol 400 µg (four puffs of 100 µg via a pressurized metered-dose inhaler), after short-acting β2-agonists had been withheld for six hours; twice-daily LABAs, oral methylxanthines, leukotriene receptor antagonists, and mast cell stabilizers for 24 hours; and once-daily LABAs for 36 hours. During the treatment period, spirometry was performed at visit 2 (baseline), visit 3 (week 4), and visit 5 (week 12) in clinically stable patients without a respiratory tract infection, after rescue salbutamol had been withheld for at least six hours. Trough FEV1 and FVC were measured before inhalation of the morning dose of study medication; at visits 3 and 5, this assessment was performed 24 (±2) hours after the previous dose. Post-bronchodilator FEV1 and FVC were measured approximately two hours (±15 minutes) after inhalation of the study medication.

The same protocol-specified spirometry procedure was used at all sites, and site staff were trained at the site initiation visits. However, spirometry was performed with each site's own spirometer, and a common spirometer model, centralized calibration standards, and central over-reading of spirograms were not specified. Because of the open-label design, spirometry operators were not blinded to treatment allocation. Patients recorded each use of rescue medication (number of puffs of salbutamol) and each dose of study medication daily in a diary card, which was reviewed at each visit. A rescue medication-free day was defined as a day on which no rescue medication was used. The proportion of rescue medication-free days at each visit was calculated as the number of rescue medication-free days since the previous visit divided by the total number of days since the previous visit; the value recorded at visit 2 (covering the screening period) served as the baseline.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or least squares (LS) mean (standard error (SE)), and categorical variables as number (percentage). The change from baseline in trough FEV1 at week 12 was analyzed using analysis of covariance (ANCOVA), with treatment as a fixed effect and the baseline value as a covariate. VIL-UME-FF was to be considered non-inferior to IND-GLY-MF if the lower limit of the two-sided 95% confidence interval (CI) for the LS mean difference (test minus reference) was greater than the non-inferiority margin of −150 mL (one-sided $\alpha = 0.025$).

The secondary continuous endpoints (trough FEV1 at week 4; trough FVC, post-bronchodilator FEV1, and post-bronchodilator FVC at weeks 4 and 12; and ACT score at weeks 4, 8, and 12) were analyzed using the same ANCOVA model. For these endpoints, the LS mean difference with its 95% CI, the F statistic with its degrees of freedom, and the p-value are reported. The change from baseline in the proportion of rescue medication-free days at each post-baseline visit was compared between groups using the independent two-sample t-test, and the mean difference with its 95% CI, the t statistic with its degrees of freedom, and the p-value are reported.

For categorical and ordinal outcomes, the ordinal GIC score was compared between groups using the Wilcoxon rank-sum test. Asthma exacerbations, TEAEs, overall tolerability grades, and categorical baseline characteristics (e.g., sex) were summarized descriptively as frequencies and percentages, and no formal hypothesis tests were prespecified or performed for these variables. All tests were two-sided, and $p < 0.05$ was considered statistically significant; no adjustment was made for multiplicity. Accordingly, the secondary efficacy analyses are considered supportive, and non-significant p-values for these endpoints are interpreted as indicating the absence of a statistically significant between-group difference rather than demonstrating equivalence. Statistical analyses were performed using SAS® version 9.4 (SAS Institute Inc., Cary, NC).

The safety population included all randomized patients who received at least one dose of study medication. The modified intention-to-treat (mITT) population included all patients in the safety population who completed at least one post-randomization visit (visit 3, 4, or 5), including those with major protocol deviations. The per-protocol (PP) population included all patients in the mITT population who completed all post-randomization visits (visits 3, 4, and 5) without any major protocol deviation; patients with only minor protocol deviations were retained.

As prespecified in the protocol, a deviation was classified as major if it was likely to affect the quality or completeness of the data, made the informed consent process inaccurate, or significantly affected the safety, rights, or welfare of patients (e.g., failure to meet eligibility criteria, wrong treatment or dosing outside the protocol, or use of prohibited medication); deviations without such impact (e.g., visits outside the permitted window, missed or incomplete study procedures or evaluations, or failure to return diary cards or study medication) were classified as minor. All deviations were reviewed and classified as major or minor.

The primary non-inferiority analysis was performed in both the PP and mITT populations, with the PP analysis considered conclusive and the mITT analysis supportive; secondary efficacy endpoints were analyzed in both populations. Baseline characteristics, safety, and tolerability were summarized in the safety

population. No imputation of missing data was planned or performed, and all analyses were based on observed data. When a baseline value was missing, the most recent available pre-treatment (screening) value was used as the baseline value.

The sample size was calculated for the primary endpoint. Assuming no true difference between the groups in the change from baseline in trough FEV1 at week 12, a common SD of 350 mL, a non-inferiority margin of 150 mL, and a one-sided significance level of 0.025, 232 evaluable patients (116 per group) were required to provide 90% power. Allowing for a 10% dropout rate, 258 patients (129 per group) were randomized in a 1:1 ratio. The non-inferiority margin of −150 mL was prespecified in the protocol approved by the DCGI. It was selected to be smaller than the minimal patient-perceivable improvement in FEV1 in asthma (approximately 230 mL) [12], thereby ensuring that a between-group difference within this margin would be unlikely to represent a clinically meaningful difference. This margin is also consistent with that used in a previous phase 3 non-inferiority trial comparing a triple-combination DPI with IND-GLY-MF in Indian patients with asthma [13].

Results

Patient disposition and baseline characteristics

Of 285 individuals screened, 258 were randomized (test group: 129; reference group: 129). All of them received at least one dose of study medication and comprised the safety population. One patient in the reference group withdrew consent before attending any post-randomization visit and was therefore excluded from the mITT and PP populations. The remaining 257 patients (test group: 129; reference group: 128) completed the study and were included in both the mITT and PP populations. Aside from this single withdrawal, no patient discontinued the study, and no major protocol deviations were recorded. Minor protocol deviations were recorded in 39 patients (30.23%; 65 deviations) in the test group and 28 patients (21.71%; 52 deviations) in the reference group. Almost all of these were related to study procedures (64 and 51 deviations, respectively), while one laboratory-related deviation occurred in the test group and one visit-schedule deviation occurred in the reference group. Because these deviations were minor, all patients were retained in the PP population; the mITT and PP populations were therefore identical, and the efficacy results were the same for both populations.

Mean treatment compliance was 98.8% ± 1.64% in the test group and 98.5% ± 6.03% in the reference group. Demographic and baseline characteristics are presented for the safety population (n = 258) in Table *1*, which therefore shows 129 patients in each group, whereas the efficacy tables show 128 patients in the reference group. The mean age was 39.9 ± 11.28 years in the test group and 41.6 ± 11.30 years in the reference group, and the male-to-female ratio was 78:51 and 86:43, respectively. Mean height (164.16 ± 7.63 cm vs. 164.22 ± 8.51 cm) and weight (61.51 ± 9.26 kg vs. 62.23 ± 8.51 kg) were similar in the two groups, and nearly 90% of patients in each group had no history of smoking. Overall, demographic and baseline characteristics were comparable between the groups (Table *1*). The CONSORT flow diagram is shown in Figure *1*.

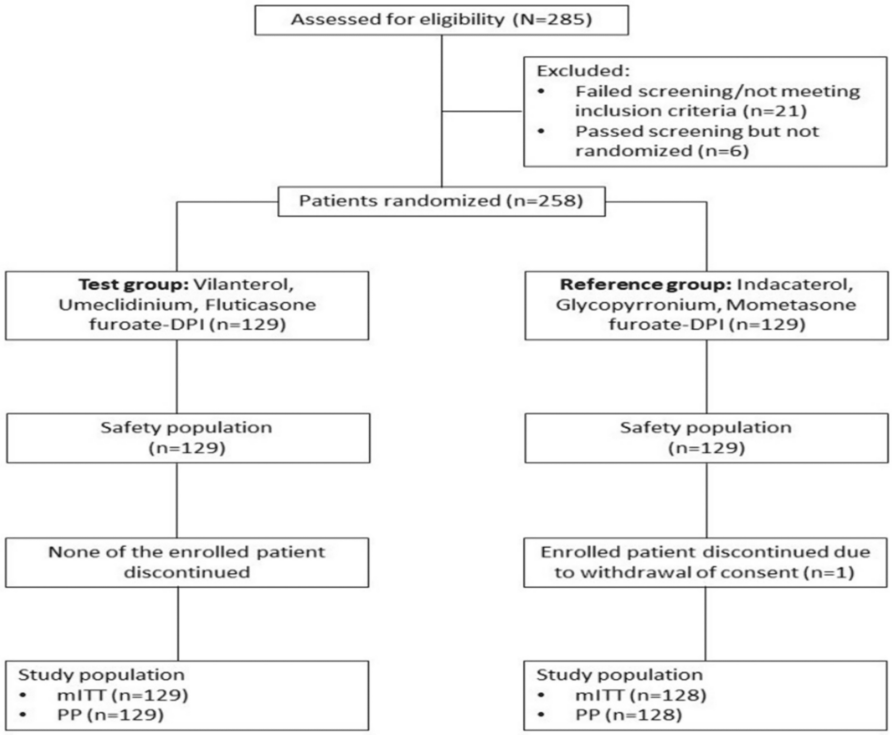


FIGURE 1: CONSORT flow diagram of patient disposition

DPI: dry powder inhaler; mITT: modified intended-to-treat; PP: per-protocol

CONSORT: Consolidated Standards of Reporting Trials

Characteristics	Test group (n = 129)	Reference group (n = 129)
Age, years		
Mean ± SD	39.9 ± 11.28	41.6 ± 11.30
Median (min-max)	39.0 (19.00-64.00)	41.0 (19.00-62.00)
Sex (male:female)	78:51	86:43
Height, cm		
Mean ± SD	164.16 ± 7.63	164.22 ± 8.51
Median (min-max)	165.00 (140.00-180.00)	166.00 (136.00-182.00)
Weight, kg		
Mean ± SD	61.51 ± 9.26	62.23 ± 8.51
Median (min-max)	62.00 (38.00-92.40)	62.10 (38.00-93.15)
BMI, kg/m², median (min-max)	23.90 (15.80-37.40)	23.50 (16.00-39.00)
Pre-bronchodilator FEV1 at screening, mL, mean ± SD*	1460.6 ± 329.18	1528.1 ± 403.87
Trough FEV1 at baseline (visit 2), mL, mean ± SD*	1555.7 ± 411.65	1608.5 ± 447.27
ACT score at screening (baseline), mean ± SD*	12.3 ± 1.44	12.2 ± 1.52

TABLE 1: Demographic details and baseline characteristics of participants (safety population)

*Lung function and ACT values are shown for the mITT population (test group, n = 129; reference group, n = 128).

Table 1 presents the safety population (all 258 randomized patients). The reference-group patient who withdrew consent before any post-randomization visit is included here but excluded from the mITT/PP efficacy analyses (n = 257; reference group, n = 128). Test group: patients received vilanterol, umeclidinium, and fluticasone furoate (from Zydus Healthcare Ltd.) – DPI formulation. Reference group: patients received indacaterol, glycopyrronium, and mometasone furoate (approved product) – DPI formulation

BMI: body mass index; DPI: dry powder inhaler; ACT: Asthma Control Test; FEV1: forced expiratory volume in 1 second; mITT: modified intention-to-treat; max: maximum; min: minimum; SD: standard deviation

Trough FEV1 response

Trough FEV1 values at baseline, week 4, and week 12 were comparable between the groups (see table in the Appendix). For the primary endpoint (PP population), the LS mean (SE) change from baseline in trough FEV1 at week 12 was 342.9 (21.27) mL in the test group and 327.6 (21.35) mL in the reference group (Table *2*). The LS mean difference (test minus reference) was 15.2 mL (95% CI: −44.19 to 74.64 mL; ANCOVA, F(1, 254) = 0.25; p = 0.6141). Because the lower limit of the 95% CI (−44.19 mL) was well above the prespecified non-inferiority margin of −150 mL, VIL-UME-FF was non-inferior to IND-GLY-MF for the change from baseline in trough FEV1 at week 12. As the mITT and PP populations were identical, the mITT analysis gave the same result. At week 4, the mean trough FEV1 was 1730.5 ± 394.09 mL in the test group and 1771.6 ± 465.62 mL in the reference group (see table in the Appendix), corresponding to mean changes from baseline of 174.7 ± 264.98 mL and 163.0 ± 251.14 mL, respectively. The between-group difference was not significant (LS mean difference: 2.3 mL; 95% CI: −58.51 to 63.18 mL; F(1, 254) = 0.01; p = 0.9398).

Change in trough FEV1 response at week 12 from baseline	Test group (n = 129)	Reference group (n = 128)
Least squares mean (SE)	342.9 (21.27) mL	327.6 (21.35) mL
Least squares mean difference (test - reference)	15.2 mL	
95% CI	(−44.19, 74.64) mL	
P-value	0.6141	
ANCOVA F statistic (df)	F(1, 254) = 0.25	

TABLE 2: Non-inferiority analysis of the change from baseline in trough FEV1 at week 12 (PP population)

LS means, the LS mean difference, its 95% CI, and the F statistic were obtained from ANCOVA with treatment as a fixed effect and baseline trough FEV1 as a covariate. Non-inferiority was concluded because the lower limit of the 95% CI was above the prespecified margin of −150 mL. The mITT population was identical to the PP population and gave identical results. Test group: patients received vilanterol, umeclidinium, and fluticasone furoate (from Zydus Healthcare Ltd.) – DPI formulation. Reference group: patients received indacaterol, glycopyrronium, and mometasone furoate (approved product) – DPI formulation

ANCOVA: analysis of covariance; CI: confidence interval; DPI: dry powder inhaler; df: degrees of freedom; FEV1: forced expiratory volume in 1 second; LS: least squares; mITT: modified intention-to-treat; PP: per-protocol; SE: standard error

Evaluation of trough FVC, post-bronchodilator FEV1 and FVC, and ACT score

Trough FVC values at baseline, week 4, and week 12 were comparable between the groups (see table in the Appendix). The mean change from baseline in trough FVC did not differ significantly between the test and reference groups at week 4 (194.7 ± 300.44 mL vs. 165.2 ± 320.44 mL; LS mean difference: 19.9 mL; 95% CI: −52.60 to 92.32 mL; F(1, 254) = 0.29; p = 0.590) or at week 12 (354.2 ± 280.78 mL vs. 344.2 ± 274.95 mL; LS mean difference: −1.0 mL; 95% CI: −63.37 to 61.31 mL; F(1, 254) < 0.01; p = 0.974) (Table *3*). Likewise, post-bronchodilator FEV1, FVC, and ACT scores were comparable between the groups (see table in the Appendix), with no significant between-group difference in the change from baseline at week 4, week 8 (ACT score only), or week 12. The LS mean differences with 95% CIs, F statistics, and p-values for all secondary continuous endpoints are presented in Table *3*.

Change from baseline in	Test group (n = 129), mean ± SD	Reference group (n = 128), mean ± SD	LS mean difference (95% CI); F(1, 254); p-value
Trough FVC (mL)			
At week 4	194.7 ± 300.44	165.2 ± 320.44	19.9 (−52.60, 92.32); 0.29; 0.590
At week 12	354.2 ± 280.78	344.2 ± 274.95	−1.0 (−63.37, 61.31); <0.01; 0.974
Post-bronchodilator FEV1 (mL)			
At week 4	186.1 ± 254.06	148.0 ± 221.43	31.2 (−26.13, 88.53); 1.15; 0.285
At week 12	329.8 ± 259.08	306.0 ± 244.85	17.5 (−43.55, 78.61); 0.32; 0.572
Post-bronchodilator FVC (mL)			
At week 4	150.8 ± 330.16	167.7 ± 289.43	−20.2 (−91.95, 51.48); 0.31; 0.579
At week 12	338.8 ± 259.61	358.1 ± 262.49	−21.7 (−83.08, 39.62); 0.49; 0.486
ACT score			
At week 4	3.4 ± 1.95	3.4 ± 2.04	0.11 (−0.36, 0.59); 0.21; 0.645
At week 8	6.0 ± 1.96	5.9 ± 2.07	0.22 (−0.26, 0.71); 0.83; 0.362
At week 12	8.4 ± 1.62	8.1 ± 1.94	0.32 (−0.10, 0.74); 2.24; 0.136

TABLE 3: Change in trough FVC, post-bronchodilator FEV1 and FVC, and ACT score (PP population)

Values in the test group and reference group columns are mean ± SD changes from baseline. LS mean differences (test − reference) with 95% CIs, F statistics (degrees of freedom 1, 254), and p-values were obtained from ANCOVA with treatment as a fixed effect and the baseline value as a covariate. The mITT population was identical to the PP population and gave identical results. Test group: patients received vilanterol, umeclidinium, and fluticasone furoate (from Zydus Healthcare Ltd.) – DPI formulation. Reference group: patients received indacaterol, glycopyrronium, and mometasone furoate (approved product) – DPI formulation

ACT: Asthma Control Test; DPI: dry powder inhaler; ANCOVA: analysis of covariance; CI: confidence interval; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; LS: least squares; mITT: modified intention-to-treat; PP: per-protocol; SD: standard deviation

Rescue medication and asthma exacerbation

At baseline (visit 2), the mean proportion of rescue medication-free days was 0.73 ± 0.383 in the test group and 0.72 ± 0.401 in the reference group. The mean proportion of rescue medication-free days at weeks 4, 8, and 12 was 0.84 ± 0.121, 0.88 ± 0.094, and 0.91 ± 0.085, respectively, in the test group and 0.85 ± 0.127, 0.88 ± 0.117, and 0.91 ± 0.127, respectively, in the reference group. The change from baseline in this proportion did not differ significantly between the groups at week 4 (mean difference: −0.016; 95% CI: −0.108 to 0.076; t(255) = −0.34; p = 0.7367), week 8 (mean difference: −0.009; 95% CI: −0.103 to 0.084; t(255) = −0.19; p = 0.8475), or week 12 (mean difference: 0.003; 95% CI: −0.093 to 0.098; t(255) = 0.06; p = 0.9554). No patient in either group experienced an asthma exacerbation during the study.

GIC

At week 12, the patient-reported GIC in disease condition was similar in the two groups (mean score: 2.2 ± 0.64 vs. 2.1 ± 0.62; Wilcoxon rank-sum test, p = 0.2564). Most patients in both groups rated their condition as much improved (test group: 56.59%; reference group: 61.72%) or very much improved (test group: 33.33%; reference group: 26.56%) (Table 4).

GIC criteria	Test group (n = 129), n (%)	Reference group (n = 128), n (%)
−3 (very much worse)	-	-
−2 (much worse)	-	-
−1 (minimally worse)	-	-
0 (no change)	1 (0.78)	1 (0.78)
+1 (minimally improved)	12 (9.30)	14 (10.94)
+2 (much improved)	73 (56.59)	79 (61.72)
+3 (very much improved)	43 (33.33)	34 (26.56)

TABLE 4: Patient-reported global impression of change in disease condition at week 12 (PP population)

Between-group comparison: Wilcoxon rank-sum test, p = 0.2564. Test group: patients received vilanterol, umeclidinium, and fluticasone furoate (from Zydus Healthcare Ltd.) – DPI formulation. Reference group: patients received indacaterol, glycopyrronium, and mometasone furoate (approved product) – DPI formulation

DPI: dry powder inhaler; GIC: global impression of change; PP: per-protocol

Overall tolerability evaluation

At week 12, the investigator-rated overall tolerability was similar in the two groups. Tolerability was rated as "excellent" in 56.59% and 54.26% of patients and as "good" in 37.98% and 38.76% of patients in the test and reference groups, respectively (Table *5*).

Visit	Tolerability grade	Test group (n = 129), n (%)	Reference group (n = 129), n (%)
Visit 5	Excellent	73 (56.59)	70 (54.26)
	Good	49 (37.98)	50 (38.76)
	Fair	7 (5.43)	8 (6.20)
	Poor	0 (0)	0 (0)

TABLE 5: Investigator-rated overall tolerability at the end of the study (safety population)

Percentages are based on the safety population (n = 129 per group); tolerability was not assessed for the reference-group patient who withdrew consent before any post-randomization visit. Tolerability was summarized descriptively; no formal statistical test was performed. Test group: patients received vilanterol, umeclidinium, and fluticasone furoate (from Zydus Healthcare Ltd.) – DPI formulation. Reference group: patients received indacaterol, glycopyrronium, and mometasone furoate (approved product) – DPI formulation

DPI: dry powder inhaler

Safety

The incidence, causality, and severity of TEAEs are summarized in Table *6*. Overall, 65 of 258 patients (25.19%) experienced 66 TEAEs: 27 patients (20.93%; 27 events) in the test group and 38 patients (29.46%; 39 events) in the reference group. Headache was the only TEAE reported in more than 4% of patients in either group (reference group: 8.53%; test group: 3.88%). TEAEs by system organ class and preferred term are presented in a table in the Appendix. Events potentially related to anticholinergic activity were infrequent: dry mouth occurred in one patient (0.78%) in each group, and constipation in one patient (0.78%) in the test group and four patients (3.10%) in the reference group; urinary retention was not reported. Tremor, palpitations, and tachycardia, which are typical of β2-agonist therapy, were not reported in either group. No deaths or serious TEAEs occurred, and all TEAEs were mild or moderate in severity. Mild TEAEs occurred in 53 patients (21 in the test group and 32 in the reference group), and moderate TEAEs in 12 patients (six in each group). All TEAEs resolved completely during the study period. No apparent differences were observed between the groups in laboratory parameters, vital signs, physical examination findings, or electrocardiograms.

Description	Test group (n = 129)	Reference group (n = 129)
Total number of TEAEs	27	39
Total number of serious TEAEs	0	0
Number of patients (%) with at least one TEAE	27 (20.93)	38 (29.46)
TEAEs (severity grade)		
Mild	21	33
Moderate	6	6
TEAEs (related to study treatment)		
Not related	10	15
Related	17	24
TEAEs (based on outcome)		
Resolved/recovered	27	39

TABLE 6: Summary of treatment-emergent adverse events by type, severity grade, relatedness to treatment, and outcome

TEAEs are summarized descriptively for the safety population (n = 258); no formal statistical test was performed. Test group: patients received vilanterol, umeclidinium, and fluticasone furoate (from Zydus Healthcare Ltd.) – DPI formulation. Reference group: patients received indacaterol, glycopyrronium, and mometasone furoate (approved product) – DPI formulation

DPI: dry powder inhaler; TEAE: treatment-emergent adverse event

Discussion

This phase 3 trial, sponsored by Zydus Healthcare Limited, compared the efficacy and safety of the VIL-UME-FF DPI with those of the approved IND-GLY-MF DPI. The trial met its primary endpoint: VIL-UME-FF was non-inferior to IND-GLY-MF for the change from baseline in trough FEV1 at week 12. The LS mean improvement in trough FEV1 from baseline was 342.9 mL with VIL-UME-FF and 327.6 mL with IND-GLY-MF, and the lower limit of the 95% CI for the between-group difference (−44.19 mL) was well above the non-inferiority margin of −150 mL. This lower confidence limit would also have excluded a more stringent margin of −50 mL.

For the secondary endpoints, once-daily VIL-UME-FF and once-daily IND-GLY-MF showed no statistically significant differences in the changes in trough FVC, post-bronchodilator FEV1 and FVC, and ACT score. No statistically significant differences were observed in rescue medication-free days or the patient-reported GIC in disease condition, and no asthma exacerbations occurred in either group. The overall tolerability and safety profile of VIL-UME-FF were similar to those of IND-GLY-MF. Because the secondary analyses were not adjusted for multiplicity and were not designed to test equivalence, these findings should be regarded as supportive of the primary non-inferiority result.

The addition of a LAMA to ICS-LABA therapy for uncontrolled asthma has been studied for many years, and the tiotropium soft mist inhaler was the first LAMA approved for this purpose [14]. More recently, clinical development has focused on single-inhaler triple therapy to improve adherence and convenience, and several phase 3 studies have shown that the complementary actions of the three components improve the control of asthma exacerbations [8,15]. The IND-GLY-MF FDC was evaluated extensively in the PLATINUM phase 3 clinical program in patients with inadequately controlled asthma [16]. Within this program, the IRIDIUM study was the first to assess once-daily IND-GLY-MF and showed that adding glycopyrronium, a LAMA, to medium- or high-dose indacaterol-mometasone furoate (IND-MF) significantly improved trough FEV1 over 26 weeks [6]. A once-daily IND-GLY-MF DPI is currently available for clinical use in India.

In a double-blind, three-period crossover, dose-ranging study of 421 patients with asthma, adding UME to FF improved trough FEV1 compared with FF alone across treatment periods (treatment difference: 0.055 L; p = 0.018), with no treatment-related effects on laboratory parameters [17]. The authors concluded that adding UME to FF may be a viable treatment option for patients with asthma. Subsequently, the double-blind, randomized, phase 3A CAPTAIN trial compared single-inhaler FF, UME, and vilanterol (FF-UME-VI) with FF-VI in patients with inadequately controlled asthma and showed significant improvements in trough FEV1 from baseline with FF-UME-VI (p < 0.0001), with small, dose-related gains attributable to UME; FF-UME-VI

was considered an effective treatment option with a favorable benefit-risk profile [18].

The VIL-UME-FF product evaluated in the present study contains the same three components at the same strengths (FF 200 µg, UME 62.5 µg, and VI 25 µg) as one of the FF-UME-VI doses evaluated in the CAPTAIN trial [18]. Whereas these studies compared UME-containing regimens with dual therapy, the present study compared VIL-UME-FF directly with an approved triple FDC, IND-GLY-MF, and showed non-inferior improvement in lung function, with no statistically significant differences in trough FVC, post-bronchodilator FEV1 and FVC, or ACT scores, and similar tolerability and TEAE profiles. These findings are consistent with those of an earlier phase 3 trial in which VIL-GLY-FF DPI was non-inferior to IND-GLY-MF DPI in Indian patients with asthma [13]. Taken together, these results indicate that VIL-UME-FF was non-inferior to the approved IND-GLY-MF FDC for the change from baseline in trough FEV1 at week 12 in Indian patients with persistent asthma.

Zydus Healthcare Limited presented the results of this phase 3 trial to the Subject Expert Committee (SEC) of the CDSCO in December 2025. According to the minutes of the meeting published on the CDSCO website, the SEC recommended the grant of permission to manufacture and market the VIL-UME-FF (25 µg/62.5 µg/200 µg) FDC DPI.

Strengths and limitations

The strengths of this study include the recruitment of patients from multiple sites across India, providing wide geographical representation; an adequately powered sample size; and comparison with a well-established, approved active triple FDC. Its main limitations are the open-label design, which may have introduced bias in patient-reported and investigator-rated outcomes; the relatively short 12-week treatment period; and the enrollment of patients from a single country (India), which may limit the generalizability of the findings to other populations. In addition, because trough FEV1 is effort-dependent, the open-label design may also have influenced the primary endpoint, and although all sites followed the same protocol-specified spirometry procedure, a common spirometer model, centralized calibration, and central over-reading of spirograms were not used.

The study was designed to test non-inferiority, not superiority. It did not include a placebo or dual-therapy (ICS-LABA) arm, and the −150 mL margin is larger than the incremental trough FEV1 benefit generally reported when a LAMA is added to ICS-LABA therapy (approximately 65-110 mL) [6,18]; therefore, the study cannot independently confirm assay sensitivity for the contribution of the LAMA component. Finally, the 12-week duration and the absence of exacerbations in either group preclude conclusions regarding comparative exacerbation reduction and long-term safety; adherence was not evaluated as an outcome, and inhaler technique was not formally reassessed after the initial instruction.

Conclusions

In this phase 3 trial, once-daily VIL-UME-FF delivered as a single DPI FDC was non-inferior to the IND-GLY-MF FDC with respect to improvement in trough FEV1 at week 12. There were no statistically significant differences in secondary efficacy endpoints, and safety and tolerability were similar over 12 weeks. This once-daily, single-inhaler ICS-LABA-LAMA combination may be a useful additional treatment option for patients with persistent asthma that remains inadequately controlled despite ICS-LABA therapy. Although once-daily, single-inhaler dosing may simplify treatment, adherence was not evaluated as an outcome in this study, and any benefit with respect to adherence remains to be demonstrated.

Appendices

Details of patient visits

Patients whose asthma was inadequately controlled despite medium- to high-dose ICS-LABA therapy were screened (visit 1) up to three days before enrollment. At the baseline visit (visit 2, day 0), eligible patients were enrolled and randomized to one of the two study groups according to their randomization number, and they were then followed up as outpatients at week 4 (visit 3), week 8 (visit 4), and week 12 (visit 5). In this parallel-group study, all enrolled patients were instructed to take the study medication for 12 weeks.

Time point	Statistics	Test group	Reference group
Baseline	N	129	128
	Mean ± SD	1556 ± 412	1609 ± 447
	Median (Min-Max)	1510 (770-3120)	1540 (740-3070)
Week 4	N	129	128
	Mean ± SD	1730 ± 394	1772 ± 466
	Median (Min-Max)	1710 (980-3170)	1750 (780-3160)
Week 12	N	129	128
	Mean ± SD	1902 ± 427	1933 ± 477
	Median	1930 (1040-3120)	1910 (1050-3160)

TABLE 7: Trough FEV1 response at baseline, week 4, and week 12 in the mITT population (mL)

Results in the mITT population were consistent with those in the PP population

FEV1: forced expiratory volume in 1 second; max: maximum; min: minimum; mITT: modified intention-to-treat; PP: per-protocol; SD: standard deviation

Time point	Statistics	Trough FVC		Post-bronchodilator FEV1		Post-bronchodilator FVC		ACT score	
		Test group	Reference group	Test group	Reference group	Test group	Reference group	Test group	Reference group
Baseline	N	129	128	129	128	129	128	129	128
	Mean ± SD	1925 ± 584	1983 ± 626	1791± 422	1849± 463	2163 ± 574	2181 ± 584	12.3 ± 1.44	12.2 ± 1.52
	Median	1870	1880	1790	1800	2150	2120	12	12
	Min-Max	960, 3930	990, 4350	1050, 3350	860, 3050	1140, 4100	1150, 3730	9, 15	8, 15
Week 4	N	129	128	129	128	129	128	129	128
	Mean ± SD	2120 ± 555	2148 ± 613	1977± 413	1997± 491	2314 ± 513	2349 ± 592	15.7 ± 2.14	15.5 ± 2.18
	Median	2070	2040	2000	1960	2310	2255	16	15
	Min-Max	990, 4130	1070, 4500	1150, 3290	910, 3650	1170, 3940	1240, 4160	11, 21	11, 20
Week 12	N	129	128	129	128	129	128	129	128
	Mean ± SD	2279 ± 526	2327 ± 576	2121 ± 452	2155± 481	2502 ± 555	2539 ± 565	20.6 ± 1.88	20.2 ± 2.00
	Median	2260	2245	2120	2140	2530	2465	20	20
	Min-Max	1160, 4000	1170, 4310	1160, 3370	1240, 3380	1310, 4360	1430, 4420	17,25	14, 25

TABLE 8: Trough FVC, post-bronchodilator FEV1 and FVC, and ACT score at baseline, week 4, and week 12 in the mITT population (FVC and FEV1 in mL)

ACT score baseline is the value at screening (visit 1), as prespecified in the protocol; the corresponding inclusion criterion was an ACT score of ≤ 15 at screening. The mean ± SD ACT score at week 8 was 18.3 ± 2.11 in the test group and 18.0 ± 2.27 in the reference group. Trough and post-bronchodilator FEV1 and FVC baselines are the values at visit 2

ACT: Asthma Control Test; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; max: maximum; min, minimum; mITT: modified intention-to-treat; SD: standard deviation

System organ class/preferred term	Test group (n = 129), n (%); events	Reference group (n = 129), n (%); events
Patients with at least one TEAE	27 (20.93); 27 events	38 (29.46); 39 events
Gastrointestinal disorders	7 (5.43); 7 events	8 (6.20); 8 events
Abdominal pain upper	1 (0.78); 1 event	0
Constipation	1 (0.78); 1 event	4 (3.10); 4 events
Diarrhoea	0	1 (0.78); 1 event
Dry mouth	1 (0.78); 1 event	1 (0.78); 1 event
Nausea	4 (3.10); 4 events	2 (1.55); 2 events
General disorders and administration site conditions	3 (2.33); 3 events	6 (4.65); 6 events
Fatigue	0	1 (0.78); 1 event
Pain	1 (0.78); 1 event	3 (2.33); 3 events
Pyrexia	2 (1.55); 2 events	2 (1.55); 2 events
Infections and infestations	2 (1.55); 2 events	2 (1.55); 2 events
Gastroenteritis	1 (0.78); 1 event	1 (0.78); 1 event
Pharyngitis	1 (0.78); 1 event	1 (0.78); 1 event
Musculoskeletal and connective tissue disorders	1 (0.78); 1 event	4 (3.10); 4 events
Back pain	1 (0.78); 1 event	4 (3.10); 4 events
Nervous system disorders	5 (3.88); 5 events	11 (8.53); 11 events
Headache	5 (3.88); 5 events	11 (8.53); 11 events
Respiratory, thoracic and mediastinal disorders	9 (6.98); 9 events	7 (5.43); 7 events
Cough	4 (3.10); 4 events	5 (3.88); 5 events
Oropharyngeal pain	3 (2.33); 3 events	1 (0.78); 1 event
Sneezing	2 (1.55); 2 events	1 (0.78); 1 event
Skin and subcutaneous tissue disorders	0	1 (0.78); 1 event
Rash maculo-papular	0	1 (0.78); 1 event

TABLE 9: Treatment-emergent adverse events by system organ class and preferred term (safety population)

Percentages are based on the number of patients in each group. Events were coded using MedDRA version 28.0

MedDRA: Medical Dictionary for Regulatory Activities; TEAE: treatment-emergent adverse event

Site	Screened	Randomized	Completed the study
IN-001	51	50	50
IN-002	42	38	38
IN-003	55	49	49
IN-004	48	45	45
IN-005	17	15	14
IN-006	45	40	40
IN-007	13	9	9
IN-010	14	12	12
Total	285	258	257

TABLE 10: Number of patients screened, randomized, and completing the study at each site

Randomization was not stratified by site. One patient at site IN-005 (reference group) withdrew consent before any post-randomization visit

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Hardik Pathak, Pankaj Vyas, Mitul Kumar Chaudhari, Jaydip Deb, Amit Bhate, Manish K. Jain, Akash Balki, Ram Kaulgud, Abhay Javia, Kevin Kansagra, Deven Parmar

Acquisition, analysis, or interpretation of data: Hardik Pathak, Pankaj Vyas, Mitul Kumar Chaudhari, Jaydip Deb, Amit Bhate, Manish K. Jain, Akash Balki, Ram Kaulgud, Abhay Javia, Kevin Kansagra, Deven Parmar

Drafting of the manuscript: Hardik Pathak, Pankaj Vyas, Mitul Kumar Chaudhari, Jaydip Deb, Amit Bhate, Manish K. Jain, Akash Balki, Ram Kaulgud, Abhay Javia, Kevin Kansagra, Deven Parmar

Critical review of the manuscript for important intellectual content: Hardik Pathak, Pankaj Vyas, Mitul Kumar Chaudhari, Jaydip Deb, Amit Bhate, Manish K. Jain, Akash Balki, Ram Kaulgud, Abhay Javia, Kevin Kansagra, Deven Parmar

Supervision: Hardik Pathak, Mitul Kumar Chaudhari, Kevin Kansagra, Deven Parmar

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. JK Orthopaedics Hospital Ethics Committee issued approval EC/JKOH/APL/APR/2025/01. The study is registered with the Clinical Trials Registry–India (CTRI), and the registration number is CTRI/2025/04/085959. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** Deven Parmar, Kevinkumar Kansagra, and Hardik Pathak are employees of Zydus Lifesciences Ltd., Ahmedabad, India. The remaining authors declare no conflicts of interest.

Acknowledgements

We thank the investigators and patients at the investigative sites for their support during the conduct of the study.

References

1. Global Initiatives for Asthma . (2024). Accessed: February 5, 2026: https://ginasthma.org/reports/.
2. World Health Organization: asthma: key facts . (2024). Accessed: February 5, 2026: https://www.who.int/news-room/fact-sheets/detail/asthma.
3. Singh S, Salvi S, Mangal DK, et al.: Prevalence, time trends and treatment practices of asthma in India: the Global Asthma Network study. ERJ Open Res. 2022, 8:26-8. 10.1183/23120541.00528-2021
4. Serebrisky D, Wiznia A: Pediatric asthma: a global epidemic . Ann Glob Health. 2019, 85:16-8. 10.5334/aogh.2416
5. Gessner C, Kornmann O, Maspero J, et al.: Fixed-dose combination of indacaterol/glycopyrronium/mometasone furoate once-daily versus salmeterol/fluticasone twice-daily plus tiotropium once-daily in patients with uncontrolled asthma: a randomised, phase IIIb, non-inferiority study (ARGON). Respir Med. 2020, 170:106021. 10.1016/j.rmed.2020.106021
6. Kerstjens HAM, Maspero J, Chapman KR, et al.: Once-daily, single-inhaler mometasone-indacaterol-glycopyrronium versus mometasone-indacaterol or twice-daily fluticasone-salmeterol in patients with inadequately controlled asthma (IRIDIUM): a randomised, double-blind, controlled phase 3 study. Lancet Respir Med. 2020, 8:1000-12. 10.1016/S2213-2600(20)30190-9
7. Blair HA: Indacaterol/glycopyrronium/mometasone: a review in asthma . Drugs. 2021, 81:709-19. 10.1007/s40265-021-01518-w
8. Rogliani P, Matera MG, Facciolo F, Page C, Cazzola M, Calzetta L: Beclomethasone dipropionate, formoterol fumarate and glycopyrronium bromide: synergy of triple combination therapy on human airway smooth muscle ex vivo. Br J Pharmacol. 2020, 177:1150-63. 10.1111/bph.14909
9. Virchow JC, Kuna P, Paggiaro P, et al.: Single inhaler extrafine triple therapy in uncontrolled asthma (TRIMARAN and TRIGGER): two double-blind, parallel-group, randomised, controlled phase 3 trials. Lancet. 2019, 394:1737-49. 10.1016/S0140-6736(19)32215-9
10. Kim LH, Saleh C, Whalen-Browne A, O'Byrne PM, Chu DK: Triple vs dual inhaler therapy and asthma outcomes in moderate to severe asthma: a systematic review and meta-analysis. JAMA. 2021, 325:2466-79. 10.1001/jama.2021.7872
11. Syed YY: Fluticasone furoate/vilanterol: a review of its use in patients with asthma . Drugs. 2015, 75:407-18. 10.1007/s40265-015-0354-5
12. Santanello NC, Zhang J, Seidenberg B, Reiss TF, Barber BL: What are minimal important changes for asthma measures in a clinical trial?. Eur Respir J. 1999, 14:23-7. 10.1034/j.1399-3003.1999.14a06.x
13. Patel C, Sheth V, Koppula R, et al.: Efficacy and safety of novel fixed dose combination of vilanterol, glycopyrronium, and fluticasone furoate dry powder inhaler: a phase 3, randomized, non-inferiority trial compared with fixed dose combination of indacaterol, glycopyrronium, and mometasone furoate dry powder inhaler in Indian asthma patients. Respir Med. 2025, 247:108293. 10.1016/j.rmed.2025.108293
14. Anzueto A, Miravitlles M: Tiotropium in chronic obstructive pulmonary disease - a review of clinical development. Respir Res. 2020, 21:199. 10.1186/s12931-020-01407-y
15. Agusti A, Fabbri L, Lahousse L, Singh D, Papi A: Single inhaler triple therapy (SITT) in asthma: systematic review and practice implications. Allergy. 2022, 77:1105-13. 10.1111/all.15076
16. Pelaia C, Crimi C, Crimi N, et al.: Indacaterol/glycopyrronium/mometasone fixed dose combination for uncontrolled asthma. Expert Rev Respir Med. 2022, 16:183-95. 10.1080/17476348.2021.2011222
17. Lee LA, Yang S, Kerwin E, Trivedi R, Edwards LD, Pascoe S: The effect of fluticasone furoate/umeclidinium in adult patients with asthma: a randomized, dose-ranging study. Respir Med. 2015, 109:54-62. 10.1016/j.rmed.2014.09.012
18. Lee LA, Bailes Z, Barnes N, et al.: Efficacy and safety of once-daily single-inhaler triple therapy (FF/UMEC/VI) versus FF/VI in patients with inadequately controlled asthma (CAPTAIN): a double-blind, randomised, phase 3A trial. Lancet Respir Med. 2021, 9:69-84. 10.1016/S2213-2600(20)30389-1