



BREZTRI[®]
AEROSPHERE[®]
budesonide / glycopyrronium / formoterol
fumarate dihydrate pressurized inhalation
suspension

ETHOS AND KRONOS PIVOTAL TRIALS¹⁻⁴



2

pivotal
trials



26

countries
worldwide



10,405

patients
enrolled

BREZTRI AEROSPHERE is indicated for the long-term maintenance treatment to reduce exacerbations of COPD and treat airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema, who are not adequately treated by a combination of an ICS/LABA or a combination of LAMA/LABA.

COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist.

KRONOS PIVOTAL TRIAL¹



Patient population

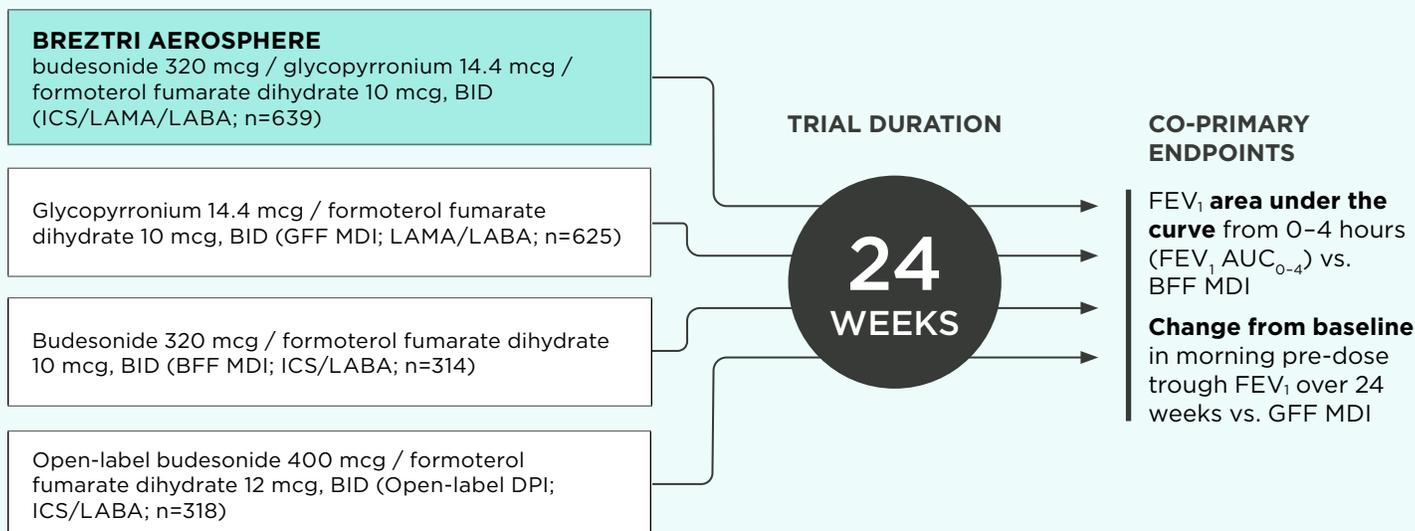
TOTAL N	KEY INCLUSION CRITERIA	DEMOGRAPHICS
1,896 patients randomized	<ul style="list-style-type: none">• Moderate to very severe COPD• No prior history of exacerbation(s) in the previous 12 months required• 74% of patients enrolled had no history of moderate/severe exacerbations in the prior year• Baseline FEV₁ ≥25% to <80% of predicted normal• Current or former smokers with ≥10 pack/year history of smoking• Symptomatic COPD while receiving ≥2 inhaled maintenance therapies for COPD for ≥6 weeks prior to screening	<ul style="list-style-type: none">• Mean age: 65 years• 55% of patients aged 65 or over• Mean post-bronchodilator % predicted FEV₁: 50% during screening• Patients on ICS-containing therapy pre-screening: 72% of patients enrolled• Most common therapy at entry: ICS + LAMA + LABA, 27% ICS + LABA, 38% LAMA + LABA, 20%



Study design

Randomized, double-blind, multicentre, chronic-dosing, parallel-group

TREATMENT ARMS



Selected secondary endpoints



- Change from baseline in morning pre-dose trough FEV₁ over 24 weeks vs. ICS/LABA
- Peak change from baseline in FEV₁ within 4 hours post-dosing over 24 weeks
- Rate of moderate or severe exacerbations



- Breathlessness (assessed by TDI)



- Quality of life (assessed by SGRQ)

AUC₀₋₄: area under the curve from 0–4 hours; BID: twice daily; BFF: budesonide/formoterol fumarate dihydrate; COPD: chronic obstructive pulmonary disease; DPI: dry powder for inhalation; FEV₁: forced expiratory volume in 1 second; GFF: glycopyrronium/formoterol fumarate dihydrate; ICS: inhaled corticosteroid; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist; MDI: metered-dose inhaler; SGRQ: St. George's respiratory questionnaire; TDI: transition dyspnea index.

ETHOS PIVOTAL TRIAL¹



Patient population

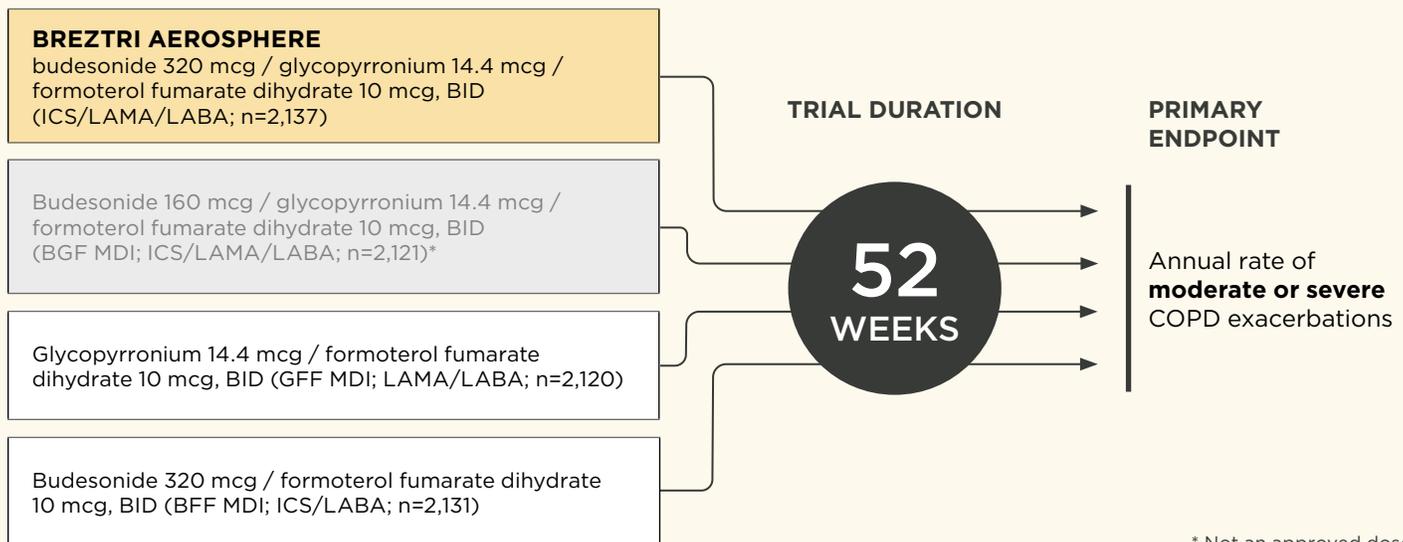
TOTAL N	KEY INCLUSION CRITERIA	DEMOGRAPHICS
8,509 patients randomized	<ul style="list-style-type: none">• Moderate to very severe COPD• History of ≥ 1 exacerbation(s) in the previous 12 months• Baseline FEV₁ $\geq 25\%$ to $< 65\%$ of predicted normal• Current or former smokers with ≥ 10 pack/year history of smoking• Symptomatic COPD while receiving ≥ 2 inhaled maintenance therapies for COPD at the time of screening	<ul style="list-style-type: none">• Mean age: 65 years• 52% of patients aged 65 or over• Mean post-bronchodilator % predicted FEV₁: 43% during screening• Patients on ICS-containing therapy pre-screening: 81%• Most common therapy at entry: ICS + LAMA + LABA, 39% ICS + LABA, 31% LAMA + LABA, 14%



Study design

Randomized, double-blind, multicentre, parallel-group

TREATMENT ARMS



Selected secondary endpoints



- Rate of severe COPD exacerbations
- Time to first moderate or severe exacerbation
- Rate of moderate or severe exacerbations in patients with ≥ 2 exacerbations in the previous year



- Time to death (all cause)



- Breathlessness (assessed by TDI)



- Quality of life (assessed by SGRQ)

BID: twice daily; BFF: budesonide/formoterol fumarate dihydrate; BGF: budesonide/glycopyrronium/formoterol fumarate dihydrate; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in 1 second; GFF: glycopyrronium/formoterol fumarate dihydrate; ICS: inhaled corticosteroid; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist; MDI: metered-dose inhaler; SGRQ: St. George's respiratory questionnaire; TDI: transition dyspnea index.

CHOOSE THE POWERFUL DEMONSTRATED EFFICACY OF BREZTRI AEROSPHERE IN COPD¹



Clinical use:

BREZTRI AEROSPHERE is not indicated for:

- Treatment of acute episodes of bronchospasm or asthma.
- Use in pediatric patients <18 years of age.

Relevant warnings & precautions:

- Risk of serious asthma-related events, including hospitalization, intubations, and death
- Should not be used in patients with deteriorating COPD
- Excessive use with other LAMA and LABA products
- Anticholinergic activity: Use with caution in patients with symptomatic prostatic hyperplasia, urinary retention, or narrow-angle glaucoma
- Cardiovascular effects, including arrhythmias, changes in pulse and blood pressure, or QTc prolongation
- Driving and operating machinery
- Candidiasis
- Risk of systemic effects, including Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, hypokalemia and hyperglycemia, cataract, intraocular pressure, and glaucoma
- Hypercorticism, adrenal suppression
- Adrenal insufficiency in patients transferred from systemic steroid

- Patients with symptomatic prostatic hyperplasia, glaucoma, convulsive disorders, thyrotoxicosis, sensitivity to sympathomimetic amines, severe hepatic impairment/hepatic disease, or urinary retention
- In rare cases, eosinophilic conditions
- Susceptibility or decreased resistance to infections
- Monitoring of hypokalemia, hyperglycemia, bone and ocular effects, and corticosteroid effects in patients with hepatic impairment
- Paradoxical bronchospasm
- Increased risk of pneumonia
- Pregnant and nursing women
- Geriatrics (≥65 years of age)

For more information:

Consult the Product Monograph at breztri-en.azpm.ca for important information regarding adverse reactions, drug interactions, and dosing. The Product Monograph is also available by calling AstraZeneca Canada at **1-800-668-6000**.

COPD: chronic obstructive pulmonary disease; LABA: long-acting beta₂-adrenergic agonist; LAMA: long-acting muscarinic antagonist.

References: **1.** BREZTRI AEROSPHERE Product Monograph. AstraZeneca Canada Inc. **2.** Rabe KF, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. *NEJM*. 2020;383(1):35-48. **3.** Ferguson GT, et al. Triple therapy with budesonide / glycopyrrolate / formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): a double-blind, parallel-group, multicentre, phase 3 randomised controlled trial. *Lancet Respir Med*. 2018(6):747-758. **4.** Study to assess the efficacy and safety of PT010 relative to PT003 and PT009 in subjects with moderate to very severe COPD (ETHOS). ClinicalTrials.gov. Available at: <https://clinicaltrials.gov/study/NCT02465567>. Retrieved December 4, 2023.

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