An overview of the

SHINE Study

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Bateman ED et al., Dual bronchodilation with QVA149 versus single bronchodilator therapy: the SHINE study

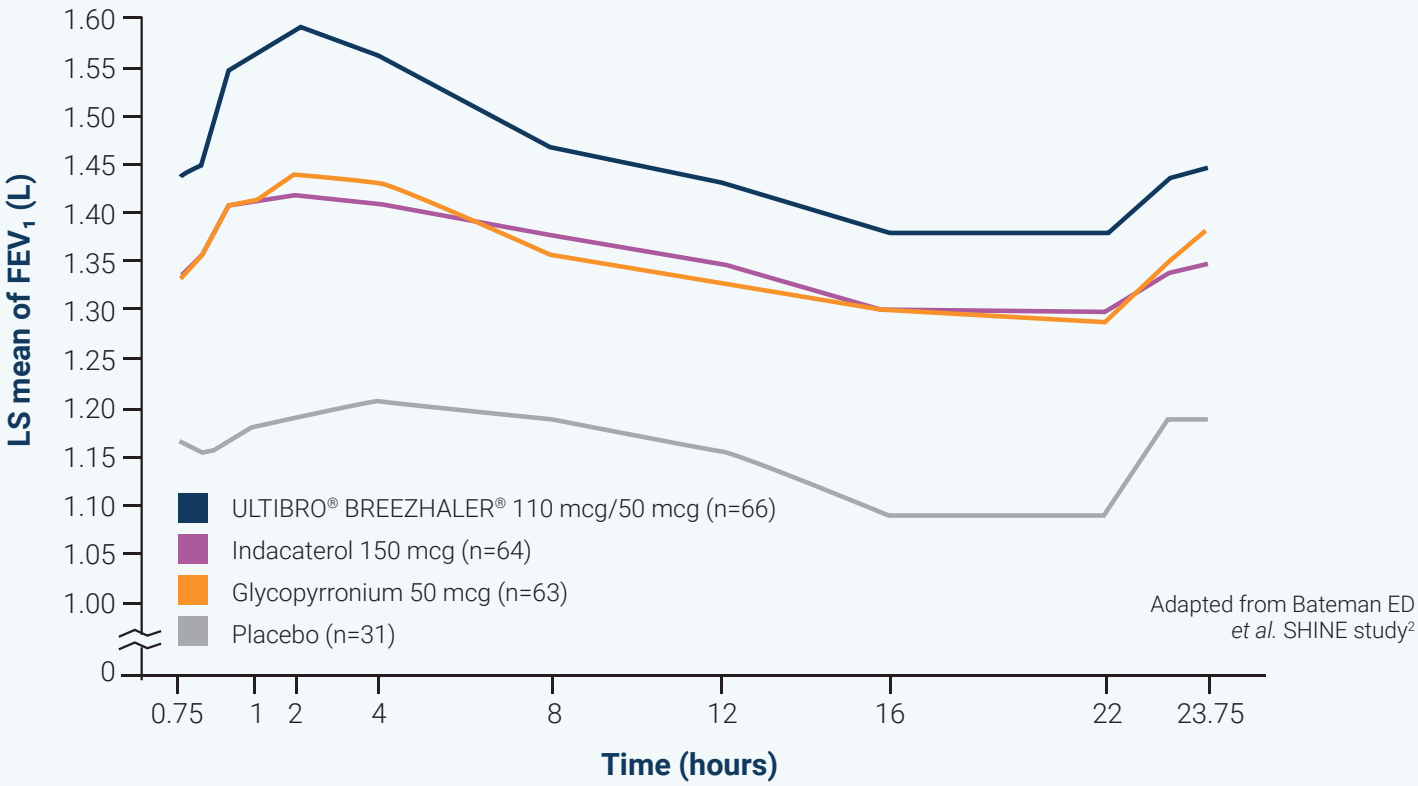
Eur Respir J 2013; 42:1484-1494

ULTIBRO® BREEZHALER®
significantly improved lung function (FEV$_1$ at week 26) *vs.* indacaterol 150 mcg,* glycopyrronium 50 mcg and placebo[2]

250-400 mL

LS mean differences of FEV$_1$ with ULTIBRO® BREEZHALER® vs. placebo demonstrated in a serial spirometry subset at week 26[1]

LS mean FEV$_1$ profile
over 24 hours at week 26



Adapted from Bateman ED *et al.* SHINE study[2]

* Indacaterol 150 mcg is not an available dosage in Canada.
FEV$_1$: forced expiratory volume in 1 second

ULTIBRO® BREEZHALER® **significantly reduced breathlessness** (TDI focal score; secondary endpoint) vs. placebo at week 26[2]

- Treatment difference in TDI focal score with ULTIBRO® BREEZHALER® vs. placebo: 1.09 units (95% CI: 0.61-1.57; *p*<0.001)
- Tiotropium was an open-label reference arm in this study

TDI: Transition Dyspnea Index.

The SHINE Study: **A 26-week, multicentre, double-blind, parallel-group, placebo- and active-controlled trial**

- Patients were randomly assigned (2:2:2:2:1) to once-daily **ULTIBRO® BREEZHALER®** 110/50 mcg, indacaterol 150 mcg*, SEEBRI® BREEZHALER® (glycopyrronium) 50 mcg, open-label tiotropium 18 mcg or placebo
- Enrolled patients (n=2144) were aged ≥40 years, had moderate to severe stable COPD (stage II or III according to GOLD 2008 criteria), a smoking history of ≥10 pack-years, and post-bronchodilator FEV_1 ≥30% and <80% of predicted value
- The primary endpoint was trough FEV_1 at week 26

Important Safety Information for ULTIBRO® BREEZHALER®

Indication:
ULTIBRO BREEZHALER (indacaterol maleate and glycopyrronium bromide) is a combination of a long-acting beta$_2$-agonist (LABA) and a long-acting muscarinic antagonist (LAMA), indicated for the long-term once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema, and for the reduction of exacerbations of COPD in patients with a history of exacerbations.

Clinical use:
- Not indicated for the treatment of acute episodes of bronchospasm
- Not indicated for asthma use
- Can be used at the recommended dose in elderly patients over 65 years of age
- Should not be used in patients under 18 years of age

Contraindications:
- Hypersensitivity to indacaterol maleate or glycopyrronium bromide, or to any other component of ULTIBRO® BREEZHALER®
- Severe hypersensitivity to milk proteins
- Not indicated for treatment of asthma

Most serious warnings and precautions:
Asthma-related death: Increased risk of asthma-related death is considered a class effect with LABAs, including indacaterol maleate. ULTIBRO® BREEZHALER® is not indicated for asthma.

Other relevant warnings and precautions:
- Not indicated for treatment of acute episodes of bronchospasm: patients who have been taking inhaled, short-acting bronchodilators on a regular basis should be instructed to discontinue regular use when beginning treatment with ULTIBRO® BREEZHALER®
- Not indicated for treatment of acutely deteriorating COPD
- Not to be used more often or at higher doses than recommended or with other LABA or LAMA products
- Occurrence of dizziness or blurred vision may influence the ability to drive and use machinery
- Caution in patients with narrow-angle glaucoma: patients should be cautioned to avoid getting the drug powder into their eyes and to be alert of signs and symptoms of acute narrow angle glaucoma
- Caution in urinary retention: risk of prostatic hyperplasia and bladder neck obstruction
- Caution in patients with cardiovascular disorders, coronary insufficiency, acute myocardial infarction, cardiac arrhythmias, and hypertension: ULTIBRO® BREEZHALER® may need to be discontinued
- Caution in patients with a known history of QTc prolongation, risk factors for torsade de pointes, or taking medications known to prolong the QTc interval
- Caution in patients with convulsive disorders, thyrotoxicosis, and patients who are unusually responsive to sympathomimetic amines
- Risk of hypokalemia: monitor serum potassium in patients predisposed to low levels of serum potassium
- Risk of hyperglycemia: monitor blood glucose in diabetic patients
- Risk of immediate hypersensitivity reactions: discontinue immediately and do not rechallenge with ULTIBRO® BREEZHALER®
- Risk of angioedema
- In severe renal impairment (estimated GFR <30 mL/min/1.73m^2) including those with end-stage renal disease requiring dialysis, use only if the expected benefit outweighs the potential risk. Patients should be monitored closely for adverse drug reactions.
- Risk of paradoxical bronchospasm: discontinue immediately
- May inhibit labour: use only if the potential benefit justifies the potential risk
- Pregnancy/nursing and delivery: use only if potential benefit justifies the potential risk
- Caution in patients with severe hepatic impairment
- ULTIBRO® BREEZHALER® capsules must not be swallowed

For more information:
Please consult the Product Monograph at https://pdf.hres.ca/dpd_pm/00054946.PDF for important information relating to adverse events, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling the Medical Information Department at 1-800-363-8883.

References:
1. ULTIBRO® BREEZHALER® Product Monograph. Novartis Pharmaceuticals Canada Inc., January 27, 2020.
2. Bateman ED et al. Dual bronchodilation with QVA149 versus single bronchodilator therapy: the SHINE study. Eur Respir J 2013(42):1484-1494.

COVIS PHARMA

REVIEWED BY PAAB

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