

## Review Article

# Dual Bronchodilation By Once Daily Fixed Dose Combined Indacaterol And Glycopyrronium, New Era For Treatment In Moderate To Severe COPD

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**Original Article-** Dual bronchodilation with QVA149 reduces patient-reported dyspnoea in COPD: BLAZE study (Ref: ERJ Express. Published on October 31, 2013 as doi: 10.1183/09031936.00124013)

**Abstract:** The effect of a dual bronchodilator (QVA149) was evaluated combining Indacaterol and Glycopyrronium, on direct patient-reported dyspnoea in moderate-to severe COPD. In this multicentre, blinded, double-dummy, three-period crossover study, once-daily QVA149 provided superior improvements in patient-reported dyspnoea and lung function versus placebo and tiotropium. These benefits were associated with improvements in other symptoms and reduced use of rescue medication.

**Key word:** QVA149- Code name used for dual bronchodilator, COPD-Chronic obstructive pulmonary disease, LABA-long-acting bronchial agonist, LAMA-long-acting muscarinic antagonist, GOLD-Global Initiative for chronic obstructive lung Disease, SAC-self assessment computerized, TDI- transition dyspnoea index, PBO-placebo, SFC-salmeterol/fluticasone combination, TIO- tiotropium, GLY- Glycopyrronium.

## Introduction

Chronic obstructive pulmonary disease (COPD) represents a significant cause of global morbidity and mortality, with a substantial economic impact. Recent changes in the Global initiative for chronic Obstructive Lung Disease (GOLD) guidance refined the classification of patients for treatment using a combination of Spirometry, assessment of symptoms, and/or frequency of exacerbations. The aim of treatment remains to reduce existing symptoms while decreasing the risk of future adverse health events<sup>1</sup>.

## Method

QVA149, a dual bronchodilator combining Indacaterol (110 µg) and Glycopyrronium (50 µg), was chosen to evaluate on direct patient-reported dyspnoea in patients with moderate-to severe COPD. In this multicentre, blinded, double-dummy, three-period crossover study, 247 patients were randomized to once-daily QVA149 110/50 µg, placebo or tiotropium 18 µg. Superiority of QVA149 versus placebo (primary objective) and

tiotropium (secondary objective) was assessed for improvement in dyspnoea via the Self Administered Computerized (SAC) version of the Baseline and Transition Dyspnoea Index (BDI/TDI) after 6 weeks<sup>4</sup>. Secondary endpoints included lung function, rescue medication use and safety. After 6 weeks, the SAC TDI total score was significantly higher with QVA149 versus and tiotropium. QVA149 provided significant improvements in lung function and lower use of rescue medications versus placebo and tiotropium. All treatments were well tolerated.

## Discussion

Long-acting bronchodilators are the mainstay of therapy due to their proven efficacy. Combinations of long-acting β<sub>2</sub>-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) are an alternative treatment recommendation for patients in GOLD Groups B to D and those who remain symptomatic when treated with a single bronchodilator<sup>2</sup>.

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In recent years we have seen growing interest in combination of long-acting muscarinic antagonists (LAMAs) like Tiotropium or Glycopyrronium (GLY), with long-acting  $\beta_2$ -agonists (LABAs), such as Indacaterol or Formoterol or Salmeterol. Most studies have examined free combinations of currently available LAMAs and LABAs, broadly showing a benefit in terms of lung function and other patient-reported outcomes. Several once- or twice-daily fixed-dose LAMA/LABA combinations are under development, most involving newly developed monotherapy components<sup>3</sup>. The IGNITE program comprises a series of randomized controlled trials that investigate the efficacy and safety of QVA149 in patients with moderate-to-severe COPD. This overview includes data from 4 multicentre, double-blind, randomized controlled trials evaluating the effect of QVA149 110/50  $\mu\text{g}$  versus IND 150  $\mu\text{g}$  alone, GLY 50  $\mu\text{g}$  alone, tiotropium (TIO) 18  $\mu\text{g}$  alone, salmeterol/fluticasone (SFC) 50/500  $\mu\text{g}$  and placebo (PBO) in patients with moderate-to-very severe COPD. Outcomes reported in terms of lung function, transitional dyspnoea index (TDI), health status and exacerbations over a certain period of time<sup>3</sup>. QVA149 provided statistically significant and clinically meaningful bronchodilation that was sustained throughout the treatment periods versus all comparators in all studies. In addition, QVA149 reduced the rate of all exacerbations by 31% and significantly delayed the time to first exacerbation versus SFC in the ILLUMINATE trial<sup>4</sup>.

## Conclusion

As data supporting the efficacy and safety of LABA/LAMA fixed-dose combinations continue to emerge, this once daily dual bronchodilation may feature increasingly in future COPD treatment algorithms<sup>3</sup>. Although like other modern treatment

options in COPD, this new treatment will emerge as an expensive one as well. More randomized control trials are ongoing to see the effect on mortality in future, but we may conclude that once daily dual bronchodilation with LABA/LAMA has significant reduction in morbidity especially in moderate to severe cases of COPD.

## References

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