Indacaterol–Glycopyrronium versus Salmeterol–Fluticasone for COPD

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ABSTRACT

BACKGROUND

Most guidelines recommend either a long-acting beta-agonist (LABA) plus an inhaled glucocorticoid or a long-acting muscarinic antagonist (LAMA) as the first choice treatment for patients with chronic obstructive pulmonary disease (COPD) who have a high risk of exacerbations. The role of treatment with a LABA–LAMA regimen in these patients is unclear.

METHODS

We conducted a 52-week, randomized, double-blind, double-dummy, noninferiority trial. Patients who had COPD with a history of at least one exacerbation during the previous year were randomly assigned to receive, by inhalation, either theLABA indacaterol (110 μg) plus the LAMA glycopyrronium (50 μg) once daily or the LABA salmeterol (50 μg) plus the inhaled glucocorticoid fluticasone (500 μg) twice daily. The primary outcome was the annual rate of all COPD exacerbations.

RESULTS

A total of 1680 patients were assigned to the indacaterol–glycopyrronium group, and 1682 to the salmeterol–fluticasone group. Indacaterol–glycopyrronium showed not only noninferiority but also superiority to salmeterol–fluticasone in reducing the annual rate of all COPD exacerbations; the rate was 11% lower in the indacaterol–glycopyrronium group than in the salmeterol–fluticasone group (3.59 vs. 4.03; rateratio, 0.89; 95% confidence interval [CI], 0.83 to 0.96; P = 0.003). The indacaterol– glycopyrronium group had a longer time to the first exacerbation than did the salmeterol–fluticasone group (71 days [95% CI, 60 to 82] vs. 51 days [95% CI, 46 to 57]; hazard ratio, 0.84 [95% CI, 0.78 to 0.91], representing a 16% lower risk; P<0.001). The annual rate of moderate or severe exacerbations was lower in the indacaterol–glycopyrronium group than in the salmeterol–fluticasone group (0.98 vs. 1.19; rate ratio, 0.83; 95% CI, 0.75 to 0.91; P<0.001), and the time to the first moderate or severe exacerbation was longer in the indacaterol–glycopyrronium group than in the salmeterol fluticasone group (hazard ratio, 0.78; 95% CI, 0.70 to 0.86; P<0.001), as was the time to the first severe exacerbation (hazard ratio, 0.81; 95% CI, 0.66to 1.00; P = 0.046). The effect of indacaterol–glycopyrronium versus salmeterol– fluticasone on the rate of COPD exacerbations was independent of the baseline blood eosinophil count. The incidence of adverse events and deaths was similar in the two groups. The incidence of pneumonia was 3.2% in the indacaterol–glycopyrronium group and 4.8% in the salmeterol–fluticasone group (P = 0.02).

CONCLUSIONS

Indacaterol–glycopyrronium was more effective than salmeterol–fluticasone in preventing COPD exacerbations in patients with a history of exacerbation during the previous year. (Funded by Novartis; FLAME ClinicalTrials.gov number, NCT01782326.)