
Comparative efficacy of indacaterol 150µg and 300µg versus fixed-dose combinations of formoterol + budesonide or salmeterol + fluticasone for the treatment of chronic obstructive pulmonary disease: a network meta-analysis

Cope S, Capkun-Niggli G, Gale R, Jardim JR, Jansen JP

CRD summary

This review concluded that indacaterol was expected to have similar effects on health status and breathlessness to salmeterol/fluticasone and similar effects on health status to formoterol/budesonide. It was also expected to be at least as good as formoterol/budesonide, and similar to salmeterol/fluticasone for lung function. These conclusions reflect the data presented and are appropriately cautious.

Authors' objectives

To compare efficacy of indacaterol (150µg and 300µg) to fixed-dose combination formoterol and budesonide and fixed-dose combination salmeterol and fluticasone for the treatment of chronic obstructive pulmonary disease.

Searching

MEDLINE and EMBASE were searched from 1989 to 2010 and full search strategies were reported in an appendix. Study documents for indacaterol studies were provided by Novartis.

Study selection

Eligible randomised controlled trials (RCTs) compared indacaterol 150µg or 300µg, fixed-dose combinations of formoterol/budesonide and salmeterol/fluticasone with each other or placebo, in adults with chronic obstructive pulmonary disease. Outcomes of interest included trough forced expiratory volume in one second (FEV₁) reported predose values at 12 weeks and six months, St. George's Respiratory Questionnaire total score at six months and transition dyspnoea index total score at six months.

All active therapies were compared with placebo and three studies directly compared indacaterol 150µg to indacaterol 300µg. No study directly compared other active treatments. The studies included patients 40 years of age or older with FEV₁/forced vital capacity of 0.70 or less and FEV₁ percent predicted less than 80% (indacaterol trials required patients to have a predicted FEV₁ 30% or above). Most studies were of patients who were current or ex-smokers with a smoking history of at least 10 years and most excluded patients with asthma or other respiratory or pulmonary diseases and other clinically significant diseases that may have affected treatment. Most studies were of predominantly Caucasian patients or reported study centres in Europe and North America.

Two reviewers independently assessed studies for inclusion.

Assessment of study quality

The authors did not state that they assessed methodological quality.

Data extraction

Data were extracted on trough FEV₁ at 12 weeks and six months, St. George's Respiratory Questionnaire total score at six months and transition dyspnoea index total score at six months. Only outcomes that were within two weeks of the time point of interest were extracted. For each outcome the difference in the change from baseline (or difference at follow-up adjusted for baseline) was extracted or calculated.

For indacaterol studies, only data from patients not using inhaled corticosteroids during the study were included.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis

Bayesian network meta-analyses were undertaken for each outcome measure and for all studies and a sub-set that excluded the three Asian studies. Summary statistics were presented for the expected absolute and relative treatment

effects, with 95% credible intervals (95% CrI). For each outcome, the probability that indacaterol was better than other treatments was also presented.

The following covariates (potential effect modifiers) were included simultaneously where possible, or in separate models where insufficient data were available: proportion of patients who were current smokers (as opposed to ex-smokers); proportion of patients with severe or very severe chronic obstructive pulmonary disease (as opposed to mild or moderate chronic obstructive pulmonary disease).

Results of the review

Eleven studies were identified from the literature search and four clinical trials of indacaterol were provided by Novartis. The total number of study participants was 10,211.

Trough FEV₁ at 12 weeks and six months:

In the analysis without covariates, all treatments were more effective than placebo. Indacaterol 150µg was associated with a greater change from baseline in FEV₁ at 12 weeks than fixed-dose combination formoterol and budesonide 9/160µg (difference in change from baseline 0.11L; 95% CrI 0.08 to 0.13) and than fixed-dose combination formoterol and budesonide 9/320µg (difference in change from baseline 0.09L; 95% CrI 0.06 to 0.11) and was comparable to fixed-dose combination salmeterol and fluticasone 50/250µg and 50/500µg. Similar results were observed for indacaterol 300µg at 12 weeks and indacaterol 150/300µg at six months. Results were not significantly altered by exclusion of the Asian studies. Adjusting for potential effect modifiers indicated that the comparison of indacaterol 150µg with fixed-dose combination formoterol and budesonide 9/320µg was sensitive to the proportion of patients with severe chronic obstructive pulmonary disease (difference became non-significant).

St. George's Respiratory Questionnaire total score at six months:

Based on the analysis of all studies without covariates, all active treatments were more effective than placebo, with the exception of fixed-dose combination formoterol and budesonide 9/160µg which included zero in the credible intervals, and indacaterol 150µg resulted in comparable improvements in St. George's Respiratory Questionnaire total score to fixed-dose combination salmeterol and fluticasone 50/500µg, fixed-dose combination formoterol and budesonide 9/160µg and formoterol/budesonide 9/320µg. Indacaterol 300µg resulted in lower scores than indacaterol 150µg, but was comparable to the alternative treatments. Excluding the Asian studies had minimal impact on the results, and no analyses adjusting for potential effect modifiers were possible.

Transition dyspnoea index total score at six months:

Based on the analysis of all studies without covariates, all active treatments were more effective than placebo. Lack of data precluded comparative estimates versus fixed-dose combination formoterol and budesonide. Indacaterol 150 and 300µg showed comparable transition dyspnoea index scores to fixed-dose combination salmeterol and fluticasone 50/250µg and fixed-dose combination salmeterol and fluticasone 50/500µg. Excluding the Asian studies produced similar results. No analyses adjusting for potential effect modifiers were possible.

Authors' conclusions

Indacaterol monotherapy was expected to be at least as good as fixed-dose combination formoterol and budesonide (9/320 and 9/160µg) and similar to fixed-dose combination salmeterol and fluticasone (50/250 and 50/500µg) in terms of lung function (trough FEV₁). Indacaterol was also expected to have similar effectiveness to fixed-dose combination formoterol and budesonide (9/320 and 9/160µg) and fixed-dose combination salmeterol and fluticasone 50/500µg for health status outcomes (St. George's Respiratory Questionnaire total) and to be similar to fixed-dose combination salmeterol and fluticasone (50/250 and 50/500µg) for breathlessness (transition dyspnoea index total).

CRD commentary

The review stated a clear objective and defined appropriate inclusion criteria. Two bibliographic databases were searched, without language restriction, for relevant studies and additional data were supplied by the industry sponsor. Study selection incorporated measures to minimise error and/or bias, but it was not clear whether similar measures were applied to the data extraction process. No assessment of the methodological quality of included studies was provided. It was therefore not possible to fully assess the reliability of the data upon which the reported meta-analyses were based.

The meta-analytic methods reported appeared robust.

The authors' conclusions reflected the data presented and were appropriately cautious.

Implications of the review for practice and research

Practice: The authors did not specify any recommendations for clinical practice.

Research: The authors did not specify any recommendations for future research.

Funding

Novartis Pharma AG.

Bibliographic details

Cope S, Capkun-Niggli G, Gale R, Jardim JR, Jansen JP. Comparative efficacy of indacaterol 150µg and 300µg versus fixed-dose combinations of formoterol + budesonide or salmeterol + fluticasone for the treatment of chronic obstructive pulmonary disease: a network meta-analysis. *International Journal of Chronic Obstructive Pulmonary Disease* 2011; 6: 329-344

PubMedID

21697997

DOI

10.2147/COPD.S18759

Original Paper URL

<http://www.dovepress.com/comparative-efficacy-of-indacaterol-150-microg-and-300-microg-versus-f-peer-reviewed-article-COPD>

Indexing Status

Subject indexing assigned by NLM

MeSH

Albuterol /administration & dosage /analogues & derivatives; Androstadienes /administration & dosage; Bronchodilator Agents /administration & dosage; Budesonide /administration & dosage; Drug Combinations; Ethanolamines /administration & dosage; Fluticasone Propionate, Salmeterol Xinafoate Drug Combination; Formoterol Fumarate; Humans; Indans /administration & dosage; Pulmonary Disease, Chronic Obstructive /drug therapy; Quinolones /administration & dosage; Randomized Controlled Trials as Topic; Treatment Outcome

AccessionNumber

12011006542

Date bibliographic record published

17/02/2012

Date abstract record published

25/05/2012

Record Status

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.