Respiratory Medicine 128 (2017) 92–101

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Efficacy and safety of indacaterol in patients with chronic obstructive pulmonary disease aged over 65 years: A pooled analysis

Pierre-Olivier Girodet, MD, PhD [a, b], Jean-Yves Jasnot, MD [c], Vincent Le Gros, MD [d], Laurent Decuypère, MD [d], Weihua Cao, PhD [e], Gilles Devouassoux, MD, PhD [f, *]

[a] Université de Bordeaux, Centre de Recherche Cardio-thoracique de Bordeaux, U1045, Département de Pharmacologie, CIC1401, F-33000 Bordeaux, France
[b] INSERM, Centre de Recherche Cardio-thoracique de Bordeaux, U1045, CIC1401, F-33000 Bordeaux, France
[c] Centre Médical Erdre-St Augustin/Clinique St Augustin, Nantes, France
[d] Novartis Pharma SAS, Rueil-Malmaison, France
[e] Novartis Pharmaceuticals Corporation, One Health Plaza, East Hanover, NJ, USA
[f] Service de Pneumologie, Hôpital de la Croix Rousse, Hospices Civils de Lyon, EA7420, Université Claude Bernard, Lyon 1, France

ARTICLE INFO

Article history:
Received 9 December 2016
Received in revised form
17 May 2017
Accepted 21 May 2017
Available online 24 May 2017

Keywords:
COPD
Elderly
Indacaterol

ABSTRACT

Background: Although the prevalence of chronic obstructive pulmonary disease (COPD) increases with age, no specific therapeutic approaches are available till date for the elderly population.
Aim: To assess the efficacy and safety of once-daily indacaterol 150 and 300 μg in elderly patients with moderate to severe COPD.
Methods: Data were pooled from 11 randomized, double-blind, placebo- and active-controlled studies (8445 patients with COPD). The patient population was stratified into age groups: young (≥40–<65 years; 52.3%), elderly (≥65–<75 years; 36.4%), and very elderly (≥75 years; 11.4%). The efficacy outcomes included improvements in trough forced expiratory volume in 1 s (FEV_1), transition dyspnea index (TDI), and health status (St. George's Respiratory Questionnaire [SGRQ]); safety was also assessed at 12 weeks.
Results: At Week 12, the mean improvement in FEV_1 with indacaterol 150 μg versus placebo was comparable in the elderly (150 mL), very elderly (160 mL), and young (170 mL) groups ($p < 0.001$ for all comparisons). Similar improvement in FEV_1 was observed with indacaterol 300 μg versus placebo in each group ($p < 0.001$). This improvement was also significantly higher with indacaterol than formoterol, salmeterol, and tiotropium in all groups ($p < 0.01$). Both TDI and SGRQ scores significantly improved with indacaterol versus placebo across age groups ($p < 0.001$) and were significantly higher than that for tiotropium ($p < 0.001$). Incidences of adverse events among indacaterol- or placebo-treated patients were similar, regardless of the age group.
Conclusions: This pooled analysis suggests that the efficacy and safety of indacaterol treatment is similar between elderly and younger patients with COPD.

© 2017 Elsevier Ltd. All rights reserved.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic progressive disorder characterized by airflow obstruction in the lungs. The incidence of COPD is higher in elderly patients [1], and was responsible for approximately 3 million deaths worldwide in 2015 [2,3]. It was ranked as the sixth leading cause of death in 1990, and is estimated to rank third worldwide by 2030 [3]. As the world population ages (16% will be > 65 years in 2050 compared with 8% in 2010) [4], the prevalence of COPD could increase.

A prospective, population-based, cohort study from the Netherlands reported that over the next 40 years, the COPD risk in a healthy 55-year-old individual would be 24% for men and 16% for women and would be higher in smokers than nonsmokers [5]. The true prevalence is likely to be even higher, because COPD is known to be highly underdiagnosed [6].

The current Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy recommends bronchodilators as the mainstay for the management of patients with COPD [7]. From stage II (moderate) COPD, regular treatment with a long-acting

* Corresponding author. Service de Pneumologie, Bâtiment I, Hôpital de la Croix Rousse, 103, Grande-Rue de la Croix-Rousse, 69317 Lyon cedex 04, France.
E-mail address: gilles.devouassoux@chu-lyon.fr (G. Devouassoux).

http://dx.doi.org/10.1016/j.rmed.2017.05.010
0954-6111/© 2017 Elsevier Ltd. All rights reserved.

Abbreviations

AE	adverse event
ANCOVA	analysis of covariance
BDI	baseline dyspnea index
bid	twice daily
BMI	body mass index
CI	confidence interval
COPD	chronic obstructive pulmonary disease
EU	European Union
FEV_1	forced expiratory volume in 1 s
FVC	forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HRQoL	health-related quality of life
ICS	inhaled corticosteroid
LABA	long-acting β_2-agonist
LOCF	last observation carried forward
LSM	least squares mean
MCID	minimum clinically important difference
MedDRA	Medical Dictionary for Regulatory Authorities
OR	odds ratio
qd	once daily
SAE	serious adverse event
SD	standard deviation
SGRQ	St. George's Respiratory Questionnaire
TDI	transition dyspnea index

bronchodilator, alone or in combination, is recommended when symptoms of dyspnea are not adequately relieved by short-acting bronchodilators or in case of exacerbations [7]. However, no specific therapeutic approaches have been developed till date for elderly patients with COPD, except for the prophylactic use of pneumococcal polysaccharide vaccine in patients aged over 65 years [6,7]. Elderly patients with COPD have more comorbidities (e.g., cardiovascular diseases) compared with a younger population [6,8].

Indacaterol is the first once-daily (qd) long-acting β_2-agonist (LABA) indicated for maintenance treatment of airflow obstruction in adult patients with COPD. However, no randomized, controlled study has assessed the efficacy and safety of indacaterol till date in elderly patients. The present pooled analysis aimed to report the efficacy and safety of indacaterol in patients with COPD aged over 65 years.

2. Methods

2.1. Study design

The efficacy and safety of indacaterol were analyzed in patients with COPD by pooling individual patient-level data from 11 Phase III/IIIb randomized, double-blinded, controlled (placebo and/or active comparator) clinical studies. Data were pooled and analyzed from 9441 patients with COPD who had the same characteristics for study inclusion and who received an indacaterol dosage of ≥75 μg for at least 12 weeks [9–19]. In the current analysis, we evaluated efficacy and safety data only for the approved doses of indacaterol (150 and 300 μg qd) versus placebo or active comparators (tiotropium 18 μg qd, formoterol 12 μg twice-daily [bid], and salmeterol 50 μg bid).

All studies completed by May 2010 were included in the present analysis. Details of each study design are summarized in Appendix Table A1 and are also provided in the individual study publications [9–19]. Two studies were excluded from the efficacy analysis: one of 12-week duration, comparing indacaterol 150 μg with salmeterol 50 μg bid, and the other of 26-week duration, comparing indacaterol 150 and 300 μg with placebo [18,19]. The reason for exclusion was that reversibility testing was done only with short-acting beta-agonists (SABA) and not with SABA and short-acting muscarinic antagonist (SAMA) like in all the other studies. Safety data from all 11 studies were analyzed.

In this analysis, patients were grouped based on their age as ≥40 to <65 years old (hereafter referred as young group), ≥65–<75 years old (hereafter referred as elderly group), and ≥75 years old (hereafter referred as very elderly group). Although all doses of indacaterol used in the studies were included in the statistical models, the efficacy and safety results are based on data for the approved 150 and 300 μg qd doses only.

2.2. Patients

Participants included in the analysis were those aged ≥40 years, with a smoking history of at least 10 pack-years and moderate to severe COPD (GOLD 2 to 3) [7], with post bronchodilator forced expiratory volume in 1 s (FEV_1) <80% and ≥30% of the predicted normal value, and post bronchodilator FEV_1/forced vital capacity (FVC) ratio <70%.

2.3. Efficacy and safety assessments

FEV_1 was analyzed if spirometric data were available at both baseline and Week 12. Baseline FEV_1 was defined as the average of the FEV_1 values recorded at the baseline visit −50 min and −15 min prior to the first dose. Trough FEV_1 at the Week 12 visit was defined as the average of the FEV_1 values recorded at 23 h 10 min and at 23 h 45 min after the previous day's dose. FEV_1 data measured within 6 h of rescue medication were excluded from this analysis, in addition to trough data outside 22–25 h after dose. A difference in trough FEV_1 of 120 mL between indacaterol and placebo was considered as the minimum clinically important difference (MCID) [9–19].

Dyspnea was assessed in terms of the transition dyspnea index (TDI) focal score [20], with a 1-unit improvement in TDI focal score regarded as the MCID [21]. Baseline dyspnea index (BDI) focal score was measured before dose on Day 1. The TDI focal score captures changes from baseline (BDI) at each visit. Health status (health-related quality of life [HRQoL]) was assessed using the St. George's Respiratory Questionnaire (SGRQ) total score, with a reduction of 4 units regarded as the MCID [22]. The baseline SGRQ total score was measured before dose on Day 1.

Adverse events (AEs) and serious adverse events (SAEs) were reported. The data cut-off was at Week 12, even if a study was of a longer duration (i.e., for a patient in a study of more than 12 weeks, any AEs that occurred at Week 13 or later were not included in the safety assessments).

2.4. Statistical analysis

The efficacy analyses were based on the full analysis set, which included all randomized patients who received at least one dose of the study drug. The change in trough FEV_1 was analyzed using a covariance model (analysis of covariance [ANCOVA]), containing

Download English Version:

https://daneshyari.com/en/article/5724972

Download Persian Version:

https://daneshyari.com/article/5724972

Daneshyari.com