Respiratory Medicine (2013) 107, 1330–1338

Available online at www.sciencedirect.com

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

Fluticasone/formoterol dry powder versus budesonide/formoterol in adults and adolescents with uncontrolled or partly controlled asthma☆

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☆ Conducted by Asthma Inhaled Research (AIR): comparing fluticasone propionate combined with formoterol versus Symbicort® — AIR Brazilian Study Group.[1]

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0954-6111/$ - see front matter
http://dx.doi.org/10.1016/j.rmed.2013.06.018

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Received 22 March 2013; accepted 23 June 2013
Available online 9 July 2013

KEYWORDS
Asthma control questionnaire;
Clinical trial;
Forced expiratory volume in 1 s;
Single inhaler;
Non-inferiority;
Morning peak expiratory flow

Summary
This 12-week study compared the efficacy and safety of a fixed combination of fluticasone propionate plus formoterol (FL/F) 250/12 μg b.i.d. administered *via* a dry powder inhaler (DPI) (Libbs Farmacêutica, Brazil) to a combination of budesonide plus formoterol (BD/F) 400/12 μg b.i.d. After a 2-week run-in period (in which all patients were treated exclusively with budesonide plus formoterol), patients aged 12—65 years of age ($N = 196$) with uncontrolled asthma were randomized into an actively-controlled, open-labeled, parallel-group, multicentre, phase III study. The primary objective was to demonstrate non-inferiority, measured by morning peak expiratory flow (mPEF).

The non-inferiority was demonstrated. A statistically significant improvement from baseline was observed in both groups in terms of lung function, asthma control, and the use of rescue medication. FL/F demonstrated a statistical superiority to BD/F in terms of lung function (FEV_1) ($p = 0.01$) and for asthma control ($p = 0.02$). Non-significant between-group differences were observed with regards to exacerbation rates and adverse events.

In uncontrolled or partly controlled asthma patients, the use of a combination of fluticasone propionate plus formoterol *via* DPI for 12-weeks was non-inferior and showed improvements in FEV_1 and asthma control when compared to a combination of budesonide plus formoterol. (Clinical Trial number: ISRCTN60408425).

Introduction

Asthma is a worldwide disease associated with a growing burden in terms of morbidity, lower quality of life, and healthcare costs [1]. The goal of therapy in asthma is to achieve and maintain clinical control by reducing the patient's exposure to factors that exacerbate asthma and by using medications for the purposes of relief and control. For patients with uncontrolled asthma treated with inhaled corticosteroids (ICS) alone, international guidelines recommend a combination of inhaled corticosteroids (ICS) and long-acting β2-agonists (LABA) [1]. The use of an ICS/LABA combination in 1 inhaler may be more effective due to convenience and ease of use by improving patient compliance and long-term control [2,3].

Fluticasone propionate is an inhaled corticosteroid with high potency in vitro [4], high topical anti-inflammatory activity [5], and a rapidly induced protective effect [6]. Fluticasone propionate has been shown to be effective in adults and children with regards to treating chronic asthma [7]. Formoterol is a LABA with a very quick onset of action [8]. It has been used as a maintenance therapy and as a relief medication in combination with an ICS [9].

The FL/F combination in a single, pressurized, metered dose inhaler has been compared with the single agent treatment of either propionate fluticasone or formoterol and with combination of either fluticasone/salmeterol or budesonide/formoterol which to the majority concluded similar efficacy and safety [10—17]. In patients with severe asthma, the combination of FL/F showed similar efficacy and similar patient tolerance [10] as compared to single agents. In patients with mild-to-moderate asthma, the FL/F combination showed superior efficacy compared to either single agent fluticasone, formoterol, or placebo [13]. FL/F in a single aerosol inhaler was also compared with fluticasone propionate plus salmeterol, resulting in similar efficacy and a faster onset of action [11]. FL/F was also compared with budesonide plus formoterol and, again, showed comparable efficacy [12].

Chronic asthma control remains suboptimal despite the continued development of improved treatments for asthma, particularly in Latin America [18,19]. The consequences of suboptimal asthma control include a poor quality of life, frequent and urgent health care visits, an increase in the risk of asthma exacerbations, and increased mortality [20]. Alternative treatment options, with different combinations and formulations, may provide more flexibility with regards to adjusting to a patient's clinical severity and device preferences. This flexibility in treatment has the potential to increase compliance and effectiveness of therapy [21,22]. The rationale behind combining fluticasone propionate and formoterol (FL/F) is to provide the benefits of a high-potency anti-inflammatory agent with the fast onset of action of a β-2 agonist in a new formulation (dry powder) using a single inhaler.

Previous studies using metered dose inhaler showed similar efficacy between FL/F and others combinations. This is the first study to evaluate the fixed combination of