



Real-world perceptions of inhaled corticosteroid/long-acting β_2 -agonist combinations in the treatment of asthma

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KEYWORDS

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Summary

Prescribing data for Europe show a shift from inhaled corticosteroids (ICSs) prescribed alone or in free combination with long-acting β_2 -agonists (LABAs) to fixed-dose single-inhaler combinations of these agents. However, existing guidelines provide little advice on selecting a specific ICS/LABA combination therapy for the treatment of asthma. European survey data indicate that the factors physicians take into account when making prescribing decisions are broadly in line with those considered to be important by experts in a Delphi process: the availability of a range of doses, the efficacy of the combination, the long-term safety and tolerability of the ICS and LABA components, the potency of the ICS and the speed of onset of the LABA. Further research is needed to help inform physician choice of ICS/LABA combinations for patients with asthma.

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Introduction

The combination of an inhaled corticosteroid (ICS) and a long-acting β_2 -agonist (LABA) is recommended by most guidelines, including those from the Global Initiative for Asthma,¹ as a treatment option for patients whose asthma is not controlled by a low-dose ICS alone.^{2,3} Several ICSs and LABAs are licensed for use as asthma therapy and four ICS/LABA combinations are available as fixed-dose treatments. Guidelines provide little advice on selecting a specific ICS/LABA combination for the treatment of asthma,¹ reflecting the lack of conclusive evidence to differentiate between available therapies.^{4,5}

In the absence of clear guidance, it is uncertain how physicians select the ICS/LABA therapy that is most appropriate for a particular patient. The aim of this article

is to provide insight into physician choice of ICS/LABA combinations, with a particular focus on a review of recent attitudinal studies that evaluated the real-world perceptions underlying these prescribing decisions.

Prescribing trends: which treatments do physicians choose?

A recent European study obtained information on the retail prescribing of ICSs (alone and in free or fixed-dose combination with LABAs) in 12 European countries (Austria, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Spain, Sweden, Switzerland and the UK) between October 2004 and September 2009.⁶ Data were collated from the MIDAS database (IMS Health, London, UK), a multinational database of sales information from wholesalers, hospitals and pharmacies in over 70 countries.

Analysis of these sales data showed that the prescription of ICSs in fixed-dose combinations increased by almost 50% over the 5-year study period, whereas the

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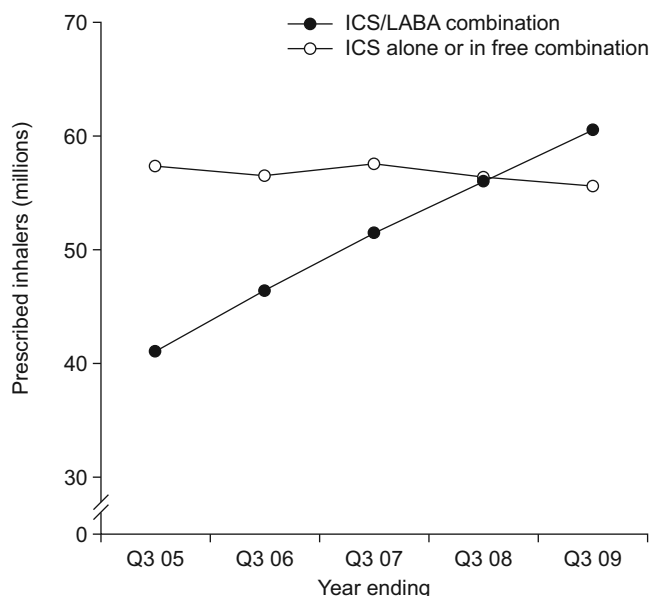


Figure 1. Retail prescribing of inhaled corticosteroids (ICSs) alone or in free combination and in fixed combination with long-acting β_2 -agonists (LABAs) for the treatment of patients with asthma in Europe, 2005–2009.⁶

prescription of ICSs as monotherapy (or in free combination) decreased slightly (Fig. 1).⁶ Beclometasone dipropionate (beclometasone) was the most commonly prescribed ICS monotherapy, accounting for 54% of ICS inhalers prescribed in the final year of the study; budesonide and fluticasone propionate (fluticasone) comprised 30% and 16% of monotherapy prescriptions, respectively.⁶ In contrast, data for ICSs prescribed as an ICS/LABA fixed-dose combination demonstrated that fluticasone was the most widely prescribed ICS in the final year of the study (59% of all fixed-dose combination inhalers prescribed). Budesonide was the second most commonly prescribed ICS (within a fixed-dose combination), accounting for 35% of inhaler sales, and beclometasone (this drug has only been available in a fixed-dose combination since 2008, despite being the oldest ICS monotherapy for asthma) was the least often prescribed ICS, accounting for just 6% of ICS/LABA inhaler sales (Fig. 2; unpublished data).

When prescription data were pooled for both ICS monotherapies and ICSs available within ICS/LABA fixed-dose combinations, they showed that fluticasone was the most widely prescribed ICS overall (accounting for 38% of all inhalers prescribed in the final year of the study), followed by budesonide (33%) and beclometasone (29%).⁶

Insight into LABA prescribing trends was gained from analysis of recent data capturing new LABA prescriptions for the treatment of respiratory disease, from January to December 2011 in France, Germany, Italy, Spain and the UK (Cegedim Strategic Data, Surrey, UK). New prescriptions were defined as those issued to patients who had not received an inhaled LABA prescription in the previous 12 months; patients who were prescribed a LABA or fixed-dose combination therapy as a replacement for an existing therapy; and patients for whom a LABA was added to their continued, original therapy. Overall, there were more than 7.44 million new

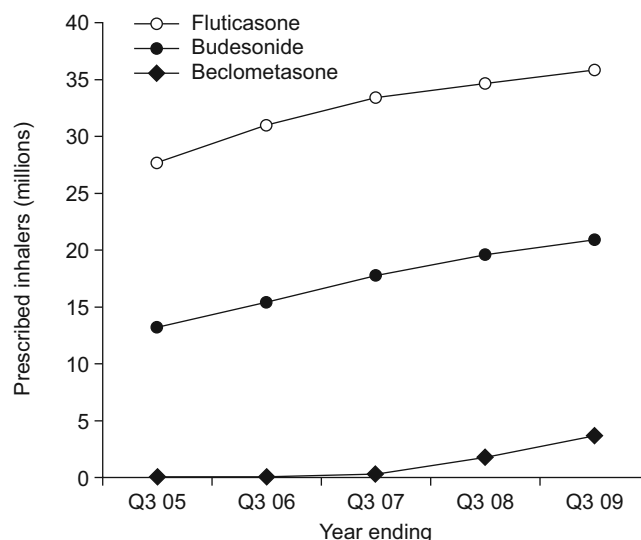


Figure 2. Retail prescribing of inhaled corticosteroids in fixed-dose combination with long-acting β_2 -agonists for the treatment of patients with asthma in Europe, 2005–2009.

prescriptions for LABAs during 2011 in these five countries, with formoterol accounting for 55% of these prescriptions, compared with 40% for salmeterol and 5% for indacaterol.⁷

A long-term study of the sales of inhalers from retail pharmacies in France, Germany, Italy, Spain and the UK for the period from Q4 2005 to Q4 2011 provides an overview of trends in device use for the treatment of respiratory disease (MIDAS database; IMS Health, London, UK). Overall, pressurized metered-dose inhalers (pMDIs) accounted for more than half of the total inhalers used in every quarter analysed, compared with use of refillable and non-refillable dry-powder inhalers (DPIs) or breath-actuated metered-dose inhalers (BA-MDIs). In the most recent quarter analysed, pMDIs accounted for 56% of inhalers used, compared with 26% for non-refillable DPIs, 15% for refillable DPIs and 3% for BA-MDIs.⁸

Prescriber attitudes: how do physicians choose an ICS/LABA combination?

Two recent attitudinal surveys explored physician attitudes and perceptions toward combinations of ICSs and LABAs for the fixed-dose combination treatment of patients with asthma.^{9,10} In the first of these studies (performed in November 2009), a group of respiratory specialists practising in the UK completed a structured online survey to evaluate the perceived effectiveness of different ICS/LABA combinations.⁹ The group of physicians was recruited via medeConnect Healthcare Insight (Abingdon, UK) from www.doctors.net.uk, which is the largest professional network of physicians in the UK. Survey respondents (n = 82) were asked to consider which combination of an ICS and a LABA they would perceive to be most effective for the treatment of asthma (whether or not the combination was commercially available as a fixed-dose therapy at the time of the survey). The most effective combination was considered to be fluticasone/formoterol (41% of the respondents, prompted answers), followed by budesonide/

Table 1

Inhaled corticosteroid (ICS)/long-acting β_2 -agonist (LABA) combinations most preferred by practising physicians in 13 European countries (n = 1007) for treating patients with asthma

ICS/LABA combination	Physicians with preference	Countries with preference ^a
Budesonide/formoterol	20%	6 (Denmark, Finland, Germany, Norway, Spain, Sweden)
Fluticasone/formoterol	15%	2 (Italy, UK)
Fluticasone/salmeterol	10%	
Ciclesonide/indacaterol	10%	
Budesonide/salmeterol	9%	1 (Austria)
Ciclesonide/formoterol	7%	1 (Netherlands)
Beclometasone/formoterol	6%	
Mometasone/indacaterol	5%	
Mometasone/formoterol	3%	
Other	15%	

^a More than one combination was equally preferred in Belgium, France and Switzerland.

formoterol (24%) and beclometasone/formoterol (20%). The most common reasons given for treatment choice were rapid onset of action (60%), high potency of ICS (39%), efficacy (15%) and experience of prescribing (13%).⁹

The second survey (performed in May and June 2010) was developed in order to obtain a wider view of the real-world attitudes and perceptions of physicians across Europe.¹⁰ The survey formed part of a European Delphi initiative (discussed in more detail below), which was recently reported by Bousquet and colleagues, on behalf of the Global Allergy and Asthma European Network.¹¹ The research set out to determine which molecules practising physicians preferred and, furthermore, the attributes that they considered to be most important when selecting an ICS/LABA combination. The survey used computer-assisted web interviews to collect information from over 1000 specialists and primary care physicians from 13 European countries (Austria, Belgium, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden, Switzerland and the UK).

In rank order, the survey results demonstrated physician preference (at least 10% of physicians) for: budesonide/formoterol, fluticasone/formoterol, fluticasone/salmeterol and ciclesonide/indacaterol (Table 1) (unpublished data). Respondents rated the improvement in patient symptoms, the potency of anti-inflammatory effect and improvement in measures of lung function as the most important factors when choosing a single-inhaler combination; rapid onset of action, sustained duration of action, a flexible dosing approach, and the safety and tolerability of the ICS and LABA were also among the attributes considered important.¹¹ In terms of the LABA component (given alone or in combination with an ICS for the maintenance treatment of asthma), formoterol (65% overall) was clearly preferred over salmeterol (33%); among the main reasons given for selecting formoterol were a rapid onset of action, long-acting effect and clinical effectiveness. Budesonide (52%) and fluticasone (25%) were the preferred ICSs (given alone or in combination with a LABA inhaler), with respondents from Sweden and Denmark showing a strong preference for

budesonide. The leading reasons for selection of budesonide included experience/familiarity with the drug (77% of physicians choosing the drug), effectiveness (61%), flexible dosing (40%) and trial evidence (34%). The main reasons for selecting fluticasone were clinical effectiveness (75%), experience/familiarity (73%), trial evidence (53%) and long-lasting action (40%). There was also a suggestion that cost may have been an important factor influencing ICS selection in countries where budesonide was the preferred ICS (unpublished data).

Expert perspective: how do experts recommend that physicians choose an ICS/LABA combination?

The attitudes of specialists and primary care physicians responsible for the routine care of patients with asthma can usefully be compared with the views of experts in the field, as demonstrated in the recent article by Bousquet and colleagues.¹¹ A Delphi process, sponsored by Mundipharma International Limited, aimed to gain the expert perspective on factors that should be considered when selecting an ICS/LABA combination for a patient with asthma.

The Delphi process is a validated technique for reaching agreement in complex areas where evidence is incomplete.¹² Anonymity, iteration and controlled feedback enable experts to refine their views in the light of the available evidence.¹² It has been used successfully to address clinically relevant issues in asthma and chronic obstructive pulmonary disease.^{13–16} Under the auspices of the Global Allergy and Asthma European Network, a Delphi process was initiated with the aim of reaching agreement on the most important criteria to consider when selecting an ICS/LABA combination therapy. Nineteen experts from seven countries (Finland, France, Germany, Italy, Spain, Sweden and the UK) took part in the process. Consensus (defined *a priori* as $\geq 66\%$ agreement) was reached on the six factors considered most important when choosing a combination therapy. The panel agreed that

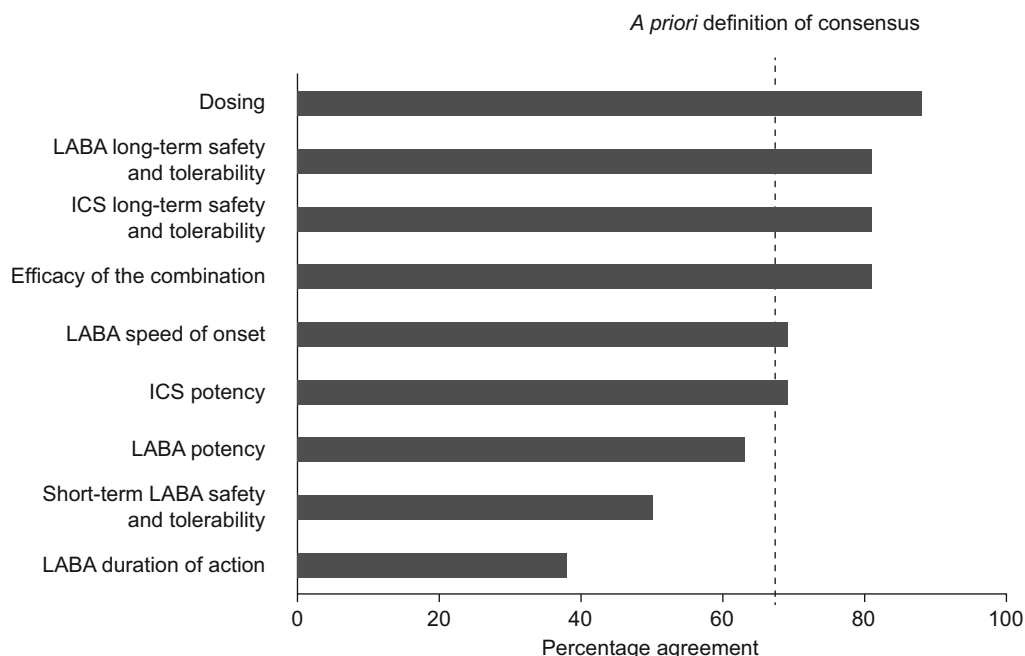


Figure 3. Results of a Delphi process (n=9) identifying the most important considerations when selecting an inhaled corticosteroid (ICS) and long-acting β_2 -agonist (LABA) for the treatment of patients with asthma.¹¹

the availability of a range of doses, the long-term safety and tolerability of both the ICS and LABA, the efficacy of the combination, the potency of the ICS and the speed of onset of the LABA (Fig. 3) were the most important considerations.¹¹

Conclusions

Several recent studies have shed light on the factors underlying physician prescribing decisions about ICS/LABA combination therapies. From an expert perspective, being able to adjust the dose to optimize efficacy (in terms of improvements in symptoms and lung function) while minimizing side effects is extremely important, with the speed of onset of bronchodilation and potency of anti-inflammatory effect being additional priorities. These views are also borne out in surveys of the wider community of respiratory physicians treating patients with asthma, with clinical experience also playing a role. Given the absence of clear guidance on the selection of a particular ICS/LABA combination, it remains important to gain further understanding of how physicians make such important decisions in clinical practice. Further research is needed to understand how physicians balance different factors when choosing which ICS/LABA combination to prescribe to an individual patient with asthma.

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Conflict of interest statement

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