

Control of asthma in adults treated with beclomethasone and formoterol in extrafine particle formulation in a real-life setting in Poland: the CASPER noninterventional, observational trial

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KEY WORDS

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formoterol
combination, extrafine
aerosol,
hydrofluoroalkanes,
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dose inhaler,

ABSTRACT

INTRODUCTION Asthma is one of the most common health problems, and its poor control can seriously affect patients' lives.

OBJECTIVES We assessed the level of asthma control in a real-life setting in Poland, in outpatients treated with a beclomethasone and formoterol combination pressurized metered-dose inhaler (BDP/F-pMDI).

PATIENTS AND METHODS The study lasted for 6 months (3 visits). Patients were aged 18 years or older, were diagnosed with asthma at least 12 months before the inclusion to the study, and had been using BDP/F-pMDI hydrofluoroalkanes (HFA) for a minimum of 2 weeks before the enrollment. Asthma control was determined in accordance with the criteria of the Global Initiative for Asthma. Patients' data were collected during study visits, using unified questionnaires with close-ended questions.

RESULTS During the first visit, 8.6% of the patients had controlled asthma; 27.6%, partly controlled asthma; and 63.9%, uncontrolled asthma. Poorer control of asthma was observed in men, smokers, patients with a longer history of asthma, higher body mass index, lower physical activity, shorter treatment with BDP/F-pMDI HFA, and inaccurate inhaler technique. After 6 months of therapy, asthma control improved in 74.2% of the patients; 60.1% of the patients met the criteria of controlled asthma; 31.4%, of partly controlled asthma; and 8.3%, of uncontrolled asthma.

CONCLUSIONS The use of BDP/F-pMDI HFA was effective in the long-term control of asthma, and one of the important factors improving treatment outcomes is the training of patients in the correct inhaler technique.

INTRODUCTION Asthma is one of the most common health problems in many countries, including Poland.^{1,2} Epidemiological data show that about 10% of the Polish population suffers from allergy, resulting in an estimated sick toll of ~4 million people,² and that asthma is the most common chronic disease in children and young adults (Juszczak G. Analysis of the health needs of working people aged 20-40 years as a forecast of changes in epidemiological structure in Poland, PhD thesis, Medical University of Warsaw, 2008; unpublished data).

Asthma is a life-long disease, which if well controlled, does not affect normal life. However, poor control may result in persistent symptoms affecting daily activity and night rest.³ As a consequence, patients with asthma are typically less efficient at school and work, have a higher rate of absence from work,⁴ and have greater difficulty retaining employment.⁵ Asthma can cause irreversible deterioration in respiratory tract efficiency, frequent exacerbations, hospitalizations, and an increased risk of premature

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TABLE 1 Assessment of asthma control according to GINA⁴

Asthma control	Asthma		
	controlled (all of the following)	partly controlled (any measure presented)	uncontrolled
daytime symptoms	none (≤ 2 /week)	> 2 /week	≥ 3 features of partly controlled asthma ^{a,b}
limitation of daily activities	none	any	
nocturnal symptoms awakening	none	any	
need for reliever/rescue treatment	none (≤ 2 /week)	> 2 /week	
lung function (PEF or FEV ₁) ^c	normal	$< 80\%$ predicted or personal best (if known)	

a Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

b By definition, an exacerbation in any week makes it an uncontrolled-asthma week.

c Without administration of bronchodilator, lung function is not a reliable test for children aged 5 years and younger.

Abbreviations: FEV₁, forced expiratory volume in 1 second; PEF, peak expiratory flow

death. Therefore, treatment of asthma aims at achieving full control of the disease,⁶ defined as no daytime symptoms or fewer than twice per week, no nocturnal symptoms, undisturbed normal life activities, normal lung function, no need for rescue treatments or their use up to twice per week, and maximum lowering of the risk of complications (caused by the disease or medication).⁷

Inhaled therapy is the primary treatment of asthma because the drug directly reaches the sites where the disease process occurs. This primary treatment is highly effective at relatively low doses that limit systemic adverse effects, but its effectiveness depends on the formulation of the delivered aerosol and on correct inhaler technique. As the result of the “Montreal Protocol on Substances that Deplete the Ozone Layer”, pressurized inhalers containing hydrofluoroalkanes (HFAs) have replaced aerosols containing chlorofluorocarbons (CFCs).⁸ The use of a propellant resulted in a beneficial change of the size and amount of particles of beclomethasone (BDP) solution delivered to the lungs. The deposition of a beclomethasone and formoterol (BDP/F) combination in a pressurized metered-dose inhaler with Modulite HFA (BDP/F-pMDI HFA) in the lung is 34% of the nominal dose in healthy volunteers; 31%, in patients with asthma; and 33%, in patients with chronic obstructive pulmonary disease.⁹⁻¹² This is an improvement in drug accessibility, resulting in a better delivery of the dose when compared with the low-percentage deposition of CFC inhalers, and even compared with more modern powder inhalers with deposition rates ranging from 17% to 28%.¹³ The mass median aerodynamic diameter, a measure of aerosol particle size (μm), is from 1.4 to 1.5 μm for the pMDI containing HFA-134a propellant, and this also ensures drug deposition in the small airways.¹⁴ The combination of beclomethasone and formoterol with the use of Modulite HFA technology is one of the three combinations of inhaled corticosteroids (ICSs) and

long-acting β_2 -agonists (LABAs) available as a single inhaler in Poland in 2010, and the only one formulated as an extrafine aerosol delivered from a new-generation pressurized inhaler. ICS/LABA combination therapy is more efficient in the control of asthma than treatments using large-particle aerosol administered in separate inhalers, despite the lower nominal daily dose of BDP.^{15,16} According to previous study results, the BDP/F-pMDI HFA proved more effective in achieving asthma control and resulted in improved quality of life.¹⁶⁻¹⁸

The objective of this noninterventional study was to assess long-term asthma control, the patient’s opinion on the pMDI and satisfaction with therapy, and safety of the extrafine aerosol formulation of the BDP/F combination in a real-life setting in Poland. The effect of training in the correct inhaler technique on asthma control in patients was also assessed.

PATIENTS AND METHODS **Study design** The CASPER study was an observational, noninterventional, prospective, multicenter trial. Outpatients, diagnosed with asthma according to routine clinical practice, were assessed in a real-life setting during 3 routine visits, scheduled every 3 months over a 6-month follow-up period. The inclusion criteria were as follows: age of 18 years or older, diagnosis of asthma established at least 12 months before enrollment, and use of BDP/F-pMDI HFA (Fostex®, Chiesi Farmaceutici, Italy) for a minimum of 2 weeks before enrollment. Only individuals meeting all criteria were eligible for the study. The choice of a therapeutic regimen was not imposed by the study protocol and was at the discretion of the treating physician. The study was conducted in the years 2010 and 2011.

Asthma control Asthma control was determined by a physician at each of the study visits based on the criteria of the Global Initiative for Asthma (GINA).⁷ The following items were assessed in the week preceding the visit: 1) frequency of

daytime symptoms; 2) limitation of activities; 3) presence of nocturnal symptoms or awakenings due to asthma; 4) frequency of the use of rescue medication; and 5) lung function expressed as peak expiratory flow (PEF) or forced expiratory volume in 1 second (FEV₁) percentage predicted. The clinical characteristics of controlled, partly controlled, and uncontrolled asthma are shown in [TABLE 1](#). Exacerbations during the previous year were also taken into consideration when categorizing the patient's status. At visits 2 and 3, patients were asked to evaluate their physical capacity and the severity and frequency of symptoms in relation to previous study visits, and define them as increased, decreased, or unchanged. The intensity of symptoms (shortness of breath and dyspnea, chest tightness, wheezing, cough) was assessed on a 4-point scale: from 0 (no symptoms) to 3 (severe limitation of daily activity). Acute asthma exacerbation was defined as the need for systemic glucocorticoids administered as rescue treatment, acute hospitalization, or any other emergency intervention.

Other variables Demographic data, including age, sex, height, weight, body mass index (BMI), educational level, smoking status, physical activity, and the duration of symptoms, were collected at visit 1. Educational level was classified as primary, secondary, incomplete university, and university. Smoking status was classified as current smoker, former smoker, or never-smoker. Based on BMI, patients were categorized as underweight (BMI <18.5 kg/m²), normal-weight (BMI, 18.5–24.9 kg/m²), overweight (BMI 25.0–29.9 kg/m²), and obese (BMI ≥30.0 kg/m²). At the same time, patients received training on the correct use of pMDI and were asked detailed questions about their opinion on and satisfaction with the use of a pMDI. Satisfaction with the inhaler device and BDP/F-pMDI HFA was recorded over subsequent study visits. A detailed assessment of the inhalation technique was performed by the physician at visits 1, 2, and 3, and any errors were highlighted and corrected.

Data regarding current asthma treatment were collected at each study visit and included the number of BDP/F-pMDI HFA doses as well as the use of any rescue therapy.

Adverse drug reactions (ADRs) were reported according to local law.

The study was conducted in accordance with the Declaration of Helsinki¹⁹ and local regulations.

Research tools Patient data were collected during routine visits, based on questionnaires filled in by the physicians. The questionnaires included demographic and anthropometric data, medical history of asthma (including asthma control, severity, and pharmacotherapy), and the assessment of the inhaler technique, patient's opinion on the inhaler, and patient's satisfaction with therapy. ADRs were recorded to assess the safety of treatment.

Statistical analysis Qualitative data were presented as percentage, and quantitative data—as mean and standard deviation or median and 95% confidence interval for the mean (95% CI). To evaluate statistical significance, the following tests were used: χ^2 test, Wilcoxon signed-rank test for dependent samples, McNemar's test for alterations in sample characteristics between the visits, analysis of variance Kruskal–Wallis tests for independent variables, and Spearman rank correlation coefficient. Adjusted odds ratios (aORs) were calculated using logistic models for binary data. The case-wise deletion of missing data was applied. For comparisons and tests of independence, the paired deletion of missing data was applied. Results with a *P* value of less than 0.05 were considered as statistically significant.

RESULTS Of 17 230 enrolled patients, 16 844 completed the study and were included in the analysis. The mean follow-up period in patients who presented at all 3 visits was 176.7 ±15.27 days.

Demographic and anthropometric characteristics of the study population Sex distribution was almost equal, and the mean age was 45.8 ±15.94 years. The majority of patients had never smoked (70.8% of women vs 55.8% of men; *P* <0.001). Sex differences were observed for the level of physical activity and mean BMI. Detailed characteristics of the patients are presented in [TABLE 2](#).

Medical history and therapy with BDP/F-pMDI HFA Asthma duration of less than 5 years was reported in 36.7% of the patients; 5 to 10 years, in 32.9% of the patients; and more than 10 years, in 30.4% of the patients. In women, the duration of asthma was slightly shorter (*P* = 0.002). The duration of asthma according to sex is presented in [TABLE 3](#). A positive family history of asthma was reported in 58.4% of the patients. The most common trigger of asthma episodes was allergy (84.6%), followed by physical exercise (46.9%) and working conditions (13.9%). These triggers were significantly more frequent in men.

The mean daily dose of BDP/F-pMDI HFA administered during the study was 315 µg.

Asthma symptoms and the level of asthma control at visit 1 The most common symptoms reported at visit 1 were cough (87.8%), breathlessness (86.2%), wheezing (79.8%), and chest tightness (74.7%). Patients also reported cough as the symptom that most frequently affected daily activity.

Daytime asthma symptoms that occurred more than twice a week during the week preceding visit 1 were reported by 79.8% of the patients, while nocturnal symptoms were reported by 58.7%. Additionally, 57.5% of the patients had to use rescue medication during the current week. Acute asthma exacerbation occurred in 18.7% of the patients.

TABLE 2 Characteristics of the study population

Parameter	Total population	Women	Men	<i>P</i> value (women vs men)
n (%)	16 844 (100)	8545 (50.7)	8299 (49.3)	–
age ^a , y	45.8 ± 15.94	45.9 ± 15.85	45.8 ± 16.07	0.649
educational level				
primary	1969 (12.4)	1016 (12.6)	953 (12.2)	0.275
secondary/vocational	7181 (45.4)	3583 (44.5)	3598 (46.2)	
incomplete university	2870 (18.1)	1471 (18.3)	1399 (18.0)	
university	3811 (24.1)	1976 (24.6)	1835 (23.6)	
smoking status				
current	3312 (19.7)	1389 (16.3)	1923 (23.2)	<0.001
former	2833 (16.8)	1097 (12.9)	1736 (21.0)	
never	10 669 (63.5)	6041 (70.8)	4628 (55.8)	
physical activity				
number of subjects	3804 (26.5)	1718 (23.5)	2086 (29.6)	<0.001
mean time, h/wk	4.0	3.7	4.3	<0.01
BMI				
BMI ^b , kg/m ²	25.98 ± 4.09	25.5 ± 4.35	26.5 ± 3.72	<0.001
underweight	193 (1.2)	159 (1.9)	34 (0.4)	
normal body mass	6821 (41.8)	4006 (48.4)	2815 (35.0)	
overweight	6887 (42.2)	2888 (35.0)	3999 (49.7)	
obesity	2412 (14.8)	1218 (14.7)	1194 (14.9)	

Data are presented as mean ± standard deviation or number (percentage of patients).

a min–max: total population, 18.1–95; women, 18–94; men, 18–95

b min–max: total population, 17.0–57.8; women, 17.0–49.9; men, 17.0–57.8

Abbreviations: BMI, body mass index

TABLE 3 Duration of asthma

Duration of asthma	Entire study population, n (%)	Women, n (%)	Men, n (%)	<i>P</i> value (women vs men)
< 5 years	5842 (36.7)	3107 (38.4)	2735 (35.0)	0.002
5–10 years	5230 (32.9)	2571 (31.7)	2659 (34.0)	
> 10 years	4840 (30.4)	2418 (29.9)	2422 (31.0)	

At visit 1, based on the GINA criteria, 63.9% of the patients had uncontrolled asthma; 27.6%, partly controlled asthma; and 8.6%, controlled asthma. The following risk factors for poor asthma control were identified: age above 40 years ($P < 0.05$), male sex ($P < 0.05$), obesity ($P < 0.001$), long history of the disease ($P < 0.001$), current smoking ($P < 0.05$), treatment with BDP/F-pMDI HFA for less than 1 month ($P < 0.001$), and improper use of the inhaler ($P < 0.001$) (FIGURE 1).

Changes in the frequency and severity of asthma symptoms and in asthma control during the follow-up period Asthma control as well as the frequency and severity of asthma symptoms observed in patients improved during the study. At visits 2 and 3, a decrease in the proportion of patients who reported coughing was reported. Similar trends were observed for other asthma symptoms such

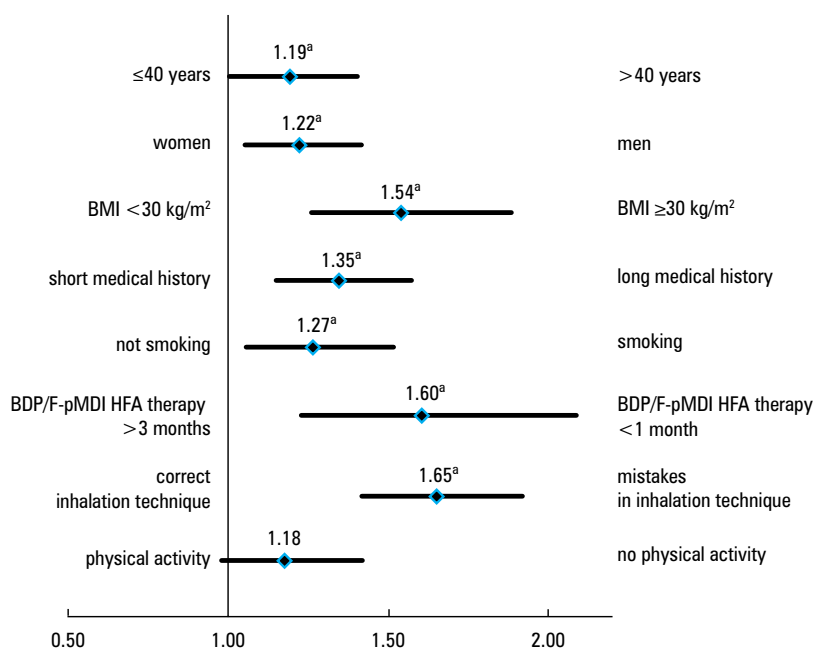
as the frequency of breathlessness, wheezing, and chest tightness. Compared with visit 1 (56.4% of the patients), only 7.6% of the patients at visit 2 and 8.1% of the patients at visit 3 reported coughing as a symptom limiting their daily activities. Breathlessness (52.3% of the patients at visit 1) was a symptom that impaired normal life in 17.0% of the patients at visit 2 and 8.0% of the patients at visit 3. A similar tendency was observed for other symptoms including wheezing and chest tightness.

The percentage of patients with any daytime asthma symptoms occurring more often than twice a week decreased during the study (visit 1; 79.8% of the patients; visit 2, 42.3% of patients; visit 3, 20.1% of patients; $P < 0.001$). The same trend was observed for any nocturnal asthma symptoms, reported by 58.7% of the patients at visit 1, 23.2% of the patients at visit 2, and 9.4% of the patients at visit 3 ($P < 0.001$).

FIGURE 1 Risk factors for poorer asthma control at visit 1

a statistically significant results ($P < 0.05$)

Abbreviations: BDP/F-pMDI HFA, beclomethasone and formoterol combination in a pressurized metered-dose inhaler with Modulite hydrofluoroalkanes; others, see [TABLE 2](#)



At visit 1, 57.5% of the patients used rescue treatment more than twice in the preceding week, compared with 20.8% and 8.2% of the patients at visits 2 and 3, respectively.

The percentage of patients reporting limited daily activities and reduced lung function decreased during the study.

Improvement of asthma control Improvement of asthma control, as compared with visit 1, was reported in 59.5% of the patients at visit 2 and 74.2% of the patients at visit 3 ([FIGURE 2](#)). At visit 2, the control of asthma, according to the GINA

criteria, was achieved in 35.5% of the patients, and at visit 3, the percentage increased to 60.1%. Uncontrolled asthma was reported in 22.4% and 8.3% of the patients at visits 2 and 3, respectively. Changes in asthma control during the study are presented in detail in [FIGURE 3](#).

Improvement in asthma control at visits 2 and 3 was positively associated with the proper inhaler technique (aOR, 1.48; 95% CI, 1.25–1.74; $P < 0.001$; and aOR, 1.66; 95% CI, 1.26–2.18; $P < 0.001$; respectively), age of less than 40 years (aOR, 1.25; 95% CI, 1.04–1.49; $P < 0.05$; and aOR, 1.41; 95% CI, 1.11–1.80; $P < 0.05$; respectively), and

FIGURE 2

Improvement of asthma control at visits 2 and 3 as defined by changes in the level of asthma control by the Global Initiative for Asthma

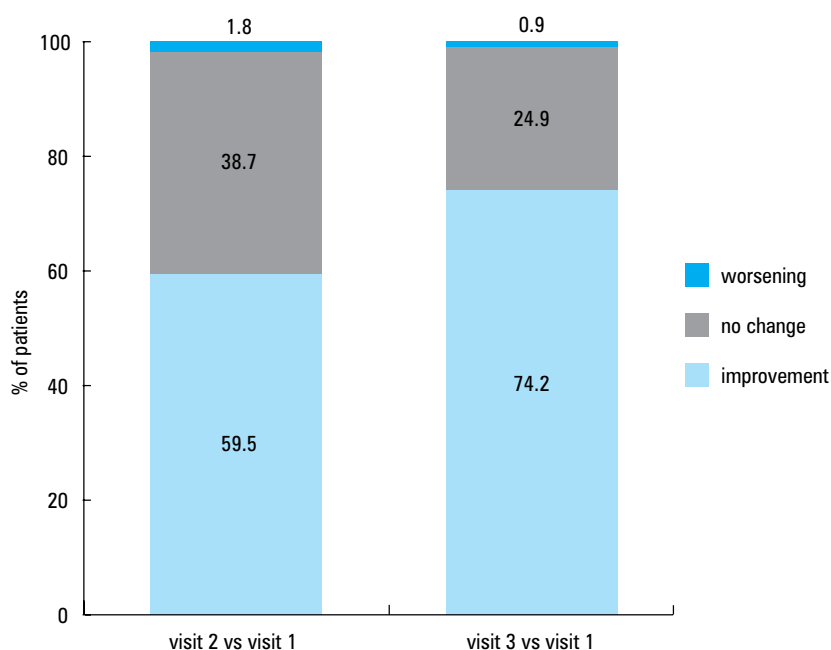
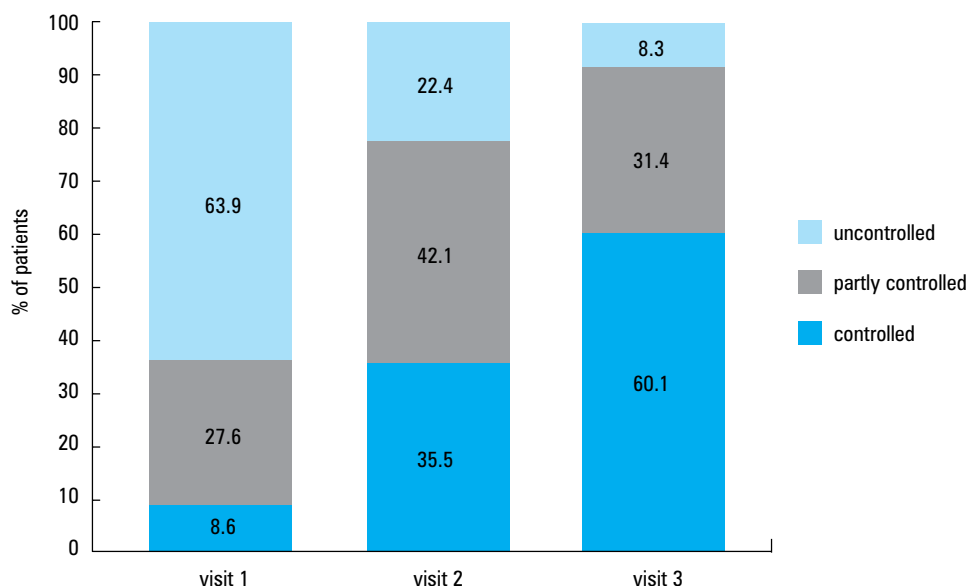


FIGURE 3 Asthma control over subsequent study visits, $P < 0.001$



a history of asthma of less than 5 years (aOR, 1.43; 95% CI, 1.21–1.69; $P < 0.001$; and aOR, 1.43; 95% CI, 1.21–1.69; $P < 0.001$; respectively).

Changes in BDP/F-pMDI HFA dosing during the follow-up period The proportion of patients treated with a lower dose of BDP/F-pMDI HFA as basic treatment (1 inhalation twice daily) decreased between visits 1 and 2 and increased between visits 2 and 3. The opposite trend was observed with higher doses (2 inhalations twice daily): the percentage of patients using higher doses increased and then decreased. The mean daily dose of BDP/F-pMDI HFA increased from $315 \pm 98.16 \mu\text{g}$ at visit 1 to $380 \pm 127.80 \mu\text{g}$ at visit 2 and then dropped to $290 \pm 101.15 \mu\text{g}$ at visit 3.

Dose changes were driven by the frequency and severity of asthma symptoms, exacerbation, and level of asthma control as assessed by the physician. In the event of poor asthma control during the period preceding the visit, the physician increased the dose of the drug. Conversely, in the event of achieving asthma control, the daily dose was lowered by the physician. It is worth noting that BDP/F-pMDI HFA at that time was not approved as a single inhaler maintenance and rescue therapy (so called SMART).

Evaluation of the proper inhaler technique and training sessions An improper inhaler technique, reported in 26.4% of the patients at visit 1, decreased to 9.7% at visit 2 and to 5.7% at visit 3. The most common error at visit 1 was not holding the breath for as long as possible, and the most common critical error was the lack of deep and slow breathing in through the mouth with simultaneous pushing of the upper side of the inhaler to release a single spray of the medication (TABLE 4).

Patient perception of the use of pressurized metered-dose inhaler and patient satisfaction with treatment At visits 2 and 3, the majority of patients reported that the frequency of their asthma symptoms had decreased since the last visit (86.1% and 77.1% of the respondents, respectively).

The self-reported severity of symptoms decreased in 85.3% and 75.9% of the patients at visits 2 and 3, respectively. Similarly, exercise efficiency was reported to improve in 81.3% of the patients at visit 2, and in 77.2% of the patients at visit 3. The proportion of patients who reported deterioration of disease symptoms was approximately 2%. During visit 3, 96.8% of the patients reported that the pressurized inhaler used for BDP/F-pMDI HFA dosing is a durable device; 98.3% of the patients declared that they can rely on it; 98.6% were satisfied with the use of inhaler; and 98.4% were satisfied with the effectiveness of the drug delivered by the inhaler. A total of 98.2% of the patients declared willingness to continue the treatment.

Adverse drug reactions During the study, 525 ADRs were reported in 422 patients (3.2% of the study population). In 27 patients (0.2%), ADRs were classified as related to the use of BDP/F-pMDI HFA. All the reported symptoms were considered as expected and were listed in the summary of product characteristics of Fostex®.

DISCUSSION Our results clearly demonstrate that the long-term use of BDP/F-pMDI HFA is associated with improved asthma control and a low number of side effects. An improvement in asthma control over the 6-month period was observed in the majority of patients, and there was a greater than 4-fold increase in the proportion of patients with full asthma control according to the GINA criteria. We also noted an overall improvement in the inhalation technique

TABLE 4 Changes in the frequency of errors in the inhalation technique during the study

Errors	Visit 1	Visit 2	Visit 3	Change (% points)	
	patients, n (%)	patients, n (%)	patients, n (%)	visit 1 vs visit 2	visit 2 vs visit 3
protective cup not removed from the mouthpiece prior to inhalation ^a	293 (1.8)	137 (0.9)	201 (1.3)	1.1 ^c	0.6 ^b
no slow, deep breath out, away from the inhaler, before inhalation	1953 (12.1)	448 (2.9)	291 (1.9)	9.6 ^c	10.5 ^c
inhaler container not held upright, with the holder facing up	872 (5.4)	274 (1.8)	255 (1.7)	3.9 ^c	NS
mouthpiece not placed between the lips ^a	699 (4.3)	299 (1.9)	303 (2.0)	2.3 ^c	NS
no deep and slow breathing in by the mouth with simultaneous pushing of the upper side of inhaler, to release a single spray of the medication ^a	1344 (8.3)	333 (2.2)	313 (2.0)	6.3 ^c	NS
breath not held as long as possible	2252 (13.9)	654 (4.2)	404 (2.6)	9.9 ^c	11.4 ^c
inhaler not removed from the mouth and no slow breathing out away from the inhaler	1967 (12.2)	791 (5.1)	559 (3.6)	7.3 ^c	8.7 ^c

a critical errors;**b** $P < 0.05$ (McNemar's test);**c** $P < 0.0001$ (McNemar's test)

during the study, and a substantial decrease in the proportion of patients mishandling their inhaler device. The latter finding is particularly important because our study showed that asthma control was affected by errors in the inhalation technique. The proper use of the inhaler is definitely a modifiable factor, which means that effective patient education and training may improve treatment effects.

Our findings are consistent with those of other studies. In a 1-year follow-up of a group of 1017 Italian patients with uncontrolled or partly controlled asthma performed in real-life conditions, the use of an extrafine BDP/F-pMDI HFA combination was associated with considerably better asthma control and improved quality of life as compared with non-extrafine fixed-dose ICS/LABA combinations with a mean daily dose of steroids 2-fold lower for extrafine BDP/F (BDP, 318 µg) compared with either budesonide and formoterol combination (BUD/F; BUD, 651 µg) or fluticasone and salmeterol combination (FP/S; FP, 750 µg).¹⁸ This beneficial effect can be due to the extrafine drug formulation, which is characterized by better deposition in the small airways, more equal distribution throughout the bronchial tree, and is less influenced by an improper inhalation technique.²⁰ Similar results were demonstrated by Muller et al,¹⁶ who compared extrafine BDP/F pMDI and dry-powder inhaler formulated with large particles in a real-life setting. In this study, patients treated with BDP/F, when compared with those treated with BUD/F or FP/S, achieved better asthma control on a significantly lower mean daily dose of ICS (321 µg, compared with 715 µg and 720 µg, respectively). Barnes et al²¹ evaluated the effectiveness of BDP-HFA versus BDP-CFC over 1 year and found that patients who received BDP-HFA were more likely

to achieve asthma control than those receiving BDP-CFC. In addition, BDP-HFA was prescribed at a median dose which was half that of BDP-CFC.

Another interesting real-life study was performed by Popov et al.²² In their study, patients with uncontrolled asthma treated with ICS/LABA fixed combination in a DPI (FP/S, 250/50 µg twice daily and BUD/F, 160/4.5 µg, 2 inhalations twice daily) were switched to BDP/F HFA (100/6 µg, 2 inhalations twice daily). After 8 weeks of treatment, significant improvements in symptoms and quality of life were observed. Patients with the best therapeutic response also demonstrated a significant decrease in some indicators of airway/systemic inflammation. These findings suggest that extrafine drug formulations of ICSs may give some extra effect owing to the ability to reach small airways in patients with uncontrolled asthma previously treated with ICS DPI.²² A favorable effect on the control of asthma in patients treated with extrafine drug formulations of ICSs versus nonextrafine formulations was also demonstrated in several randomized controlled trials.²³⁻²⁵

In the present study, BDP/F-pMDI HFA was shown to have a good safety profile. The frequency of ADRs observed in the study was similar to the occurrence of ADRs related to ciclesonide (another ICS in a prodrug formulation) in routine medical care.²⁶ The safety profile was also investigated in head-to-head randomized controlled trials comparing BDP/F with BUD/F²⁷ and with FP/S.²⁸ No significant difference was found between the groups in the proportion of patients with adverse events and ADRs; no serious adverse effects were observed for the total study period; and no patient had to discontinue the study because of adverse effects. No changes in heart rate and systolic blood pressure

were observed in the BDP/F (400/24 µg) and FP/S (500/100 µg) groups. In the second study, when comparing BDP/F (400/24 µg) and BUD/F (800/24 µg), no significant differences were observed between the treatment groups. Adverse effects were reported by 15 patients (13.8%) in the BDP/F group and 18 in the BUD/F group (16.5%) (nonsignificant), but none were classified as serious. Thus, it seems that the safety profile for each combination at the above doses is comparable.^{27,28}

Smoking was identified as one of the risk factors for poor asthma control. Nevertheless, it is worth noting that the use of extrafine inhaled drug formulations is associated with a better control of asthma and improved pulmonary function independently of the smoking status.²⁹ This can be explained by the finding that the interaction between drug particles and tobacco smoke occurs during the first few seconds after drug inhalation, and these few seconds are critical for drug resistance.³⁰ In other words, it may be interpreted that patients who administer extrafine BDP/F-pMDI HFA in the air free of tobacco smoke may experience treatment benefits to the same extent as nonsmokers, independently from their overall smoking status.

Although a long history of asthma was found to be a risk factor for worsened disease control at the beginning of BDP/F-pMDI HFA treatment, it did not weaken the overall drug response. This and other previously described findings can also be explained by a considerable improvement in patients' inhaler technique, as observed in our study. As shown by Melani et al,³¹ mishandling of the inhaler device severely affects therapeutic outcomes in asthmatic patients.³¹ The authors list advanced age, low educational level, and the lack of adequate instructions on the inhaler technique as being among the most important factors contributing to an incorrect use of the inhaler device. The results of our study seem to confirm that the proper education of patients, provision of training, and routine assessment of the inhaler technique are critical modifiable factors that can minimize the misuse of the inhaler device. The importance of the instructions provided by caregivers was also emphasized by the majority of our study patients. A positive effect of patient education and training in the inhalation technique and compliance with therapy was demonstrated in a meta-analysis by Cochrane et al.³²

Despite the findings of the present study, some researchers suggested that the clinical outcomes of treatment with a pMDI delivering extrafine particles is less dependent on the inhaler technique than large-particle drug combinations. This can be explained by the fact that lung deposition of extrafine BDP/F is to a lower degree influenced by the inhalation flow and hand-mouth coordination.^{33,34}

The majority of patients in our study were satisfied with their pMDI and considered it reliable.

This is of particular importance because patient satisfaction with therapy correlates with patient compliance and asthma control. The results of a real-life observational study by Small et al³⁵ demonstrated that improved clinical and patient-reported outcomes such as the quality of life, exacerbations, or sleep disturbances due to asthma symptoms are closely associated with the level of satisfaction with the inhaler device. A number of other factors should also be taken into account when choosing the inhaler device, including clinical condition, financial burden, and availability of the drug in a particular device. It is worth noting that if adequately adjusted to an individual patient's capabilities and preferences, available inhaler devices show no clinically important differences in therapeutic outcomes.^{36,37}

Finally, we should highlight the fact that our results obtained in a real-life observational study reflect daily clinical practice and not treatment patterns as approved by regulatory authorities. Even though the BDP/F-pMDI HFA should be used as maintenance therapy, the changes in doses observed in our study suggest that it has been prescribed both as a maintenance and rescue treatment. The dose changes were driven by the level of asthma control according to the GINA criteria and drug characteristics, that is, by the frequency and severity of asthma symptoms, exacerbations, and level of asthma control assessed by the physician, meaning an increase of the dose in the event of poor asthma control and a decrease of the dose when asthma was well controlled. The strength of observational studies lies in the fact that they provide insight into real-life treatment patterns and drug use, and our findings should be viewed in this light.

Study limitations When interpreting the results of the CASPER study, certain limitations inherent to the observational study design must be acknowledged. Owing to the potential effect of bias or unrecognized confounding factors, it is difficult to make firm conclusions regarding causality, and the outcomes should be analyzed with caution. However, the larger sample size as well as representativeness and the diversity of patients observed in real-life conditions allow wider applicability of the collected data to the general population.

In conclusion, BDP/F-pMDI HFA is effective in the long-term control of asthma and has a good safety profile. The results of our study also indicate that patient education related to an accurate inhaler technique is a potent tool, which considerably improves treatment outcomes.

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Kontrola astmy w warunkach codziennej praktyki w Polsce u dorosłych leczonych beklometazonem i formoterolem podawanym w aerozolu superdrobnocząsteczkowym – nieinterwencyjne obserwacyjne badanie CASPER

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SŁOWA KLUCZOWE

aerozol superdrobno-
cząsteczkowy,
beklometazon
i formoterol – lek
złożony, inhalator
ciśnieniowy dozujący,
hydrofluoroalkany,
kontrola astmy

STRESZCZENIE

WPROWADZENIE Astma to jeden z najbardziej powszechnych problemów zdrowotnych, a słaby poziom jej kontroli może znacząco wpływać na życie pacjentów.

CELE Oceniano stopień kontroli astmy w warunkach codziennej praktyki w Polsce u pacjentów ambulatoryjnych leczonych beklometazonem/formoterolem w ciśnieniowym inhalatorze dozującym (BDP/F-pMDI).

PACJENCI I METODY Badanie trwało 6 miesięcy (3 wizyty). Pacjenci byli w wieku ≥ 18 lat, astmę zdiagnozowano u nich ≥ 12 miesięcy przed włączeniem do badania i stosowali BDP/F-pMDI z nośnikiem hydrofluoroalkanowym (HFA) przez minimum 2 tygodnie przed rozpoczęciem badania. Poziom kontroli astmy został określony zgodnie z wytycznymi Global Initiative for Asthma. Dane dotyczące pacjentów zbierano podczas wizyt za pomocą zunifikowanych kwestionariuszy zawierających pytania zamknięte.

WYNIKI Podczas pierwszej wizyty u 8,6% pacjentów stwierdzono astmę kontrolowaną, u 27,6% – częściowo kontrolowaną, a u 63,9% – niekontrolowaną. Gorszy stopień kontroli astmy stwierdzono u mężczyzn, palaczy, osób dłużej chorujących, z większym BMI, mniejszą aktywnością fizyczną, krótszym czasem stosowania BDP/F-pMDI HFA i niewłaściwą techniką inhalacji. Po 6 miesiącach leczenia stopień kontroli astmy poprawił się u 74,2% badanych, u 60,1% pacjentów stwierdzono astmę kontrolowaną, u 31,4% – częściowo kontrolowaną, a u 8,3% – niekontrolowaną.

WNIOSKI Stosowanie BDP/F-pMDI HFA było skuteczne w zapewnieniu długoterminowej kontroli astmy, a jednym z ważnych czynników wpływających na polepszenie wyników leczenia jest nauczanie pacjentów odpowiedniej techniki inhalacji.

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