

# Budesonide Inhalation Suspension in Adults With Poorly Controlled Asthma or Chronic Obstructive Pulmonary Disease

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## **ABSTRACT**

Inhaled corticosteroids (ICSs) are recommended as first-line therapy for patients with persistent asthma and as adjunctive therapy in patients with chronic obstructive pulmonary disease (COPD) who experience exacerbations. Administration of nebulized budesonide inhalation suspension (BIS) may be an appropriate alternative in certain patients with asthma or COPD that are uncontrolled with ICS delivery via dry powder inhaler (DPI) or pressurized metered-dose inhaler (MDI). In the U.S.A., BIS is approved for children aged 12 months to 8 years with asthma. In many other countries BIS also is approved for use in adults. In this case series, 12 patients with poorly controlled

asthma aged 31 - 72 years and 13 patients with poorly controlled COPD aged 54 - 84 years were initiated on ICS therapy with nebulized BIS or transitioned from their usual ICS treatment to nebulized BIS and observed for  $\geq 1$  year. Changes in the number of exacerbations requiring oral corticosteroids and forced expiratory volume in 1 second ( $FEV_1$ ) from the previous year (during which patients received their usual asthma or COPD therapy) to the following year (during which patients received nebulized BIS) were assessed. The number of exacerbations requiring oral corticosteroids decreased by an average of 3.6 exacerbations in patients with asthma and by an average of 2.5 exacerbations in patients with COPD during BIS treatment compared with the previous year. Clinical improvements in  $FEV_1$  occurred in 58% of these patients with long-standing disease. Reported improvements in asthma control and pulmonary function suggest that BIS

administered via a nebulizer may be a treatment option for adults with asthma or COPD that remains suboptimally controlled on ICS-based therapy administered via DPI or MDI.

## INTRODUCTION

Inhaled corticosteroids (ICSs) are the most effective controller therapy available for patients with persistent asthma.<sup>1</sup> As such, daily ICS use is recommended for all patients with persistent asthma, regardless of severity.<sup>1</sup> For patients with chronic obstructive pulmonary disease (COPD), the addition of a daily ICS to inhaled long-acting bronchodilator therapy is recommended to reduce exacerbations and improve health status in patients with stage III to stage IV disease and a history of repeat exacerbations.<sup>2</sup>

For adult patients with asthma or COPD, important considerations in choosing an inhalation device include patient age, patient ability to use the device correctly, availability of medication(s) in a given device (eg, nebulized formulation), cost, and reimbursement.<sup>3</sup> Because patient satisfaction may improve adherence with therapy, patient preference also should be considered.<sup>4</sup>

Aerosol therapy generally is administered via a metered-dose inhaler (MDI) or dry powder inhaler (DPI); however, these devices may be a suboptimal method of inhaled drug delivery for some adult patients. Among patients with asthma or COPD, inhaler technique often is poor.<sup>5,6</sup> Poor technique can decrease drug deposition in the lungs<sup>7</sup> and lead to asthma instability.<sup>8</sup> Studies in adult patients show that the incorrect use of DPIs and MDIs increases with age.<sup>5,8,9</sup> For some elderly patients, reduced hand strength<sup>10</sup> or subclinical cognitive impairment or dyspraxia<sup>11</sup> may make proper use of an inhaler difficult, despite adequate instruction and repeated demonstration.

Administration of ICS therapy via

nebulization provides a delivery system that is effective with normal breathing and requires less manual dexterity than traditional handheld inhalers. In the U.S.A., nebulized budesonide inhalation suspension (BIS) is approved for children aged 12 months to 8 years with asthma. In many countries outside of the U.S.A., BIS also is approved for use in adults.<sup>12</sup> A review of the few nebulized ICS studies suggested that use of BIS in adults is an effective treatment option for asthma or COPD.<sup>12</sup> However, these studies were conducted in limited patient populations. Early studies in adults included only patients with severe oral corticosteroid-dependent persistent asthma and showed that addition of treatment with nebulized BIS (2 - 8 mg/day) enabled oral corticosteroid treatment to be reduced or discontinued.<sup>13,14,15</sup> A study showing that BIS was effective in adults with noncorticosteroid-dependent moderately severe asthma uncontrolled on ICS therapy included only 26 patients.<sup>16</sup> A large (N=758) 12-week, randomized U.S.A. study was conducted to establish the efficacy of BIS in patients aged  $\geq 12$  years with moderate to severe persistent asthma previously receiving ICSs via DPI or MDI. No difference in predose forced expiratory volume in 1 second ( $FEV_1$ ), the primary end point, was demonstrated between BIS 2 mg twice daily and BIS 0.5 mg once daily, which may have several explanations. One possible reason is that the patients' asthma severity based on prestudy ICS dose was overestimated, resulting in the inclusion of patients with mild asthma who would have been controlled with lower doses of ICS. Therefore, definitive conclusions regarding the efficacy of BIS in U.S.A. adults could not be drawn from this study.<sup>17</sup> The study, however, did not include a placebo comparator. An alternate conclusion may have been that using BIS did not improve outcomes

among patients previously receiving traditional ICS therapy. Finally, studies suggest that BIS is effective for treating an acute exacerbation of COPD,<sup>18,19</sup> but studies of daily use for COPD are lacking.

To describe the effectiveness of daily BIS therapy in a usual practice setting, I report exacerbation rates and pulmonary function outcomes for 25 adult patients with poorly controlled asthma or COPD who were initiated on BIS or transitioned from traditional ICS therapy administered via DPI or MDI to nebulized BIS. The rationale for the initiation of nebulized BIS, or the transition from other ICSs to nebulized BIS, varied based on individual patient characteristics.

## METHODS

The medical charts for 25 consecutive adult patients with asthma or COPD who were initiated on ICS therapy with BIS (Pulmicort Respules<sup>®</sup>; AstraZeneca LP, Wilmington, DE) or transitioned from ICS therapy delivered via MDI or DPI to nebulized BIS were reviewed retrospectively. On discontinuation of any previous ICS therapy, all patients received BIS 0.5 mg administered twice daily via a jet nebulizer. Jet nebulizer/compressor systems varied among patients, with most patients using the same system that they used for as-needed administration of bronchodilators. BIS doses were not stepped up or stepped down after initiation of therapy but remained the same throughout a 1-year observation period. In some patients, changes in the dosage form of concomitant asthma or COPD therapies were made at the time of the transition to BIS. Controller medications were prescribed per labeled dosages, and rescue bronchodilator therapy was used as needed. The primary outcome was the number of exacerbations requiring the use of oral corticosteroids during the 1-

year period after the initiation of BIS or transition to BIS compared with the number during the year before the transition. Pulmonary function based on FEV<sub>1</sub> was assessed before and 3 months after initiation of BIS treatment.

## RESULTS

Patients ranged in age from 31 to 84 years (mean age, 65 years) with a similar percentage diagnosed with asthma and COPD (Table 1). More female patients (n=18) than male patients (n=7) were included. Nineteen patients were initiated on BIS or transitioned to BIS as part of their treatment regimen because of a failure of their previous therapy (Table 2) to control frequent exacerbations despite adherence checks and repeated instruction on ICS inhaler use. All 12 asthma patients previously were receiving ICS plus adjunctive therapy at step 3 or higher based on the 2002 U.S.A. asthma guidelines that were in place at the time therapy was initiated.<sup>20</sup> Four of the 12 asthma patients received omalizumab (Xolair<sup>®</sup>; Genentech Inc, South San Francisco, CA) for  $\geq 3$  months before the transition to BIS but continued to experience frequent asthma symptoms. Six patients, all with COPD, were transitioned (n=4) or initiated (n=2) on BIS because they had no prescription coverage and because Medicare at that time did not have a medication benefit option to cover ICS MDI or DPI formulations. One of these patients had a tracheotomy and was unable to use any other method of ICS delivery.

During treatment with BIS, patients used as-needed rescue bronchodilator medications, including short-acting  $\beta_2$ -adrenergic agonists (SABAs) and anticholinergics, and additive controllers, including leukotriene modifiers and long-acting  $\beta_2$ -adrenergic agonists (LABAs) (Table 2). At the time that these patients were initiated on or transitioned to BIS, LABAs were not avail-

**Table 1. Patient characteristics.**

Patient	Age (years)	FEV <sub>1</sub> (% predicted)	Comorbidities	Reason for Switch to BIS
With asthma				
1	64	64	—	Frequent exacerbations
2	54	20	Sjögren's syndrome	Frequent exacerbations
3	72	54	Coronary artery disease	Frequent exacerbations
4	46	63	Allergic rhinitis	Frequent exacerbations
5	57	67	Nasal polyps	Frequent exacerbations
6	65	42	Hypertension, osteoporosis	Frequent exacerbations
7	62	63	—	Frequent exacerbations
8	45	21	Pulmonary hypertension	Frequent exacerbations
9	58	38	Hypertension	Frequent exacerbations
10	52	46	—	Frequent exacerbations
11	31	55	—	Frequent exacerbations
12	58	77	Colon cancer	Frequent exacerbations
With COPD				
13	76	35	Sleep apnea	Frequent exacerbations
14	67	36	Diabetes mellitus, coronary artery disease	Frequent exacerbations
15	74	40	Hypertension, atrial fibrillation	Frequent exacerbations
16	77	44	Hypertension	Insurance
17	83	65	—	Insurance
18	82	80	Polymyalgia rheumatica	Frequent exacerbations
19	83	24	Prostate cancer	Frequent exacerbations
20	79	70	Coronary artery disease	Frequent exacerbations
21	63	18	Hypertension	Insurance
22	84	83	Hypertension	Insurance
23	54	61	Hypertension	Frequent exacerbations
24	72	50	Rheumatoid arthritis	Insurance
25	77	—	Laryngeal cancer	Insurance, tracheotomy

BIS=budesonide inhalation suspension; COPD=chronic obstructive pulmonary disease; FEV<sub>1</sub>=forced expiratory volume in 1 second.

**Table 2.** Medications before and during BIS\* treatment for patients with asthma and COPD.

Patient	Before		During	
	Daily	As-needed	Daily	As-needed
Asthma				
1	Fluticasone HFA 110 µg MDI Montelukast, omalizumab	Albuterol MDI	BIS 0.5 mg/2 mL Montelukast, omalizumab	Albuterol MDI
2	Fluticasone/salmeterol 250/50 µg DPI	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI	Levalbuterol inhalation solution
3	Budesonide 200 µg DPI Formoterol DPI, omalizumab	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Formoterol DPI, omalizumab	Levalbuterol inhalation solution
4	Budesonide 200 µg DPI Formoterol DPI, montelukast, omalizumab	Albuterol MDI	BIS 0.5 mg/2 mL Formoterol DPI, montelukast, omalizumab	Albuterol MDI
5	Beclomethasone 80 µg MDI Salmeterol DPI, montelukast	Albuterol MDI	BIS 0.5 mg/2 mL Salmeterol DPI, montelukast	Albuterol MDI
6	Fluticasone HFA 220 µg MDI Methylprednisolone 4 mg daily, salmeterol DPI, montelukast	Albuterol MDI	BIS 0.5 mg/2 mL Methylprednisolone 4 mg daily, salmeterol DPI, montelukast	Albuterol MDI
7	Fluticasone HFA 220 µg MDI Montelukast	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Montelukast	Levalbuterol inhalation solution
8	Budesonide 200 µg DPI Formoterol DPI, theophylline	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Formoterol DPI, theophylline	Levalbuterol inhalation solution
9	Budesonide 200 µg DPI Formoterol DPI, omalizumab	Albuterol MDI	BIS 0.5 mg/2 mL Formoterol DPI, omalizumab	Albuterol MDI
10	Fluticasone/salmeterol 250/50 µg DPI Montelukast	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI, montelukast	Levalbuterol inhalation solution
11	Fluticasone/salmeterol 500/50 µg DPI Zafirlukast	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI, zafirlukast	Levalbuterol inhalation solution
12	Budesonide 200 µg DPI Methylprednisolone 4 mg daily, formoterol DPI, Zafirlukast	Albuterol MDI	BIS 0.5 mg/2 mL Methylprednisolone 4 mg daily, salmeterol DPI, † zafirlukast	Albuterol MDI

COPD				
13	Fluticasone/salmeterol 250/50 µg DPI Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Ipratropium 0.5 mg/ albuterol 2.5 mg inhalation solution	BIS 0.5 mg/2 mL Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Ipratropium 0.5 mg/ albuterol 2.5 mg inhalation solution
14	Fluticasone/salmeterol 250/50 µg DPI Tiotropium DPI	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Levalbuterol HCl inhalation solution, † tiotropium DPI	Levalbuterol inhalation solution
15	Fluticasone/salmeterol 250/50 µg DPI Ipratropium MDI, theophylline	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI, tiotropium DPI, theophylline	Levalbuterol inhalation solution
16	Budesonide 200 µg DPI Formoterol DPI, tiotropium DPI	Albuterol 2.5 mg inhalation solution	BIS 0.5 mg/2 mL Formoterol DPI, tiotropium DPI	Albuterol 2.5 mg inhalation solution
17	Fluticasone/salmeterol 250/50 µg DPI	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI	Levalbuterol inhalation solution
18	Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL	Levalbuterol inhalation solution
19	Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Levalbuterol inhalation solution
20	Fluticasone/salmeterol 250/50 µg Theophylline	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI, theophylline	Levalbuterol HCl inhalation solution
21	Fluticasone/salmeterol 250/50 µg Theophylline	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI, theophylline	Levalbuterol inhalation solution
22	Fluticasone/salmeterol 250/50 µg DPI Tiotropium DPI	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Salmeterol DPI, tiotropium DPI	Levalbuterol inhalation solution
23	Ipratropium 0.5 mg/albuterol inhalation solution	Ipratropium 0.5 mg/ albuterol 2.5 mg inhalation solution	BIS 0.5 mg/2 mL Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Ipratropium 0.5 mg/ albuterol 2.5 mg inhalation solution
24	Ipratropium and albuterol MDI Theophylline	Ipratropium 0.5 mg/ albuterol 2.5 mg inhalation solution	BIS 0.5 mg/2 mL Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution, theophylline	Ipratropium 0.5 mg/ albuterol 2.5 mg inhalation solution
25	Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Levalbuterol inhalation solution	BIS 0.5 mg/2 mL Ipratropium 0.5 mg/albuterol 2.5 mg inhalation solution	Levalbuterol inhalation solution

BIS=budesonide inhalation suspension; COPD=chronic obstructive pulmonary disease; DPI=dry powder inhalation; MDI=metered dose inhaler; HCl=hydrochloride; LABA=long-acting β<sub>2</sub>-adrenergic agonist.

\*BIS 0.5 mg/2 mL is administered twice daily.

†Long-acting β<sub>2</sub>-adrenergic agonist changed because of formulation issues.

‡Used instead of a LABA as daily treatment.

able as nebulized formulations. Thus, patients previously receiving ICS/LABA therapy via 1 inhaler (n=11) were switched from their previous ICS to nebulized BIS and a LABA administered via DPI. The same LABA was continued in all but 3 patients: 2 COPD patients (#13 and #14) were discontinued from LABA therapy, and 1 asthma patient (#12) had a prescription benefit formulary with a specific LABA product requirement. One COPD patient (#15) was switched from ipratropium to tiotropium DPI, and 1 COPD patient discontinued ipratropium (#18) at the time of the transition to BIS. For all other asthma and COPD patients, concomitant therapies (eg, montelukast, formoterol or salmeterol DPI, theophylline) remained the same during the transition to BIS. In 6 asthma patients and 9 COPD patients, rescue SABA therapy was continued with nebulized levalbuterol (Xopenex®; Sepracor Inc, Marlborough, MA) at the time of the transition to nebulized BIS. When concomitant therapy included a nebulized medication, the medication was administered simultaneously with BIS, which is not indicated in the prescribing information<sup>21</sup> but is commonly recommended by clinicians to reduce the time needed for nebulization.

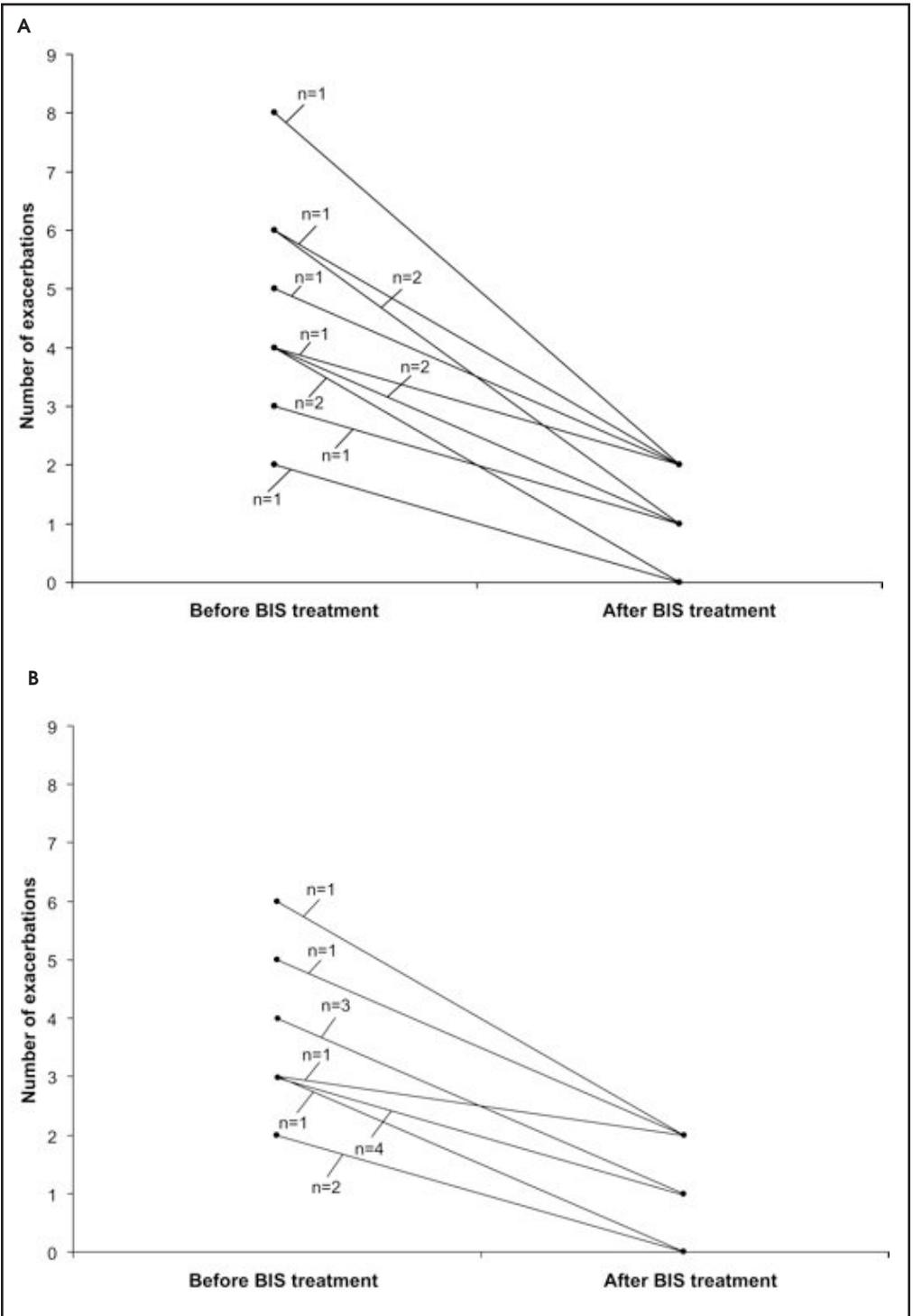
Figure 1 shows the number of exacerbations experienced by each patient before and after the transition to BIS. The number of exacerbations decreased for all patients. The total number of exacerbations in patients with asthma decreased from 56 before the transition to BIS to 13 during BIS treatment (mean decrease, 3.6/patient or 77% overall). For patients with COPD, exacerbations decreased from 45 to 13 (mean decrease, 2.5/patient or 71% overall). Three patients with asthma had no exacerbations while receiving BIS. In 1 patient with asthma (#6), exacerbations decreased from 8 in the year

before the transition to BIS to only 2 after the transition. Clinical improvements after 3 months in absolute FEV<sub>1</sub> values (L) of ≥ 13% in patients with asthma and ≥ 9% in patients with COPD were observed in 83% (10/12) of patients with asthma and 33% (4/12) of patients with COPD (Fig. 2). Patients who did not demonstrate an improvement in absolute FEV<sub>1</sub> after 3 months maintained similar FEV<sub>1</sub> values; none of the patients exhibited a significant decrease in FEV<sub>1</sub>. Assessment of FEV<sub>1</sub> was not performed in 1 patient with COPD (#25) because of a tracheotomy. Finally, BIS was well tolerated. None of the patients reported any adverse events.

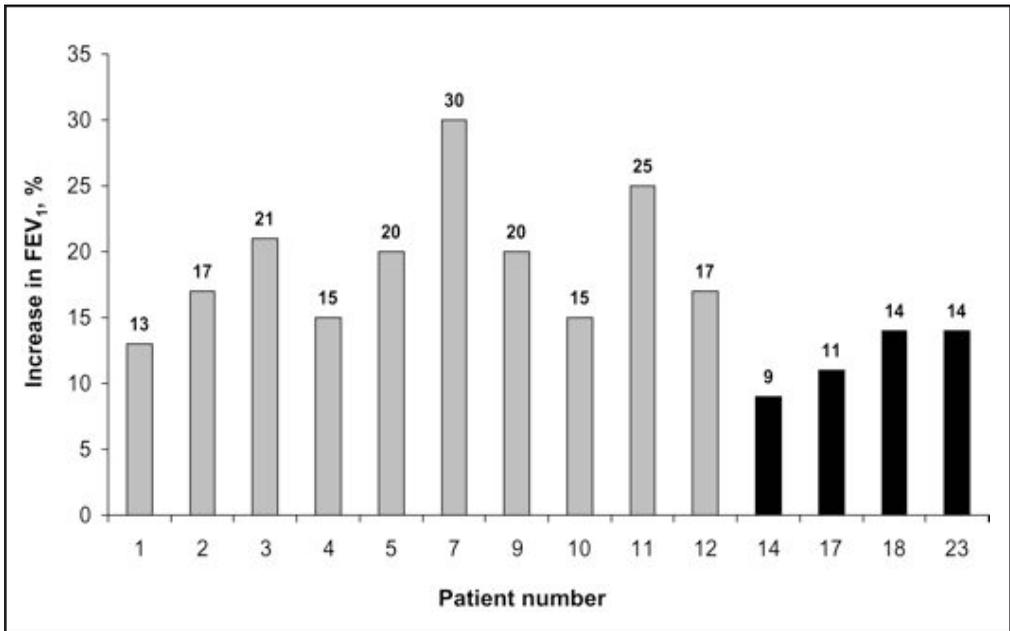
## DISCUSSION

In this series of 25 consecutive patients with poorly controlled asthma or COPD, a transition from commonly used ICS formulations administered via DPI or MDI to nebulized BIS or initiation of ICS treatment with BIS provided marked improvement in disease control for all patients and was well tolerated. Exacerbations decreased by more than 70% in patients with asthma or COPD. Moreover, despite a long-standing history of pulmonary disease, 83% of patients with asthma and 33% with COPD demonstrated clinical improvement in FEV<sub>1</sub> while receiving BIS during the 1-year observation period. Some patients continue to be treated with BIS, while others have been lost through attrition. All of the patients who still are treated actively in the practice continue to receive BIS.

These findings are in agreement with previous research of nebulized ICS use in adults. Early studies, however, focused on the addition of BIS and not replacement of traditional ICS with BIS.<sup>13,14,15,18,22</sup> Additionally, a retrospective cohort study of medical and pharmacy claims data showed that older adults (≥ 50 years) who persistently used



**Figure 1.** Numbers of exacerbations of asthma (a) or chronic obstructive pulmonary disease (b) requiring the use of oral corticosteroids before and during treatment with budesonide inhalation suspension (BIS).



**Figure 2.** Percentage increase in absolute forced expiratory volume in 1 second (FEV<sub>1</sub>; L) in the 10 patients with asthma (gray bars) and the 4 patients with chronic obstructive pulmonary disease (black bars) whose FEV<sub>1</sub> improved while on budesonide inhalation suspension (BIS). Ten patients had FEV<sub>1</sub> values during BIS treatment that were unchanged from baseline; 1 patient with a tracheotomy was unable to perform spirometry.

nebulized ICS therapy required fewer courses of oral corticosteroids in the 6-month period after their first nebulized ICS prescription compared with the previous 6-month period.<sup>18</sup> Gawchik reported that 3 women (aged ~45 years) with uncontrolled asthma experienced decreases in the number of urgent care visits, and 2 of the 3 women required fewer oral corticosteroid courses after switching from ICSs delivered via DPI or MDI to BIS delivered via a jet nebulizer and compressor. By the end of Gawchik's 5-year observation, BIS was reduced from 1 mg twice daily to 0.5 mg twice daily in 2 patients and to 0.5 mg once daily in 1 patient while maintaining good asthma control.<sup>22</sup> These dosages are consistent with those reported for adults and children aged  $\geq 12$  years in the international product monograph, which recommends a BIS starting dosage of 1 - 2 mg twice daily followed by a maintenance dosage of 0.5 - 1

mg/day once asthma control has been established.<sup>23</sup> In the present case series, administration of BIS 0.5 mg twice daily improved control of asthma and COPD in a real-world setting of older patients.

The efficacy of BIS in total daily doses ranging from 0.5 - 8 mg as the only ICS therapy has been assessed in 2 controlled clinical studies in adolescent and adult patients with asthma.<sup>16,17</sup> In a small crossover study (N=26), BIS 1- and 4-mg twice-daily dosages were at least as effective as budesonide 800  $\mu$ g administered twice daily via MDI with spacer in adults with moderately severe unstable asthma despite treatment with ICS.<sup>16</sup> A larger (N=758), more recent study demonstrated similar maintenance of asthma control in adolescents and adults with moderate to severe persistent asthma transitioned from ICS via DPI or MDI to BIS 0.5 or 1 mg once daily, BIS 1 or 2 mg twice daily, or budesonide DPI 400  $\mu$ g twice daily.<sup>17</sup>

The authors also suggested that longer nebulization times for the 2-mg twice-daily BIS dosage (4 ampules of BIS 0.5 mg/2 mL twice daily) (20 - 30 minutes) compared with the 0.5-mg once-daily dosage (2 ampules of BIS 0.25 mg/2 mL once daily) (10 - 20 minutes) may have resulted in numerically lower adherence, higher withdrawal rates, and lower-than-expected FEV<sub>1</sub> in the higher dosage group.<sup>17</sup> At the time the study was conducted, the 1 mg/2 mL BIS ampule was not available; a 4-mg/day dosage can now be given twice daily as 2 ampules of BIS 1 mg/2 mL,<sup>21</sup> reducing nebulization time. Finally, the study population included patients who generally would not have a preference or need for nebulized ICS therapy.<sup>17</sup> Of the 603 patients who received BIS, approximately 5% were aged  $\geq$  65 years.<sup>17</sup>

In the present case series, 6 patients with COPD (mean age, 76 years) received BIS therapy because of insurance-related issues. In the U.S.A., not all ICS delivery devices (eg, spacers) may be covered by commercial insurers. Moreover, the government's health insurance program for the elderly (Medicare Part A and Part B) generally did not cover outpatient prescription drugs; however, the cost of nebulizers and the medications used in the nebulizers were covered through Part B. This reimbursement discrepancy holds true despite the introduction of Medicare Part D, which is a voluntary prescription benefit plan that includes large out-of-pocket expenses. Nebulized medications covered by Medicare Part B before the Part D prescription drug program became available still are covered under Medicare Part B, but some U.S.A. providers and patients may not be aware of this information. Although most pharmacies stock medications for nebulization, only certain pharmacies or durable medical equipment suppliers usually are able to bill for nebulized medications

under Medicare Part B. Despite the limited age indication for nebulized BIS in the U.S.A., Medicare does reimburse for the branded product (code J7626; 0.5 mg/2 mL).

Mixing of nebulized medications may potentially increase the inhaled mass of medications because of increased volume in the nebulizer cup.<sup>24</sup> Although increased volume prolongs nebulization time, some patients may prefer 1 treatment. In the present case series, simultaneous administration of BIS with other nebulized medications (eg, levalbuterol) enabled simpler dosing of add-on therapy for those patients who required concomitant therapy. Previous data have shown BIS to be stable chemically and compatible physically when administered simultaneously with respiratory medications, including albuterol sulfate inhalation solution (Proventil<sup>®</sup>; Schering Corporation, Kenilworth, NJ), ipratropium bromide inhalation solution (Atrovent<sup>®</sup>; Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, CT), and levalbuterol inhalation solution.<sup>24</sup> Although not commercially available at the time when my patients were transitioned to BIS, arformoterol tartrate inhalation solution 15  $\mu$ g/2 mL (Brovana<sup>®</sup>; Sepracor Inc, Marlborough, MA) also has been shown to be stable physically and chemically when mixed with BIS 0.25 mg/2 mL or 0.5 mg/2 mL.<sup>25</sup> These studies only assessed chemical compatibility; other variables related to administration of admixing solutions, such as potential changes in inhaled mass, the emergence of new adverse events, or clinical efficacy, have not been evaluated.<sup>24,25</sup> The prescribing information recommends that BIS be administered separately from other medications in the nebulizer.<sup>21</sup>

In the present case series, inhaler technique was reviewed and proper inhaler use was demonstrated in the clinic setting at nearly every follow-up

visit. Despite these measures, many patients achieved suboptimal outcomes with ICS-based controller therapy delivered by MDI or DPI. Nebulization therapy relies on normal tidal breathing and obviates the manual dexterity needed to properly use handheld aerosol devices. These patients may have experienced improved ICS delivery to the airways with nebulizer use, contributing to the effectiveness of BIS in this patient population of older adults. In a survey of patients' views on home nebulizer treatment for chronic pulmonary disease (n=82; median age, 71.5 years) conducted by Barta et al,<sup>26</sup> a majority of patients reported an increased feeling of personal well-being, better symptom control, and increased confidence to be the main advantages of nebulizer use.

Approximately 75% of patients felt their nebulizer was superior to inhalers for symptom relief and that its use would keep them out of the hospital.<sup>26</sup> Moreover, many patients felt they would "be lost" without their nebulizers.<sup>26</sup> Patient preference for home nebulizer treatment and the perception of greater symptom control offer additional support for the use of nebulized therapy in older patients with asthma and COPD.

In conclusion, decreased exacerbations in patients with asthma and COPD, along with ease of use for older patients or those who have issues with other types of inhalation devices, suggest that BIS administered via a nebulizer may be a treatment option for adults with asthma or COPD who remain suboptimally controlled on ICS-based therapy administered via DPI or MDI.

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