

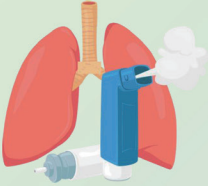



Short-acting β_2 -agonist prescriptions in patients with asthma: findings from the South Korean cohort of SABINA III

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Short-acting β_2 -agonist prescriptions in patients with asthma: findings from the South Korean cohort of SABINA III

Aims	Methods	Results		
 <p>To find out the describe prescription patterns of Short-Acting β_2-Agonist (SABA), and clinical outcomes</p>	<p>Cross-sectional study</p>  <ul style="list-style-type: none"> asthma aged ≥ 12 years ≥ 3 consultations with the same healthcare provider medical records containing data for ≥ 12 months prior to the study visit 	Prescription patterns	83.7%	Treated by specialist
			91.0%	Moderate to severe asthma
7.6%	Over-prescription of SABA (≥ 3 canisters)			
47.4%	Over-prescription of SABA in addition to maintenance therapy			
		Clinical outcomes	91.6%	Well-controlled/partly-controlled
			29.6%	Experienced ≥ 1 severe asthma exacerbation
Conclusion		SABA over-prescription was reported in nearly 50% of patients prescribed SABA in addition to maintenance therapy, underscoring the need to align clinical practices with the latest evidence-based recommendations and educate physicians and patients on appropriate SABA use.		

Background/Aims: Despite short-acting β_2 -agonist (SABA) overuse being associated with poor asthma outcomes, data on SABA use in South Korea is scarce. Herein, we describe prescription patterns of SABA and other asthma medications in patients from the South Korean cohort of the SABA use IN Asthma (SABINA) III study.

Methods: This study included patients with asthma aged ≥ 12 years, who had ≥ 3 consultations with the same healthcare provider, and medical records containing data for ≥ 12 months prior to the study visit. Patients were classified by investiga-

tor-defined asthma severity (per 2017 Global Initiative for Asthma recommendations) and practice type (primary or specialist care). Data on disease characteristics, asthma treatments, and clinical outcomes in the 12 months before the study visit were collected using electronic case report forms.

Results: Data from 476 patients (mean age, 55.4 years; female, 63.0%) were analyzed. Most patients were treated by specialists (83.7%) and had moderate-to-severe asthma (91.0%). Overall, 7.6% of patients were prescribed ≥ 3 SABA canisters (defined as over-prescription). In patients prescribed SABA in addition to maintenance therapy, 47.4% were over-prescribed SABA. Most patients (95.4%) were prescribed a fixed-dose combination of an inhaled corticosteroid and a long-acting β_2 -agonist as maintenance therapy. Although asthma was well-controlled/partly-controlled in 91.6% of patients, 29.6% experienced ≥ 1 severe asthma exacerbation.

Conclusions: SABA over-prescription was reported in nearly 50% of patients prescribed SABA in addition to maintenance therapy, underscoring the need to align clinical practices with the latest evidence-based recommendations and educate physicians and patients on appropriate SABA use.

Keywords: Anti-asthmatic agents; Anti-inflammatory agents; Asthma; Bronchodilator agents; Glucocorticoids; South Korea

INTRODUCTION

Asthma is a heterogeneous, chronic inflammatory disease of the airways, which affects approximately 339 million patients worldwide [1]. In South Korea, the prevalence of asthma has steadily risen over the past decade [2], with approximately 2.9% of the population diagnosed with asthma in 2017 [3]. Despite recent advances in asthma management and the availability of international evidence-based treatment guidelines, asthma remains poorly controlled across the world, including Asia [4-6]. This is likely due to, in part, a long-held paradox of asthma management, whereby for over 20 years, the Global Initiative for Asthma (GINA) recommended as-needed short-acting β_2 -agonists (SABAs) as the preferred reliever for patients with mild asthma, even though they have no inherent anti-inflammatory activity [7]. However, with accumulating evidence that SABA overuse (≥ 3 canisters/year) is associated with an increased risk of exacerbations, hospitalizations, and mortality [8,9], GINA no longer recommends as-needed SABAs without concomitant inhaled corticosteroid (ICS) and instead recommends as-needed low-dose ICS-formoterol as the preferred reliever for adults and adolescents with mild asthma (GINA treatment steps 1–2) and for those with moderate-to-severe asthma (GINA treatment steps 3–5) who are prescribed ICS-formoterol maintenance therapy [10].

Insights on asthma medication prescribing patterns, particularly for SABA prescriptions, will provide clinicians and healthcare policymakers with a better understanding of

the extent of SABA use and ensure that treatment practices align with the latest evidence-based treatment recommendations. However, although South Korea has several well-established databases, such as the National Health Insurance Service (NHIS) [11] and the Health Insurance Review & Assessment Service (HIRA), there is a paucity of data on potential SABA overuse across the country, with only one previous study examining trends of annual SABA use and overuse and the impact of SABA overuse on mortality [12].

To bridge this gap and provide a global view of SABA prescriptions, the SABA use IN Asthma (SABINA) program was initiated to describe asthma treatment prescription patterns, the extent of high SABA prescription, and its impact on asthma-related clinical outcomes through a series of global studies [13]. Results from SABINA I and II, retrospective observational studies conducted in the United Kingdom and Europe, respectively, demonstrated that SABA overprescription (≥ 3 canisters/year) was common and associated with poor clinical outcomes [8,14]. The SABINA III arm of the program, conducted in 23 countries across Asia-Pacific, Africa, the Middle East, Latin America, and in Russia, used electronic case report forms (eCRFs) to overcome the lack of robust national healthcare databases in many of the participating countries [15]. Here, we report results from the South Korean cohort of the SABINA III study, to provide real-world evidence on asthma treatment practices in this country.

METHODS

Study design and population

Detailed methodology for SABINA III has been published previously [15]. In brief, this observational, cross-sectional study was conducted at 16 sites (6 primary, 1 secondary, and 9 tertiary care sites) across South Korea, with patient recruitment between July 2019 and November 2019 (Supplementary Table 1). The primary and specialist care study sites were selected using purposive sampling with the aim of obtaining a sample representative of how patients with asthma were being treated in their country.

Retrospective data were obtained from existing medical records, and patient data were collected during a study visit and entered into an eCRF. The study was conducted in compliance with the Declaration of Helsinki and Good Clinical Practice guidelines, and each study site received approval from the Institutional Review Board (Clinical Trial Center, Konkuk University Hospital; IRB reference number: KUMC 2019-06-017).

Patients aged ≥ 12 years with a documented diagnosis of asthma, ≥ 3 recorded consultations with their healthcare provider, and medical records containing data for ≥ 12 months prior to the study visit were enrolled [15]. Patients with other chronic respiratory diseases or limiting acute or chronic conditions were excluded. Signed informed consent was obtained from all patients.

Study variables and outcomes

Patients were characterized based on practice type (primary or specialist care) and investigator-classified asthma severity (guided by GINA 2017 treatment steps: steps 1–2, mild asthma and steps 3–5, moderate-to-severe asthma) [16]. Sociodemographic characteristics and disease characteristics were recorded during the study visit. Sociodemographic characteristics included age, sex, body mass index (categorized according to the Asia-Pacific classification [17]); education (primary and/or secondary school, high school, or university and/or post-graduate education); healthcare reimbursement (not reimbursed, partially reimbursed, or fully reimbursed); and smoking history (active smoker, former smoker, or never smoker).

Asthma medication prescriptions in the preceding 12 months, including SABA, ICS, ICS–long-acting β_2 -agonist (LABA) fixed-dose combinations, oral corticosteroid (OCS) burst treatment (defined as a short course of intravenous

corticosteroid or OCS administered for 3–10 days or a single dose of an intramuscular corticosteroid to treat an exacerbation), long-term OCS treatment (defined as any OCS treatment for > 10 days), and antibiotics prescribed for asthma (regardless of duration of use), were recorded. SABA prescriptions were categorized as 0, 1–2, 3–5, 6–9, 10–12, or ≥ 13 canisters, with over-prescription defined as ≥ 3 canisters in the 12 months before the study visit [8–10]. ICS prescriptions were categorized by prescribed average daily dose (low, medium, or high) [16].

Severe asthma exacerbations in the 12 months before the study visit were defined based on the European Respiratory Society/American Thoracic Society guidelines as a worsening of asthma symptoms requiring hospitalization, an emergency room visit, or the need for OCS burst treatment [18]. During the study visit, patients were questioned about their level of asthma control, which was evaluated using the GINA 2017 assessment for asthma control and categorized as well-controlled, partly controlled, or uncontrolled by the investigator [16].

Statistical analysis

Descriptive analyses characterized patients according to sociodemographic and clinical characteristics. Continuous variables were described as number (%), mean (standard deviation [SD]), and median (minimum, maximum). Categorical variables were summarized by frequency counts and percentages.

RESULTS

Overall, 476 patients were analyzed; however, data on practice type were unavailable for 4 patients (Supplementary Fig. 1). Most patients were treated by specialists (83.7%) and had investigator-classified moderate-to-severe asthma (91%).

The mean \pm SD age of patients was 55.4 ± 15.1 years (Table 1). The majority of patients were female (63.0%), overweight or obese (64.7%), had never smoked (66.8%), and reported partially reimbursed healthcare (90.1%). Patients had a mean \pm SD asthma duration of 6.5 ± 6.1 years, with most at GINA treatment step 3 (42.4%) or 4 (38.0%). Overall, 84.7% of patients had ≥ 1 comorbidity.

Table 1. Sociodemographic and disease characteristics presented by practice type and investigator-classified asthma severity

Variable	All (n = 472) ^{a)}						
	All (n = 476)	Primary care (n = 77)		Specialist care (n = 395)			
		Mild asthma (n = 1)	Moderate-to-severe asthma (n = 76)	All (n = 77)	Mild asthma (n = 42)	Moderate-to-severe asthma (n = 353)	All (n = 395)
Age (yr)							
Mean ± SD	55.4 ± 15.1	81.0 ± NA	52.3 ± 15.1	52.7 ± 15.4	51.9 ± 16.9	56.4 ± 14.8	55.9 ± 15.1
Age group (yr) ^{b)}							
18–55	199 (41.8)	0 (0.0)	43 (56.6)	43 (55.8)	20 (47.6)	135 (38.2)	155 (39.2)
≥ 55	277 (58.2)	1 (100.0)	33 (43.4)	34 (44.2)	22 (52.4)	218 (61.8)	240 (60.8)
Sex							
Female	300 (63.0)	1 (100.0)	49 (64.5)	50 (64.9)	24 (57.1)	223 (63.2)	247 (62.5)
BMI (kg/m ²)							
Mean ± SD	24.7 ± 4.0	27.7 ± NA	24.0 ± 3.6	24.0 ± 3.6	24.6 ± 3.6	24.9 ± 4.1	24.9 ± 4.0
BMI group (kg/m ²) ^{c)}							
< 18.5	18 (3.8)	0 (0.0)	4 (5.3)	4 (5.2)	1 (2.4)	13 (3.7)	14 (3.5)
18.5–22.9	150 (31.5)	0 (0.0)	29 (38.2)	29 (37.7)	14 (33.3)	106 (30.0)	120 (30.4)
23.0–24.9	105 (22.1)	0 (0.0)	19 (25.0)	19 (24.7)	8 (19)	76 (21.5)	84 (21.3)
≥ 25.0	203 (42.6)	1 (100.0)	24 (31.6)	25 (32.5)	19 (45.2)	158 (44.8)	177 (44.8)
Education level							
Primary and/or secondary school	52 (10.9)	0 (0.0)	5 (6.6)	5 (6.5)	4 (9.5)	42 (11.9)	46 (11.6)
High school	71 (14.9)	0 (0.0)	12 (15.8)	12 (15.6)	5 (11.9)	54 (15.3)	59 (14.9)
University and/or post-graduate education	138 (29.0)	0 (0.0)	35 (46.1)	35 (45.5)	17 (40.5)	85 (24.1)	102 (25.8)
Unknown	215 (45.2)	1 (100.0)	24 (31.6)	25 (32.5)	16 (38.1)	172 (48.7)	188 (47.6)
Healthcare insurance/medication funding							
Not reimbursed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Partially reimbursed	429 (90.1)	1 (100.0)	75 (98.7)	76 (98.7)	41 (97.6)	308 (87.3)	349 (88.4)
Fully reimbursed	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.4)	5 (1.3)
Unknown	42 (8.8)	0 (0.0)	1 (1.3)	1 (1.3)	1 (2.4)	40 (11.3)	41 (10.4)
Smoking status history							
Active smoker	52 (10.9)	0 (0.0)	8 (10.5)	8 (10.4)	1 (2.4)	43 (12.2)	44 (11.1)
Former smoker	106 (22.3)	0 (0.0)	8 (10.5)	8 (10.4)	12 (28.6)	86 (24.4)	98 (24.8)

Table 1. Continued

Variable	All (n = 472) ^{b)}					
	Primary care (n = 77)		Specialist care (n = 395)			
	Mild asthma (n = 1)	Moderate-to-severe asthma (n = 76)	All (n = 77)	Mild asthma (n = 42)	Moderate-to-severe asthma (n = 353)	All (n = 395)
Never smoker	1 (100.0)	60 (78.9)	61 (79.2)	29 (69.0)	224 (63.5)	253 (64.1)
Asthma duration (yr)						
Mean ± SD	2.0 ± NA	5.6 ± 4.5	5.6 ± 4.5	5.4 ± 4.2	6.9 ± 6.5	6.7 ± 6.3
Median (range)	2.0 (2.0–2.0)	4.5 (1.0–22.0)	4.0 (1.0–22.0)	4.0 (1.0–17.0)	5.0 (1.0–52.0)	5.0 (1.0–52.0)
GINA treatment step ^{d)}						
Step 1	1 (100.0)	0 (0.0)	1 (1.3)	9 (21.4)	0 (0.0)	9 (2.3)
Step 2	0 (0.0)	0 (0.0)	0 (0.0)	33 (78.6)	0 (0.0)	33 (8.4)
Step 3	0 (0.0)	40 (52.6)	40 (51.9)	0 (0.0)	160 (45.3)	160 (40.5)
Step 4	0 (0.0)	33 (43.4)	33 (42.9)	0 (0.0)	146 (41.4)	146 (37.0)
Step 5	0 (0.0)	3 (3.9)	3 (3.9)	0 (0.0)	47 (13.3)	47 (11.9)
Comorbidities						
None	0 (0.0)	17 (22.4)	17 (22.1)	7 (16.7)	48 (13.6)	55 (13.9)
1–2	0 (0.0)	38 (50.0)	38 (49.4)	22 (52.4)	169 (47.9)	191 (48.4)
3–4	1 (100.0)	17 (22.4)	18 (23.4)	9 (21.4)	83 (23.5)	92 (23.3)
≥ 5	0 (0.0)	4 (5.3)	4 (5.2)	4 (9.5)	53 (15.0)	57 (14.4)

Values are presented as number (%).

BMI, body mass index; GINA, Global Initiative for Asthma; NA, not available; SD, standard deviation.

^{a)}Data on practice type were not available for 4 patients.

^{b)}Patients in the 12–17-year age group were not recruited in the study.

^{c)}BMI is categorized according to the Asia-Pacific classification as underweight (< 18.5 kg/m²), normal (18.5–22.9 kg/m²), overweight (23.0–24.9 kg/m²), and obese (≥ 25.0 kg/m²) [17].

^{d)}Based on the 2017 GINA recommendations [16].

Asthma treatments in the 12 months before the study visit

SABA prescriptions

Overall, 7.6% of patients were prescribed ≥ 3 SABA canisters in the previous 12 months, defined as over-prescription (Fig. 1). However, 83.8% of patients received no SABA prescriptions. A higher proportion of patients under specialist care were prescribed ≥ 3 SABA canisters compared with those under primary care (8.9 vs. 1.3%).

Only 1 patient was prescribed SABA monotherapy, with a prescription of 1–2 SABA canisters in the previous 12 months. However, 16.0% of patients were prescribed SABA in addition to maintenance therapy, with 47.4% prescribed ≥ 3 SABA canisters (Table 2). In primary care, 5.2% of patients, all of whom had moderate-to-severe asthma, were prescribed SABA in addition to maintenance therapy. In specialist care, 18.2% of patients (21.4% with mild asthma and 17.8% with moderate-to-severe asthma) were prescribed SABA in addition to maintenance therapy; of these, all patients with mild asthma and 41.3% of those with moderate-to-severe asthma were prescribed ≥ 3 SABA canisters. Overall, only 0.6% of patients were prescribed a short-acting muscarinic antagonist.

ICS prescriptions

Overall, ICS monotherapy was prescribed to 6.3% of patients, all of whom were treated by specialists. The majority of these patients were classified with mild asthma, with 80% prescribed low-dose ICS (Table 2).

Most patients (95.4%) were prescribed an ICS-LABA

fixed-dose combination as maintenance therapy, with 50.0% prescribed low-dose ICS (Table 2). With the exception of 1 patient, primary care physicians prescribed ICS-LABA to all patients with moderate-to-severe asthma, with 70.7% prescribed low-dose ICS. In specialist care, a greater proportion of patients with moderate-to-severe asthma were prescribed ICS-LABA compared with those with mild asthma (99.7 vs. 52.4%). Of these, 45.7% and 42.2% were prescribed low- and medium-dose ICS, respectively.

Other prescriptions for asthma

One or more OCS burst was prescribed to 25.0% of patients, with this occurring in more patients in primary care compared with specialist care (32.5 vs. 23.3%; Table 2). In primary care, all patients with moderate-to-severe asthma were prescribed ≥ 1 OCS burst. In specialist care, 11.9% of patients with mild asthma and 24.6% of patients with moderate-to-severe asthma were prescribed ≥ 1 OCS burst.

Long-term OCS maintenance therapy was prescribed to 6.7% of patients, with higher prescription rates observed in specialist care compared with primary care (7.3 vs. 3.9%; Table 2). All patients prescribed long-term OCS treatment in primary care had moderate-to-severe asthma. In specialist care, 2.4% of patients with mild asthma and 7.9% with moderate-to-severe asthma were prescribed long-term OCS treatment.

Additionally, 13.3% of patients were prescribed antibiotics for asthma, with higher prescription rates observed in primary care compared with specialist care (26.0 vs. 10.9%; Table 2).

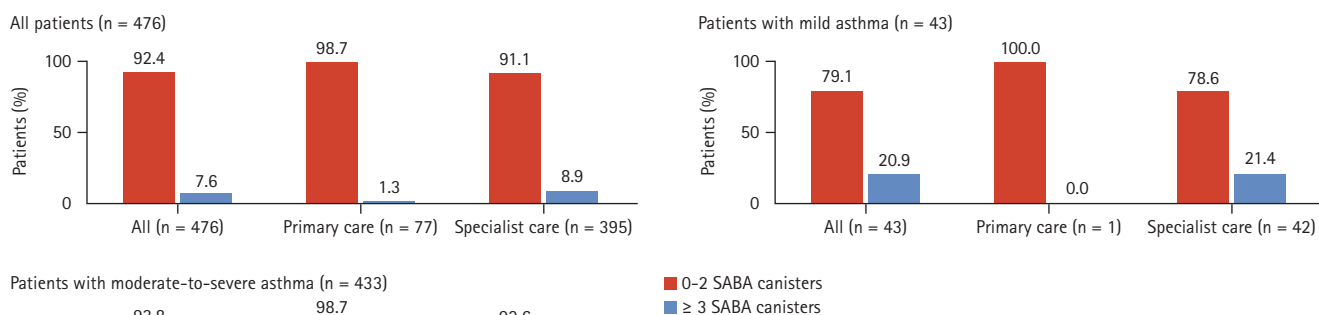


Figure 1. SABA prescriptions in the 12 months before the study visit by practice type and investigator-classified asthma severity. Data on practice type were not available for 4 patients. SABA, short-acting β_2 -agonist.

Table 2. Prescription of asthma medication in the 12 months before the study visit by practice type and investigator-classified asthma severity

Variable	All (n = 472) ^{a,b)}					
	Primary care (n = 77)			Specialist care (n = 395)		
	All (n = 476)	Mild asthma (n = 1)	Moderate-to-severe asthma (n = 76)	All (n = 77)	Mild asthma (n = 42)	Moderate-to-severe asthma (n = 353)
Patients prescribed SABA in addition to maintenance therapy						
Yes	76 (16.0)	0 (0.0)	4 (5.3)	4 (5.2)	9 (21.4)	63 (17.8)
SABA canisters or inhalers prescribed in the past 12 months ^{c)}						
Mean ± SD	6.4 ± 24.0	NA	53.5 ± 104.3	53.5 ± 104.3	4.8 ± 1.5	3.6 ± 4.5
Median (range)	2.0 (1.0–210.0)	NA	1.5 (1.0–210.0)	1.5 (1.0–210.0)	5.0 (3.0–7.0)	2.0 (1.0–30.0)
SABA canisters or inhalers prescribed in the past 12 months by groups						
Total	76	0	4	4	9	63
1–2	40 (52.6)	NA	3 (75.0)	3 (75.0)	0 (0.0)	37 (58.7)
3–5	17 (22.4)	NA	0 (0.0)	0 (0.0)	7 (77.8)	10 (15.9)
6–9	15 (19.7)	NA	0 (0.0)	0 (0.0)	2 (22.2)	13 (20.6)
10–12	NA	NA	NA	NA	NA	NA
≥ 13	4 (5.3)	NA	1 (25.0)	1 (25.0)	0 (0.0)	3 (4.8)
Patients prescribed ICS monotherapy ^{d)}						
Yes	30 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	20 (47.6)	10 (2.8)
ICS canisters or inhalers prescribed in the past 12 months ^{c)}						
Mean ± SD	15.7 ± 40.0	NA	NA	NA	20.0 ± 48.0	7.2 ± 12.7
Median (range)	4.5 (1.0–217.0)	NA	NA	NA	6.0 (1.0–217.0)	3.0 (1.0–42.0)
Total daily ICS dose prescribed						
Total	30	0	0	0	20	10
Low dose	24 (80.0)	NA	NA	NA	18 (90.0)	6 (60.0)
Medium dose	6 (20.0)	NA	NA	NA	2 (10.0)	4 (40.0)
High dose	NA	NA	NA	NA	NA	NA
Patients prescribed ICS-LABA fixed-dose combination						
Yes	454 (95.4)	1 (100.0)	75 (98.7)	76 (98.7)	22 (52.4)	352 (99.7)
Total daily ICS dose prescribed						
Total	454	1	75	76	22	352
Low dose	226 (50.0)	0 (0.0)	53 (70.7)	53 (69.7)	12 (57.1)	158 (45.0)

Table 2. Continued

Variable	All (n = 472) ^{a,b}					
	All (n = 476)		Primary care (n = 77)		Specialist care (n = 395)	
	Mild asthma (n = 1)	Moderate-to-severe asthma (n = 76)	All (n = 77)	Mild asthma (n = 42)	Moderate-to-severe asthma (n = 353)	All (n = 395)
Medium dose	1 (100.0)	20 (26.7)	21 (27.6)	9 (42.9)	148 (42.2)	157 (42.2)
High dose	0 (0.0)	2 (2.7)	2 (2.6)	0 (0.0)	45 (12.8)	45 (12.1)
Missing values ^e	2	0	0	1	1	2
Patients prescribed OCS burst treatment/short course ^f						
Yes	119 (25.0)	25 (32.9)	25 (32.5)	5 (11.9)	87 (24.6)	92 (23.3)
Patients prescribed long-term OCS as maintenance treatment ^g						
Yes	32 (6.7)	3 (3.9)	3 (3.9)	1 (2.4)	28 (7.9)	29 (7.3)
Patients prescribed antibiotics for asthma						
Yes	63 (13.3)	20 (26.3)	20 (26.0)	3 (7.1)	40 (11.4)	43 (10.9)
Missing values ^e	2	0	0	0	2	2

Values are presented as number (%).

ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; NA, not available; OCS, oral corticosteroid; SABA, short-acting β_2 -agonist; SD, standard deviation.

^aData on practice type were not available for 4 patients.

^bOnly 1 patient with mild asthma, who was treated in specialist care, was prescribed SABA monotherapy, with a prescription of 1–2 SABA canisters in the past 12 months.

^cThe data represents the mean and median number of canisters.

^dICS monotherapy refers to ICS alone as controller treatment.

^eMissing values are not included in the calculation of percentages.

^fOCS burst treatment was defined as a short course of OCS typically administered for 3–10 days to treat an exacerbation.

^gLong-term OCS as maintenance treatment was defined as any OCS treatment for > 10 days.

Table 3. Asthma-related severe exacerbations^{a)} and asthma symptom control by practice type and investigator-classified asthma severity

Variable	All (n = 472) ^{b)}					
	All (n = 476)		Primary care (n = 77)		Specialist care (n = 395)	
	Mild asthma (n = 1)	Moderate-to-severe asthma (n = 76)	All (n = 77)	Mild asthma (n = 42)	Moderate-to-severe asthma (n = 353)	All (n = 395)
Number of severe asthma exacerbations in the past 12 months						
Mean ± SD	0.5 ± 1.1	0.0 ± NA	0.8 ± 1.5	0.2 ± 0.7	0.5 ± 1.1	0.5 ± 1.0
Median (range)	0.0 (0.0–8.0)	0.0 (0.0–0.0)	0.0 (0.0–8.0)	0.0 (0.0–4.0)	0.0 (0.0–8.0)	0.0 (0.0–8.0)
Number of severe asthma exacerbations in the past 12 months by groups						
None	335 (70.4)	1 (100.0)	49 (64.5)	36 (85.7)	247 (70.0)	283 (71.6)
1	86 (18.1)	0 (0.0)	12 (15.8)	4 (9.5)	69 (19.5)	73 (18.5)
2	30 (6.3)	0 (0.0)	7 (9.2)	1 (2.4)	22 (6.2)	23 (5.8)
3	10 (2.1)	0 (0.0)	4 (5.3)	0 (0.0)	6 (1.7)	6 (1.5)
> 3	15 (3.2)	0 (0.0)	4 (5.3)	1 (2.4)	9 (2.5)	10 (2.5)
Level of asthma symptom control						
Well-controlled	294 (61.8)	1 (100.0)	26 (34.2)	35 (83.3)	230 (65.2)	265 (67.1)
Partly controlled	142 (29.8)	0 (0.0)	45 (59.2)	5 (11.9)	91 (25.8)	96 (24.3)
Uncontrolled	40 (8.4)	0 (0.0)	5 (6.6)	2 (4.8)	32 (9.1)	34 (8.6)

Values are presented as number (%).

NA, not available; OCS, oral corticosteroid; SD, standard deviation.

^{a)}Severe asthma exacerbations in the 12 months before the study visit were defined based on the European Respiratory Society/American Thoracic Society guidelines as a worsening of asthma symptoms requiring hospitalization, an emergency room visit, or the need for intravenous corticosteroids or OCS for ≥ 3 days or a single intramuscular corticosteroid dose.

^{b)}Data on practice type was not available for 4 patients.

Asthma-related clinical outcomes

Patients reported a mean \pm SD of 0.5 ± 1.1 severe asthma exacerbations in the previous 12 months, with 29.6% experiencing ≥ 1 severe exacerbation (Table 3, Supplementary Fig. 2). The proportion of patients with ≥ 1 severe exacerbation was the lowest in those prescribed ICS-containing therapy (ICS monotherapy or ICS-LABA fixed-dose combination) and the highest in those prescribed ≥ 1 OCS burst (Supplementary Fig. 2).

Asthma symptom control was assessed as well-controlled in 61.8%, partly controlled in 29.8%, and uncontrolled in 8.4% of patients (Table 3). Almost twice as many patients treated in specialist care had well-controlled asthma compared with those treated in primary care (67.1% vs. 35.1%). In specialist care, a higher percentage of patients with mild asthma were well-controlled compared with those with moderate-to-severe asthma (83.3% vs. 65.2%).

DISCUSSION

This cross-sectional study [15] provides valuable real-world insights into asthma treatment practices in patients predominantly under specialist care in this South Korean cohort of the SABINA III study [15]. Although SABA over-prescription was observed in only 7.6% of patients, in the 16% of patients prescribed SABA in addition to maintenance therapy, almost half (47.4%) were prescribed ≥ 3 SABA canisters in the preceding 12 months (over-prescription), underscoring the need for improvements in asthma care across the country.

Compared with country-aggregated data from SABINA III [15], patients from South Korea appeared to be more effectively managed and treated, with lower rates of SABA over-prescription (38 vs. 7.6%). Furthermore, compared with the overall SABINA III cohort [15], a higher percentage of patients from the Korean cohort reported well-controlled asthma (43.3 vs. 61.8%), with a lower proportion experiencing ≥ 1 severe exacerbation in the preceding 12 months (45.4 vs. 29.6%). These differences were observed despite the relatively similar sociodemographic and disease characteristics between the overall SABINA III [15] and South Korean cohorts, with most patients from both datasets treated under specialist care and classified as having moderate-to-severe asthma. Although some differences were observed between the 2 cohorts, for example, compared with the overall SABINA III cohort [15], patients from the South

Korean cohort had a lower mean asthma duration and body mass index, with a greater percentage being active and former smokers and reporting ≥ 5 comorbidities, it is unlikely that these factors contributed to the improved patient outcomes observed in the South Korean cohort.

Notably, over 80% of patients received no SABA prescriptions, with only 1 patient prescribed SABA monotherapy in the preceding 12 months. Additionally, relatively few patients (16%) were prescribed SABA in addition to maintenance therapy, of whom nearly half were prescribed ≥ 3 SABA canisters. Although limited studies to date have evaluated the extent and burden of SABA over-prescription in South Korea, our findings align with previous country-specific studies that have documented similar low rates of SABA use [12,19]. This low SABA use has been attributed to SABA being considered an “emergency medication” and not a rescue medication in Korea, with most patients only using SABA following an acute exacerbation and not for the prevention of exacerbations [12]. However, some factors specific to this study may have also contributed to the low SABA prescription rates observed. The majority of patients were treated by specialists who are generally more familiar with current asthma treatment guidelines and have the expertise and knowledge to provide optimal asthma care [20]. Additionally, most patients in this study were treated at tertiary or primary care centers, with only 1 secondary care site enrolled. This may have influenced SABA prescribing habits, with evaluation of data from the HIRA nationwide database (2013–2014) revealing lower SABA prescription rates in tertiary (41.7%) and primary (23.6%) care compared with secondary care (71.5%) [21].

The availability of SABA in Korea is strictly regulated [22]. Based on results from a cross-sectional epidemiologic study using the NHIS-National Sample Cohort database (2002–2012) where SABA overuse (≥ 3 canisters/year) was associated with all-cause mortality (adjusted odds ratio [OR], 1.72; 95% confidence interval [CI], 1.61–1.84) and asthma-related mortality (adjusted OR, 3.25; 95% CI, 2.72–3.89) [12], it would be advantageous for other countries to follow the lead of South Korea to drive policy changes that regulate the purchase of SABA over-the-counter (OTC) to ensure optimal asthma management.

Previous surveys and nationwide population-based studies from South Korea have reported low ICS prescription rates in patients with asthma, particularly those treated in primary care [12,20,21,23,24]. In contrast, in our study,

most patients were prescribed ICS-containing therapy (ICS monotherapy, 6.3%; ICS-LABA fixed-dose combination, 95.4%), which was in alignment with over 90% being classified as having moderate-to-severe asthma. Among patients prescribed ICS-LABA fixed-dose combinations, 50.0% and 39.6% were prescribed low- and medium-dose ICS, respectively, suggestive of the use of an ICS-LABA combination inhaler as both maintenance and reliever therapy (MART), which is common practice in South Korea. In addition, over 50% of patients with mild asthma treated by specialists were prescribed an ICS-LABA fixed-dose combination, which did not conform to GINA recommendations at the time this study was conducted [16]. This observation may reflect physician preference for an ICS-LABA fixed-dose combination over ICS monotherapy, to maximize patient adherence and ensure that even those with mild symptoms receive anti-inflammatory medication to prevent exacerbations. Overall, the high rate of ICS prescribing observed in this study may be attributable to a patient population treated largely under specialist care.

Studies based on NHIS and other databases have reported high OCS prescription rates across South Korea [12,19,21,23]. Notably, annual qualitative assessments of asthma management provided by the HIRA from 2015 to 2016 consistently reported high OCS prescription rates without ICS, ranging from 28.2 to 30.4% [25]. Unsurprisingly, OCS bursts were prescribed to 25.0% of all patients in this study, with prescription rates being higher in primary care compared with specialist care. Although lower than that reported in previous reports, this remains a matter of concern, since even short dosing periods (3–7 d) of OCS are associated with an increased risk of adverse events, including decreased bone density, hypertension, and gastrointestinal ulcers/bleeds [26]. In line with the findings of previous reports from Korea [25] and considering that 10.1% of patients who were prescribed an OCS burst in this cohort did not experience severe exacerbations, OCS may have been used as a reliever medication to treat acute episodes of symptom worsening in this study. Furthermore, the high percentage of patients prescribed OCS bursts may be due to some physicians prescribing OCS as a standby medication in patients' asthma action plans in the event of worsening asthma symptoms. However, these findings may also reflect physician beliefs and patient preferences, with both physicians at primary, secondary, and tertiary teaching hospitals in South Korea [20] and patients from South Korea

[27] and other parts of Asia [28,29] reporting a preference for oral medications. Interestingly, 13.3% of patients were prescribed antibiotics for asthma, suggesting a lack of familiarity with asthma guidelines as GINA does not support the routine use of antibiotics without a strong evidence of lung infection [10].

Overall, 61.8% of patients from this South Korean cohort of the SABINA III study had well-controlled asthma, which was higher than that observed in the overall SABINA III cohort (43.3%) [15] and in Korean patients from the multinational Asthma Insight and Management survey (27%) [27]. Several factors may have contributed to this improved level of asthma control. Although not captured in this study, most patients were treated by specialists who are more likely to prescribe MART, which may have improved asthma control and reduced as-needed medication use [30,31]. Indeed, most patients were prescribed an ICS-LABA fixed-dose combination, which is associated with positive asthma outcomes [32]. Additionally, the low level of SABA prescriptions, combined with the strict prohibition of SABA purchase OTC in South Korea [22], may possibly have further contributed to improved patient outcomes. Finally, the robust healthcare infrastructure in South Korea, in particular, the provision of compulsory health insurance and availability of medical aid may have potentially had a favorable impact on asthma control by ensuring access to essential asthma medications and optimizing patient adherence to prescribed therapies [11]. Nevertheless, even though most patients in this study had well-controlled asthma, 29.6% of patients still experienced ≥ 1 severe exacerbation in the previous 12 months [10]. Such findings may indicate potential over-estimation of disease control by both physicians and patients, leading to under-treatment of asthma [33-35]. Consequently, this study emphasizes the need for educational initiatives targeting both patients and physicians to further improve asthma care in South Korea.

There are some limitations to this study. First, prescription data may not reflect actual medication use; therefore, rates of treatment compliance or noncompliance were unknown. Second, since data entry into the eCRF relied on clinician assessment, findings may have been impacted by misinterpretation of instructions, incorrect patient classification based on asthma severity, or recall bias. Third, the majority of patients were recruited from specialist care, resulting in most patients being classified with moderate-to-severe asthma, and precluding comparisons across asthma sever-

ities. A possible explanation for this could be the lack of a well-established primary care system in South Korea [36], together with inherent challenges commonly encountered in conducting clinical trials at a primary care level. Thus, the study population represents a “better case scenario” and is not truly representative of the overall asthma patient population in South Korea. Therefore, additional studies are required to gain a more comprehensive understanding of asthma treatment patterns in both primary and specialist care across South Korea. Fourth, data on patients prescribed a MART regimen were not recorded. Finally, due to the relatively small sample size, it was not feasible to examine the association between SABA prescriptions and asthma-related clinical outcomes. However, overall findings from SABINA III indicated that ≥ 3 SABA prescriptions/year (vs. 1–2 SABA prescriptions) were associated with increasingly lower odds of controlled or partly controlled asthma and higher rates of severe exacerbations across many countries, healthcare settings, and asthma severities [15]. Nevertheless, this study provides comprehensive real-world data on current prescription patterns of asthma medications in patients in this South Korean cohort of the SABINA III study.

In conclusion, results from the South Korean cohort of SABINA III demonstrated that SABA over-prescription (≥ 3 canisters/year) occurred in $< 10\%$ of patients. However, despite treatment predominantly under specialist care, SABA over-prescription occurred in almost half of all patients prescribed SABA in addition to maintenance therapy. Although approximately 60% of patients reported well-controlled asthma, nearly 30% experienced ≥ 1 severe asthma exacerbation in the previous 12 months. These findings reinforce the need to continue aligning clinical practices with the latest evidence-based treatment recommendations to ensure further improvements in asthma management across South Korea.

KEY MESSAGE

1. Findings from this South Korean cohort of the SABINA III study revealed that SABA over-prescription (≥ 3 canisters/year) was relatively low, occurring in $< 10\%$ of all patients.
2. However, despite treatment predominantly under specialist care, SABA over-prescription was reported in almost half of all patients prescribed SABA in addition to maintenance therapy.

3. Although asthma was well-controlled/partly controlled in 91.6% of patients, 29.6% of patients experienced ≥ 1 severe asthma exacerbation in the 12 months prior to the study visit, underscoring the need for improvements in asthma care across the country.

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Received : February 23, 2023

Revised : July 31, 2023

Accepted : August 11, 2023

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Acknowledgments

Medical writing and editorial support were provided by Tejaswini Subbannayya, PhD, of Cactus Life Sciences (part of Cactus Communications, Mumbai, India), in accordance with Good Publication Practice (GPP3) guidelines (<http://www.ismpp.org/gpp3>), which was fully funded by AstraZeneca.

Credit authorship contributions

Kwang-Ha Yoo: data curation, formal analysis, writing - original draft, writing - review & editing, visualization, project administration, funding acquisition; Sang-Ha Kim: data curation, formal analysis, funding acquisition, project administration, visualization, writing - original draft, writing - review & editing; Sang-Heon Kim: data curation, formal analysis, funding acquisition, project administration, visualization, writing - original draft, writing - review & editing; Ji-Yong Moon: data curation, formal analysis, funding acquisition, project administration, visualization, writing - original draft, writing - review & editing; Heung-Woo Park: data curation, formal analysis, funding acquisition, project administration, visualization, writing - original draft, writing - review & editing; Yoon-Seok Chang: data curation, formal analysis, funding acquisition, project administration, visualization, writing - original draft, writing - review & editing; Maarten J.H.I. Beekman: conceptualization, data curation, formal analysis, funding acquisition, methodology, project administration, visualization, writing - original draft, writing - review & editing

Conflicts of interest

Kwang-Ha Yoo has advised pharmaceutical companies, including GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Novartis, Takeda, Nycomed, Teva Pharmaceuticals, MSD Pharmaceuticals, Mundipharma, Hyundai, and Hankook Pharmaceuticals regarding the conduct of clinical trials in asthma, COPD, and pneumonia and has spoken at meetings supported in whole or in part by these companies. Maarten J.H.I. Beekman was an employee of AstraZeneca when the study was conducted. Sang-Ha Kim, Ji-Yong Moon, Heung-Woo Park, and Yoon-Seok Chang declare that there is no conflict of interest.

Funding

AstraZeneca funded the study; was involved in the study design, protocol development, study conduct, and statistical analysis; and was given the opportunity to review the manuscript before submission.

Data sharing

Data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data sharing policy described at <https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure>.