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A Multi-country study on the Prescription Patterns of Short Acting Beta-2 Agonist (SABA) and its potential effects on asthma control: A Cross-Sectional Study on SABA use in Asthma

(SABA in Asthma International *SABINA-International*)

An observational, multi-country, cross sectional study describing SABA prescription and potential effects among asthma patients, using real-time electronic data collection methods in local healthcare settings.

Sponsor:	AstraZeneca
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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or special term	Explanation
ANOVA	Analysis of variance
AZ	AstraZeneca
BTS	British Thoracic Society
BNF	British National Formulary
COPD	Chronic obstructive pulmonary disease
eCRF	Electronic Case Report Form
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GINA	Global Initiative for Asthma
GORD	Gastro oesophageal reflux disease
GP	General practitioner
HRU	Healthcare Resource Utilisation
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICS	Inhaled corticosteroids
NIS	Non-interventional study
OCS	Oral corticosteroids
PEFR	Peak expiratory flow rate
SABA	Short-acting beta-2-agonist
SAS	Statistical Analysis System

RESPONSIBLE PARTIES

Name	Professional Title	Role in Study	Affiliation	Email Address

STUDY REPORT SUMMARY (ABSTRACT)

A multi-country study on the prescription patterns of Short Acting Beta-2 Agonist (SABA) and its potential effects on asthma control: a cross-sectional study on SABA use in asthma using real-time electronic data collection methods in local healthcare settings.

SABINA-International

Background/Rationale:

Asthma is a common, chronic disease that affects millions of patients worldwide, though mild cases remain the most prevalent. The Global Initiative for Asthma (GINA), recommends and defines a pharmacological, stepwise approach to managing asthma patients. This treatment strategy involves progressively adjusting medication dosage and introducing different classes of drugs to achieve asthma control. For example, the 2017 GINA guidelines recommend treating mild asthma patients according to Steps 1 and 2, both of which feature low dose medications. Step 1 treatment uses only a short-acting beta-2-agonist (SABA) to relieve symptoms as needed, while Step 2 includes SABA and daily, low dose inhaled corticosteroids (ICS). At each step, patients can use a reliever medication as well as their controller medication(s) to manage acute worsening of symptoms. However, under-prescription of ICS and over-prescription of SABA among asthma patients has emerged as a common problem that may cause increased healthcare resource utilisation (HRU) and patient morbidity. Experts increasingly agree that the underlying process provoking these symptomatic episodes worsens inflammation. Thus, first-line asthma treatment should always begin with an anti-inflammatory medication (such as ICS), rather than an approach that relies solely on managing symptoms with a bronchodilator (e.g. SABA). In 2019, GINA made a fundamental change to its asthma management strategy, recommending that all adults and adolescents with asthma receive ICS-containing controller treatment instead of starting with SABA-only treatment. The updated recommendations seek to reduce the risk of serious asthma exacerbation and to control symptoms.

Increasing evidence points to the adverse effects of SABA monotherapy. As such, recent adjustments to the GINA treatment guidelines aim to prevent SABA overuse and reduce the risk of asthma-related exacerbations. However, little research exists on patient over-reliance on SABA and the severity of this practice in a real-world setting, particularly in regions outside of Europe and North America. This observational, cross-sectional study describes the characteristics and treatment strategies of asthma patients in 24 countries in 5 continents, offering an improved global understanding of SABA over-prescription and use.

Objectives and Hypotheses:

The main objective of this study is to describe the demographic characteristics, medical background and treatment patterns of asthma patients, with a specific focus on SABA prescriptions. We investigate a possible correlation between SABA prescription patterns and patient health outcomes, symptom control (defined by the GINA Assessment of Asthma Control© 2017 Global Strategy Asthma Management and Prevention, all rights reserved. Use is by express license from the owner), and history of severe asthma exacerbations.

Methods:

This is a non-hypothesis driving, multi-country, cross-sectional, observational study describing SABA prescription patterns. Retrospective data were collected electronically in real-time, over a period starting from March 2019 to January 2020. The study included data collected from healthcare practitioners (HCPs) and selected asthma patients from the HCP's centres. The inclusion criteria for patients in the study were as follows: 12 years of age or older with a documented diagnosis of asthma; the absence of additional chronic respiratory diseases; a history of at least 3 consultations with their HCP or the HCP practice at the study start date; signed informed consent documentation by the patient or his/her legal guardian. Once the patient sample was established, data was collected through electronic Case Report Forms (eCRFs).

Our observational, cross-sectional study did not supply a specific medicinal product. Rather, information about patient exposure to treatments as part of routine care were sourced from eCRFs (e.g. exacerbation frequency, treatment, duration of diagnosis).

Results:

Patients who met all of the inclusion criteria described in the previous section were included in the final analysis group. This group included a total of 8351 patients from 215 healthcare centres located in 24 countries. The average patient age was 49.4 years and 68.1% of the group was female. In terms of asthma severity, 1,958 (23.4%) patients had a mild diagnosis, 6,388 (76.5%) patients had a moderate-to-severe diagnosis, and 5 (0.1%) patients were missing this value. In the past 12 months, 45.4% of patients had at least one severe exacerbation. We observed that SABA alone and ICS therapies were mainly used to treat mild patients, while ICS/LABA (fixed dose combination) was used to treat almost all moderate-to-severe patients. SABA was used as an add-on treatment for over half of the patients with a mild diagnosis as well as the patients with a moderate-to-severe diagnosis. Based on our analyses of asthma treatment patterns, we found that 37.9% of the patients included in the study had been prescribed 3 or more canisters of SABA, which is regarded as over-prescription. In general, mild asthma patients were more likely to receive prescriptions of 3 or more canisters of SABA than moderate-to-severe patients. Finally, we found that 43.3% of patients had asthma that was well-controlled, while 24.4% had asthma that was uncontrolled. For the next phase of our analysis, we separated our patients into four geographic regions, including Latin America, Middle East, Africa and Asia. The scope of our analysis for each region was similar to what was used in the full study sample. We found that, even with the significant diversity in patient characteristics, healthcare systems and geographies across the four regions, patients were overprescribed SABA and with increased SABA over-prescription frequently experienced worse health outcomes. We created three models to further investigate the association of SABA prescription patterns and health outcomes. Each of these models confirmed the adverse effect of SABA prescription of 3 or more canisters on the health outcomes of asthma patients. Specifically, increased SABA prescription was associated with worse asthma control, increased incidence rates of exacerbation and increased usage of OCS short bursts. Other covariables introduced in the models influenced patient health outcomes as well, including smoking status, healthcare insurance, number of co-morbidities, gender, GINA step and patient education level.

MILESTONES

Milestone	Planned date
July 2018	Development of Study Concept Sheet
October 2018	Final Protocol
December 2018	Study Start Up: contracts in place, regulatory submissions, initiation visits
March 2019	FSI
Mid-December 2019	LSI for overall analysis
Mid-January 2020	First Database lock
February 2020	TFLs
November 2020	LSI in last country
December 2020	Second Database Lock & Data Extraction
December 2020	Development of Analytic Datasets
December 2020	Statistical Analyses
December 2020	Abbreviated Study Report and manuscript