Study report	
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Assessment of treatment patterns of severe asthmatic patients across the Gulf region- SevEos study

SevEos: A cross-sectional, multi-centre, non-interventional, observational study aimed to describe the treatment patterns in 250 severe asthmatic patients across the Gulf region. In addition, the study determines the current level of asthma control and quality of life in these patients; describes the exacerbation patterns; and determines the current levels of blood eosinophils for the enrolled patients.

Sponsor: AstraZeneca FZ LLC – Gulf - GCC

Dubai HealthCare City, Ibn Sina, Block D

Building 27, Level 2, PO BOX 505070

Dubai, UAE

T: +971 4 3624888 ext:190
F: +971 4 3624898/99

Author:

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or special term	Explanation
ACQ	Asthma Control Questionnaire
AE	Adverse events
AED	Arab Emirates Dirhams
AIR	Asthma Insights and Reality
AIRGNE	Asthma Insights and Reality in the Gulf and the Near East
AQLQ(S)	Standardized version of the Asthma Quality of Life Questionnaire
AZ	AstraZeneca
BMI	Body mass index
CI	Confidence interval
CFC	Chlorofluorocarbon propellant
COPD	Chronic Obstructive Pulmonary Disease
CRF	Case report form
CRO	Clinical research organization
DPI	Dry powder inhaler
ECRHS	European Community Respiratory Health Survey
eCRF	electronic Case Report Form
ED	Emergency Department
EDC	Electronic data capture
EOS	Eosinophil
ER	Emergency Room
FeNO	Fraction of exhaled nitric Oxide
FEV_1	Forced Expiratory Volume in the first second
FVC	Forced Vital Capacity
GBD	Global Burden of Disease
GCP	Good Clinical Practices
GERD	Gastroesophageal reflux disease
GINA	Global Initiative for Asthma
HCRU	Health Care Resource Use
HDM	House Dust Mite
HFA	Hydrofluoroalkane propellant
ICF	Informed consent form
ICS	Inhaled Corticosteroids

Abbreviation or special term	Explanation
IgE	Immunoglobulin E
IL	Interleukins
IQR	Interquartile range
ISAAC	International Study of Asthma and Allergies in Childhood
IU/mL	International Units per Millilitre
KD	Kuwaiti Dinar
LABA	Long-Acting Beta Agonist
LAMA	Long-Acting Muscarinic Antagonist
LTRA	Leukotriene Receptor Antagonist
OCS	Oral Corticosteroids
OMR	Omani rial
PEF	Peak Expiratory Flow
ppb	Parts per billion
QASMA	Qatar Asthma in Adult
QoL	Quality of Life
SABA	Short-Acting Beta-Agonist
SAMA	Short-Acting Muscarinic Antagonists
SAS	Statistical Analysis Software
SD	Standard deviation
SLIT	Sublingual immunotherapy
TMF	Trial Master File
UAE	United Arab Emirates
USD	United States Dollar
Vit D	Vitamin D

RESPONSIBLE PARTIES

Name	Professional title	Role in study	Affiliation	E-mail address

STUDY REPORT SYNOPSIS

Assessment of treatment patterns of severe asthmatic patients across the Gulf region- SevEos study

SevEos: A cross-sectional, multi-centre, non-interventional, observational, study aimed to describe the treatment patterns in 250 severe asthmatic patients across the Gulf region. In addition, the study determines the current level of asthma control and quality of life in these patients; describes the exacerbation patterns; and determines the current levels of blood eosinophils for the enrolled patients.

Milestones:	First Patient In: 31 December 2017 Last Patient Out: 03 January 2019 Data Base Lock: 15 April 2019 Final Study Report: 26 March 2020
Phase of development:	Observational, Non-Interventional
Sponsor:	AstraZeneca Gulf - GCC
Author:	

This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.

Background/rationale:

Due to scarcity of data on current treatments in patients with severe asthma across the Gulf region, it was decided to conduct this study "Assessment of treatment patterns of severe asthmatic patients across the Gulf region" with a particular focus on the role of blood eosinophil (EOS) levels in this population.

Objectives:

Primary Objective

To describe the treatment patterns of severe asthmatic patients across four Gulf countries during the past year.

Secondary Objectives

1. To determine the current level of asthma control in these patients. In addition, a comparison of uncontrolled asthma between those with a normal eosinophilic count and those with an eosinophilic count ≥ 300 cell/µl were made.
2. To describe the frequency of exacerbations during the past year.
3. To assess the current quality of life (QoL) of these patients.
4. To determine the current and past year levels of blood eosinophils, and the percentage of patients with elevated eosinophilic level ≥ 150 cells/µL and ≥ 300 cells/µL
5. To determine the past year levels of serum Immunoglobulin E (IgE).

Exploratory objective

To determine the past year levels of other inflammatory biomarkers like periostin and fraction of exhaled nitric oxide (FeNO).

Study design:

SevEos was a cross-sectional, multi-centre, non-interventional study. This study was designed to capture real-world data on patients' characteristics and the clinical management of patients with severe asthma.

Data source:

In most cases, the source documents were contained in the patient's medical record and data collected on the case report forms (CRFs) matched the data in the medical records. In some cases, the CRF, or part of the CRF, also served as source documents. In these cases, a document was available at the investigator's site and clearly identified those data that were recorded in the CRF, and for which the CRF stood as the source document.

Study population:

The study population included diagnosed severe asthmatic patients. The study aimed to enrol approximately 250 patients from a total of approximately 9-12 sites in 4 countries across the

Gulf region (Kuwait, Oman, United Arab Emirates [UAE], and Qatar), over a 12-month recruitment period.

Inclusion criteria:

Patients who met the following criteria were considered for enrolment:

1. Age above 12 years.
2. Body weight of ≥ 40 kg.
3. Diagnosed by a physician with severe asthma, who requires regular treatment with medium or high dosage ICS (patients aged 12-17 years) OR high-dosage ICS plus LABA for at least 1 year before enrolment. [Note that the value of the medium/high dosage is dependent on the type of ICS.]

Exclusion criteria:

Patients who met any of the following criteria were excluded from the study:

1. Patient refuses to consent.
2. Another clinically important pulmonary disease is considered to be the primary diagnosis, other than severe asthma (i.e.: Chronic Obstructive Pulmonary Disease [COPD], major bronchiectasis, active tuberculosis, and other conditions considered by the Principal Investigator).
3. Mentally disabled patient or inability to understand the study questions.
4. Unable to read/write.

Statistical methods:

The primary objective was addressed through 3 statistical methods: (1) Descriptive statistics on treatment patterns during the past 12 months; (2) Time-to-event analyses to assess the patients' time to progression between Global Initiative for Asthma (GINA) treatment steps (Step 4 to Step 5 and Step 5 to Step 4) ; and (3) Sankey diagram to illustrate treatment changes from baseline to 12 months.

Descriptive statistics on the Asthma Control Questionnaire (ACQ) were provided to assess current level of asthma control. Comparison of eosinophil count (normal eosinophilic count <300 cells/µL and eosinophilic count ≥ 300 cell/µl) between uncontrolled vs. controlled asthma patients was assessed with Chi-square test providing relative p-values and 95% CI. Additionally, descriptive statistics were provided on: frequency of asthma exacerbation in the past 12 months; QoL as assessed through the standardized version of the Asthma Quality of Life Questionnaire (AQLQ[S]); and levels of blood eosinophils, serum IgE and FeNO levels in the past 12 months.

Results:

A total of 243 (96.4%) patients were enrolled in the study. Most of the patients were enrolled from Kuwait (n=88; 36.2%), followed by Oman (n=57; 23.5%), UAE (n=51; 20.9%) and Qatar (n=47; 19.4%).

Overall, ICS/LABA combination was the most commonly used asthma medication (n=240; 98.8%), followed by LTRA (n=190; 78.2%), biologics (n=120; 49.4%), and LAMA (n=118;48.6%). In total there were 61 patients who progressed from GINA step 4 to 5 (from the time of step 4 diagnosis up to the enrolment date). The median (95% CI) time to progress from GINA step 4 to 5 was 34.5 (24.3, 62.6) months. There were no patients who moved from GINA step 5 to 4 in this study. There were no observed treatment group switches over the past 12 months.

Overall, the majority of patients had uncontrolled asthma: ACQ score of >1.25 (n=173; 71.2%). There were 31 (12.8%) patients with borderline uncontrolled asthma: ACQ score >0.75 - ≤1.25; and 35 (14.4%) patients with controlled asthma: ACQ score ≤0.75. There was no statistically significant difference in eosinophil count between the uncontrolled vs. controlled asthma groups (p=0.69). Overall, the majority of patients (n=206; 84.8%) experienced at least one exacerbation over the past 12 months, and 129 (53.1%) patients experienced 2 or more exacerbations. A total of 56 (23.1%) patients responded they were at least "moderately limited" in relation to all activities performed during the last 2 weeks, per the AQLQ(S).

Overall, most of the patients had at least one blood eosinophil measurement during the past 12 months (n=212; 87.2%). Almost half of all patients had 2 eosinophil measurements (n=112; 46.1%). There were only 53 (21.8%) patients who had 3 eosinophil measurements; all other measurements (measurements 4 to 10), were each undertaken by less than 10% of patients. In total, 439 blood eosinophil measurements were conducted over the past 12 months. The majority of these eosinophil measurements were >300 cells/µL (n=183; 41.7%), followed by 150-300 cells/µL (n=138; 31.4%), and <150 cells/µL (n=118; 26.9%). Overall, most patients had at least one serum IgE measurement during the past 12 months (n=148; 60.9%). There were few patients with second (n=17; 7.0%) and third measurements (n=2; 0.8%). In total, 167 IgE measurements were conducted over the past 12 months. The majority of the IgE measurements were ≥ 30 IU/mL (n=157; 94.0%) and only 10 (6.0%) of IgE measurements were <30 IU/mL. This study did not identify any recordings of periostin measurements during the past 12 months. FeNO levels were measured a maximum of 2 times over the past 12 months among patients. Overall, there were only 38 (15.6%) patients with a first FeNO measurement and only 1 (0.4%) patient with a second FeNO measurement. The mean (SD) for the 1st FeNO measurement was 45.7 (46.0) parts per billion (ppb).

Conclusion: