Clinical Study Report Synopsis	
Drug Substance	NA
Study Code	D8111R00016
Edition Number	1.0
Date	14 March 2024
EudraCT Number	
NCT Number	05282017

LatInamerican Vaccine Effectiveness against hospitalizations due to circulating COVID-19 VoC RWE study (LIVE)

Study dates:	First subject enrolled: 01 Feb 2022 Last subject last visit: 19 Apr2023
Phase of development:	Non Interventional
International -Cordinating Investigator:	*NA*
Sponsor's Responsible Medical Officer:	Medical Director LatAm AstraZeneca S.A. de C.V.

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centre(s)

Country	Site ID	Site name
Brazil	BRA01	Instituto IDOR
Brazil	BRA02	Instituto IDOR
Brazil	BRA03	Instituto IDOR
Colombia	COL01	Fundación Neumológica Colombiana
Colombia	COL03	Centro de Estudios en Infectología Pediátrica S.A.S.
Costa Rica	CRC01	Instituto de Investigaciones en Ciencias Médicas (ICIMED)
Panama	PAN01	INDICASAT
Mexico	MEX01	Hospital Agustin O´Horan
Mexico	MEX02	Hospital Civil Guadalajara
Mexico	MEX03	Hospital de Especialidades Centro Médico Nacional Siglo XXI

Publications

Abstract presented at SLIPE 2023 (Clinical Characteristics of hospitalized COVID-19 from a real-world study of AZD1222 vaccine effectiveness (VE) in Latin America).

Objectives and criteria for evaluation

Table S1 Objectives and Endpoints
Co-Primary
• To estimate overall VE against hospitalisation due to severe COVID-19 disease among subjects who have been vaccinated with at least 1 dose with AstraZeneca COVID-19 Vaccine, among those subjects who belong/ed to target group(s) for vaccination.
• To estimate overall VE against hospitalisation due to severe COVID-19 among subjects who have been vaccinated fully vaccinated with the AstraZeneca COVID-19 Vaccine, among those subjects who belong/ed to target group(s) for vaccination.
Secondary
• To describe AstraZeneca and other COVID-19 vaccines variant-specific effectiveness against hospitalisation due to severe COVID-19 among subjects who have been vaccinated with at least 1 dose of existing vaccines at each country. • To describe overall and variant-specific VE against hospitalisation due to severe COVID-19 disease among subjects vaccinated with at least 1 dose of the AstraZeneca and/or other COVID-19 vaccines by type(s) of vaccine received, number of doses, dose interval, and time since vaccination. • To describe overall and variant-specific VE against hospitalisation due to severe COVID-19 disease among subjects vaccinated with 1 dose/fully vaccinated with the AstraZeneca COVID-19 and other COVID-19 vaccines available Vaccine by age group, other subgroups of interest (e.g. immunocompromised or other specific co-morbid conditions), and HIV status (for settings with more than 5% prevalence of HIV). • To describe overall and variant-specific VE against hospitalisation due to severe COVID-19 disease among healthcare workers who received 1 dose/fully vaccinated with the AstraZeneca COVID-19 and/or other COVID-19 vaccines. • To estimate VE against hospitalisation due to severe COVID-19 disease among subjects who have been vaccinated with 1 dose/ fully vaccinated with the AstraZeneca COVID-19 Vaccine and other COVID-19 vaccines available by level of disease severity.
Exploratory
To describe the characteristics of breakthrough cases of COVID-19 among fully vaccinated patients.

Study design

Observational prospective active-surveillance hospital-based study, with a test-negative case-control design (TNCC) of hospitalized COVID-19 like cases undergoing testing for SARS-CoV-2 by RT-PCR or rapid antigen test.

Target subject population and sample size

The sample size calculations was performed to guide study design and site selection to produce estimates that detect a minimum vaccine effectiveness (VE) estimate of 70% with sufficient precision (95% CI width of ≤50%).

A simulation-based sample size calculation was performed to estimate the required number of cases for crude and adjusted VE estimates. The adjusted sample size estimated were obtained by inflating the crude sample size by 20%.We proposed a total of 444 COVID +ve cases for each country, or 2,664 COVID +ve cases overall (across the 5 countries), for the study. This number would enable us to detect an anticipated VE of 70% with sufficient precision (95% CI width ≤50%) in all of the following scenarios:

- Low control: case ratios of ≥ 0.25 (i.e., 1 control for up to 4 cases)
- Overall vaccine coverage of ≥40% (40% fully vaccinated, 70% receiving at least 1 dose and 30% completely unvaccinated) and AZ-specific proportion of ≥30% (in each country)

Allow for adjusted vaccine effectiveness estimates (crude sample size estimates inflated by 20%)The sample size calculations was based on the following assumptions:

1) COVID-19 vaccination has no effect on test negative symptomatic disease aetiologies
2) COVID-19 vaccination coverage in test negative controls is similar to the overall vaccination coverage in the source population
3) High specificity RT-PCR testing is used to ascertain cases (and controls)
4) Overall health status is similar in test positive cases and test negative controls
5) The parameters used in the sample size estimation are consistent with the intended source population (e.g. age-restrictions etc.)

The sample size estimations for ChAdOx1 and other COVID-19 vaccines available VE estimates were challenging as they strongly depend on the SARS-CoV-2 attack rate and ChAdOx1 and other COVID-19 vaccines available vaccination coverage, with both parameters being difficult to predict. Due to these challenges, the study was not able to reach the required sample size to estimate VE of ChAdOx1

Investigational product and comparator(s): dosage, mode of administration and batch numbers

NA

Duration of treatment

NA

Statistical methods

The analytical dataset excluded individuals with incomplete data on vaccine exposure, specifically the brand and vaccination dates. Those without information on the administered vaccine brand and corresponding dates, as well as subjects vaccinated against SARS-CoV-2 without the AZ vaccine or with missing onset dates, were excluded.

The descriptive analysis focused on describing baseline characteristics, including demographics and risk factors, for the subjects included. The data was stratified by COVID-19 variants and country, with continuous variables summarized using means, standard deviations, medians, and interquartile range (IQR), and categorical variables presented as counts and proportions.

To address the primary objectives, crude and adjusted VE estimates of the COVID-19 AZ vaccine (compared to fully unvaccinated) were estimated. Country-specific analyses were performed, where the VE were estimated as follows:

VE = (1-OR) X100

The OR in the formula above denotes the odds ratio for AZ COVID-19 vaccination amongst COVID-19 positive cases against COVID-19 negative controls. For crude VE estimates, the OR will be unadjusted. For adjusted VE estimates, we used multivariable logistic regression models to obtain confounder-adjusted OR which we will then use in the VE calculation. The multivariable logistic regression model will include a list of pre-specified variables which is expected to include:

1. Sociodemographic factors: age at first vaccination, sex, socioeconomic group, chronic pre-existing medical conditions (including those that define vaccination priority groups, and those that have known to be associated with a lower VE)
2. Adherence to non-pharmaceutical interventions
3. Time: Date of illness onset

Study population

The study population consists of patients presenting at the participating hospitals during the study period who:

- Met the inclusion criteria, and didn't met the exclusion criteria

  AND

- Were hospitalized with COVID-19 like case

Conclusion(s)

The changing epidemiological situation and evolution of the COVID-19 pandemic, the changes in COVID-19 diagnostic indications and the increase of vaccination coverage due

booster doses had a negative impact on the number of potential subjects that could participate in the study, limiting the amount of data obtained and the statistical analysis to obtain results with statistical significance of the effectiveness of AstraZeneca's COVID-19 vaccine against hospitalizations due to circulating COVID-19 VoC in the five participating Latin American countries (786 subjects enrolled). This study collected data on the demographic characteristics of COVID-19 patients in Latin America and can support future decisions in these countries. The information obtained could also be helpful to tailor public health measures, vaccine development strategies, and treatment modalities.