Clinical trial results:
A Phase IIa Randomised, Double Blind, Placebo Controlled, Parallel Arm, Multi-Centre Study to Evaluate the Efficacy and Safety of Mitiperstat (AZD4831), for 12-24 Weeks, in Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD)

Summary

EudraCT number	2022-002441-18
Trial protocol	DK ES NL IT BG DE
Global end of trial date	30 October 2024

Results information

Result version number	v1
This version publication date	14 August 2025
First version publication date	14 August 2025

Trial information

Trial identification

Sponsor protocol code	D6582C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05492877
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 May 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 August 2024
Global end of trial reached?	Yes
Global end of trial date	30 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of mitiperstat (AZD4831) as compared to placebo on the time to first COPDCompEx event in patients with moderate to severe COPD.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the

Declaration of Helsinki and are consistent with International Council for Harmonisation (ICH)/Good Clinical Practice (GCP), and applicable regulatory requirements. All participant must meet all inclusion criteria and not meet any exclusion criteria before receiving investigational product. IDMC was formed to monitor potential risk in the study

Background therapy:

Participants need to be on stable regimen of triple therapy or dual therapy for ≥ 3 months prior to enrolment (change of inhaler device or change of medication in the same drug class is allowed). Triple therapy may consist of an appropriate combination of ICS + LABA + LAMA. Dual therapy consists of either inhaled ICS + LABA or LABA + LAMA where the treating physician deems the participant unsuitable for ICS (eg, blood eosinophil count ≤ 100 cells/μL on 2 separate occasions, or on the basis of previous or perceived risk of significant AEs from ICS-based therapy, such as previous episodes of pneumonia or significant oral candidiasis).

Evidence for comparator:

Not applicable as there was no comparator arm in the study

Actual start date of recruitment	14 November 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	United States: 41
Country: Number of subjects enrolled	Bulgaria: 28
Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Türkiye: 20
Country: Number of subjects enrolled	Denmark: 34
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	United Kingdom: 52
Country: Number of subjects enrolled	Argentina: 26
Country: Number of subjects enrolled	Mexico: 14

Country: Number of subjects enrolled	South Africa: 10
Country: Number of subjects enrolled	Germany: 55
Worldwide total number of subjects	381
EEA total number of subjects	194

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	158
From 65 to 84 years	223
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 101 centers in 14 countries (Argentina, Bulgaria, Canada, Denmark, Germany, Italy, Mexico, Netherlands, Poland, South Africa, Spain, Turkey, UK and USA).

Pre-assignment

Screening details:

A total of 381 participants were randomized and received at least one dose of study drug.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Blinding implementation details:

Participant was randomised using an interactive web response system to receive either 5mg mitiperstat or placebo. Participants, investigators and the sponsors are blinded with regard to the actual dose information.

Arms

Are arms mutually exclusive?	Yes
Arm title	Mitiperstat

Arm description:

Participants received an oral tablet of mitiperstat 5mg once daily.

Arm type	Experimental
Investigational medicinal product name	Mitiperstat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg once daily

Arm title	Placebo

Arm description:

Participants receive an oral tablet of placebo matched to mitiperstat once daily.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily

Number of subjects in period 1	Mitiperstat	Placebo
Started	189	192
Treated	189	192
Completed	165	170
Not completed	24	22
Adverse event, serious fatal	1	-
Physician decision	1	2
Consent withdrawn by subject	3	7
Adverse event, non-fatal	11	7
Lost to follow-up	1	1
Reason not specified	6	4
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Mitiperstat
Reporting group description:	
Participants received an oral tablet of mitiperstat 5mg once daily.	
Reporting group title	Placebo
Reporting group description:	
Participants receive an oral tablet of placebo matched to mitiperstat once daily.	

Reporting group values	Mitiperstat	Placebo	Total
Number of subjects	189	192	381
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	75	83	158
From 65-84 years	114	109	223
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	66.2	65.7	
standard deviation	± 6.65	± 7.03	-
Sex: Female, Male Units:			
Female	77	74	151
Male	112	118	230
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	26	27	53
Not Hispanic or Latino	163	165	328
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	3
White	182	183	365
More than one race	0	0	0
Unknown or Not Reported	3	6	9

End points

End points reporting groups

Reporting group title	Mitiperstat
Reporting group description:	
Participants received an oral tablet of mitiperstat 5mg once daily.	
Reporting group title	Placebo
Reporting group description:	
Participants receive an oral tablet of placebo matched to mitiperstat once daily.	

Primary: To evaluate the effect of mitiperstat (AZD4831) as compared to placebo on the time to first COPD Composite Exacerbation (CompEx) event in patients with moderate to severe COPD.

End point title	To evaluate the effect of mitiperstat (AZD4831) as compared to placebo on the time to first COPD Composite Exacerbation (CompEx) event in patients with moderate to severe COPD.
End point description:	
COPDCompEx is a composite endpoint of exacerbations and events defined from participant e-Diaries and peak expiratory flow (PEF). COPDCompEx defined exacerbations as one or more of the following: hospitalization, emergency room visit, treatment with systemic corticosteroids (injected and/or oral), or treatment with antibiotics. Diary COPDCompEx events are defined by threshold and slope criteria being met for >= 2 consecutive days using the following diary and home spirometry variables: overall symptom rating, night-time awakenings due to symptoms, reliever medication use, PEF. COPDCompEx also includes patient withdrawals for treatment failure. The analysis population used was the Full Analysis Set, which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation	
End point type	Primary
End point timeframe:	
From baseline to up to 24 weeks	

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: Participants				
Count of Participants with a COPDCompEx event	125	125		

Statistical analyses

Statistical analysis title	Cox proportional hazard model
Comparison groups	Mitiperstat v Placebo

Number of subjects included in analysis	381
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.599 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.071
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.869
upper limit	1.32

Notes:

[1] - The p-value was based on a 2-sided log rank test stratified by region

Secondary: To assess the PK of mitiperstat (AZD4831) in patients with moderate to severe COPD

End point title	To assess the PK of mitiperstat (AZD4831) in patients with moderate to severe COPD[2]

End point description:

Measurement of Time to Reach Maximum Plasma Concentration (Tmax) at week 12.

The analysis population used was the PK set which included all participants who had received mitiperstat and had evaluable PK data for mitiperstat, with no important protocol deviations that were thought to have impacted the analysis of the PK data.

End point type	Secondary

End point timeframe:

At week 12

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There is no PK data for placebo arm. There is no PK data at baseline

End point values	Mitiperstat			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: hours				
median (full range (min-max))	1.292 (0.42 to 2.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: To assess the pharmacokinetics (PK) of mitiperstat (AZD4831) in patients with moderate to severe COPD.

End point title	To assess the pharmacokinetics (PK) of mitiperstat (AZD4831) in patients with moderate to severe COPD.[3]

End point description:

Measurement of Maximum Plasma Concentration (Cmax) at week 12.

The analysis population used was the PK set which included all participants who had received mitiperstat

and had evaluable PK data for mitiperstat, with no important protocol deviations that were thought to have impacted the analysis of the PK data.

End point type	Secondary

End point timeframe:

At week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There is no PK data for placebo arm. There is no PK data at baseline

End point values	Mitiperstat			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: nmol/L				
geometric mean (geometric coefficient of variation)	38.786 (± 39.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the effect of mitiperstat (AZD4831) as compared to placebo on the time to first moderate or severe exacerbation.

End point title	To evaluate the effect of mitiperstat (AZD4831) as compared to placebo on the time to first moderate or severe exacerbation.

End point description:

A COPD exacerbation was considered moderate if it required treatment with systemic corticosteroids and/or antibiotics for at least 3 days or resulted in emergency room visit< 24 hours requiring intensive treatment; and did not result in hospitalization or death.
A COPD exacerbation was considered severe if it resulted in hospitalization (defined as an inpatient admission ≥ 24 hours in the hospital, an observation area, the emergency department, or other equivalent healthcare facility depending on the country and healthcare system) or death due to COPD.

The analysis population used was the Full Analysis Set (FAS), which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation.

End point type	Secondary

End point timeframe:

From baseline to up to week 24

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: Participants				
Count of participants with an exacerbation event	53	44		

Statistical analyses

Statistical analysis title	Cox proportional hazard model
Comparison groups	Mitiperstat v Placebo
Number of subjects included in analysis	381
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.234
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.882
upper limit	1.726

Secondary: To assess the effects of mitiperstat (AZD4831) as compared to placebo on post-bronchodilator (BD) forced expiratory volume in the first second (FEV1) in patients with moderate to severe COPD.

End point title	To assess the effects of mitiperstat (AZD4831) as compared to placebo on post-bronchodilator (BD) forced expiratory volume in the first second (FEV1) in patients with moderate to severe COPD.

End point description:

The mean change from baseline in Post-BD FEV1 at Week 12 was estimated using a repeated measures mixed effects analysis of covariance. Only subjects with non-missing covariates are included in the analysis. FEV1 was measured by spirometry at clinic.

The analysis population used was the Full Analysis Set (FAS), which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation.

End point type	Secondary

End point timeframe:

From baseline to week 12

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	136		
Units: Litre				
least squares mean (standard error)	-0.049 (± 0.0178)	-0.031 (± 0.0175)		

Statistical analyses

No statistical analyses for this end point

Secondary: To assess the effect of mitiperstat (AZD4831) compared to placebo on respiratory symptoms in patients with moderate to severe COPD - EXACT.

End point title	To assess the effect of mitiperstat (AZD4831) compared to placebo on respiratory symptoms in patients with moderate to severe COPD - EXACT.

End point description:

Change from baseline in EXAcerbations of Chronic Pulmonary Disease Tool (EXACT) which is a 14-item ePRO instrument developed to assess the frequency, severity and duration of COPD exacerbations. It has a theoretical range of 0 to 100, with higher values indicating a more severe condition. The EXACT will be performed at on-site visits using the e-Diary.

The analysis population used was the Full Analysis Set (FAS), which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation.

End point type	Secondary

End point timeframe:

From baseline to week 12 and week 24

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: Units on a scale				
least squares mean (standard error)				
Week 12	0.1 (± 0.97)	-2.4 (± 0.95)		
Week 24	-1.9 (± 1.32)	-3.7 (± 1.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: To assess the effect of mitiperstat (AZD4831) compared to placebo on respiratory symptoms in patients with moderate to severe COPD - BCSS.

End point title	To assess the effect of mitiperstat (AZD4831) compared to placebo on respiratory symptoms in patients with moderate to severe COPD - BCSS.

End point description:

Change from baseline to Week 12 and week 24 in mean Breathlessness, Cough and Sputum Scale (BCSS) score is reported. The BCSS was a 3-item daily diary that assesses the severity of the 3 symptoms: breathlessness, sputum, and cough, each on a 5-point Likert scale ranging from 0 (no symptoms) to 4 (severe symptoms). Item scores were summed to yield a total score ranging from 0 to 12; wherein higher total score indicated more severe symptoms. The BCSS was captured each evening via eDiary.

The analysis population used was the Full Analysis Set (FAS), which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation.

End point type	Secondary

End point timeframe:

From baseline to week 12 and week 24

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: Units on a scale				
least squares mean (standard error)				
Week 12	0.16 (± 0.130)	0.15 (± 0.127)		
Week 24	0.11 (± 0.166)	-0.17 (± 0.172)		

Statistical analyses

No statistical analyses for this end point

Secondary: To assess the effect of mitiperstat (AZD4831) compared to placebo in disease impact in patients with moderate to severe COPD.

End point title	To assess the effect of mitiperstat (AZD4831) compared to placebo in disease impact in patients with moderate to severe COPD.

End point description:

Change from baseline to Week 12 and week 24 in cough Visual Analogue Scale (VAS) score is reported. Participants were asked to complete a cough severity VAS (100-point linear scale marked with a horizontal line by the participant, with 0 representing ''no cough'' and 100 representing "worst cough") that measured subjective assessment by the participant of the prior 24 hrs for severity of cough symptoms. It was completed each evening in the eDiary.

The analysis population used was the Full Analysis Set (FAS), which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation.

End point type	Secondary

End point timeframe:

From baseline to week 12 and week 24

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: Units on a scale				
least squares mean (standard error)				
Week 12	-1.25 (± 1.183)	-3.05 (± 1.160)		
Week 24	-2.64 (± 1.540)	-3.48 (± 1.562)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 in total COPD Assessment Test (CAT)

End point title	Change from baseline to Week 12 in total COPD Assessment Test (CAT)

End point description:

COPD Assessment Test (CAT) is designed to measure how COPD impacts on a patient's daily life and how this might change over time. It consists of 8 questions that ask the patient to rate items relating to symptoms and impact on quality of life (such as normal activity and sleep). Each question is performed on a 5-point Likert scale from 0 (no symptoms/no impact) to 5 (severe symptoms/impact). The CAT will be completed by participants at on-site visits using the e-Diary.

The analysis population used was the Full Analysis Set (FAS), which included all randomized participants who received at least one dose of study intervention. The 'while on treatment' estimand strategy was followed, meaning that if an intercurrent event occurred, all subsequent data for that subject was excluded from the evaluation.

End point type	Secondary

End point timeframe:

From baseline to Week 12

End point values	Mitiperstat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	134		
Units: Units on a scale				
least squares mean (standard error)	-1.2 (± 0.62)	-1.2 (± 0.64)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until the end of the follow-up period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	PLACEBO
Reporting group description: -	
Reporting group title	AZD4831
Reporting group description: -	

Serious adverse events	PLACEBO	AZD4831	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 192 (6.77%)	23 / 189 (12.17%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour pulmonary			
subjects affected / exposed	1 / 192 (0.52%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 192 (0.52%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Carotid artery thrombosis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	5 / 192 (2.60%)	14 / 189 (7.41%)	
occurrences causally related to treatment / all	0 / 5	1 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 192 (0.52%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 192 (1.04%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			

subjects affected / exposed	1 / 192 (0.52%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	0 / 192 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 192 (1.56%)	5 / 189 (2.65%)	
occurrences causally related to treatment / all	1 / 3	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 192 (0.52%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	PLACEBO	AZD4831	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 192 (23.44%)	52 / 189 (27.51%)	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	36 / 192 (18.75%)	45 / 189 (23.81%)	
occurrences (all)	55	62	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 192 (6.25%)	10 / 189 (5.29%)	
occurrences (all)	14	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2022	Clinical Study Protocol Version 2. Version 1 of the protocol was not published or used. Version 2 was the first version to be submitted to any Health Authority/Ethics committee
13 January 2023	Clinical Study Protocol Version 3. Exclusion criterion which excluded participants with a positive diagnostic lateral flow test for SARS-CoV-2 at screening was removed (exclusion criterion 1). Changes were made in response to the requirements of various health authorities. For example, contraceptive requirements.
28 April 2023	Clinical Study Protocol Version 4. To add the optional substudies which affect only selected sites in selected countries where the substudies will be conducted. A substantial change was made to remove history of treatment with cardiotoxic medications from the list of exclusion criteria (exclusion criterion 22).
07 December 2023	Clinical Study Protocol Version 5. To increase the sample size, due to changes in statistical assumptions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No significant methodological limitations, protocol deviations or study conduct changes were identified that may have impacted upon the validity or interpretation of the results

Notes: