Clinical trial results:
A Multicenter, Open-label, Single-arm, Expanded Access Protocol of Sotorasib (AMG 510) for the Treatment of Subjects in Select European Countries with Previously Treated Locally Advanced and Unresectable or Metastatic Non-small Cell Lung Cancer with KRAS p.G12C Mutation

Summary

EudraCT number	2020-005279-11
Trial protocol	IT ES
Global end of trial date	11 August 2022

Results information

Result version number	v1 (current)
This version publication date	21 May 2023
First version publication date	21 May 2023

Trial information

Trial identification

Sponsor protocol code	20190442

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, medinfo@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, medinfo@amgen.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	11 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to provide expanded access and to characterize the safety profile of sotorasib in participants with previously treated locally advanced unresectable/metastatic non-small cell lung cancer (NSCLC) with Kirsten rat sarcoma viral oncogene homolog (KRAS) p.G12C mutation.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 75
Country: Number of subjects enrolled	Spain: 44
Worldwide total number of subjects	119
EEA total number of subjects	119

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)	45
From 65 to 84 years	72
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 40 centers in Italy and Spain from 08 July 2021 to 11 August 2022.

Pre-assignment

Screening details:

A total of 130 participants were screened for enrollment into this study. Of those, 119 participants were enrolled. A total of 118 participants received at least 1 dose of sotorasib.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Sotorasib

Arm description:

Participants received sotorasib 960 mg orally once daily (QD). Treatment cycles were 28 days long, with no treatment-free intervals. Participants were treated with sotorasib until disease progression, intolerance of protocol treatment, start of another anti-cancer therapy, death, withdrawal of informed consent, or for up to 6 months (if in accordance with local laws and regulations) of treatment for an individual participant after sotorasib received marketing authorization approval for the treatment of NSCLC in the participant's country, whichever occurred first. Participants with previously treated locally advanced unresectable/metastatic NSCLC with KRAS p.G12C mutation who were not eligible or did not have the opportunity to enroll in an ongoing sotorasib interventional clinical study and who met the eligibility criteria outlined in the protocol were considered for participation in this study.

Arm type	Experimental
Investigational medicinal product name	Sotorasib
Investigational medicinal product code	
Other name	AMG 510 Lumakras® Lumykras®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received sotorasib 960 mg once daily (QD) in each 28 day cycle.

Number of subjects in period 1	Sotorasib
Started	119
Completed	79
Not completed	40
Consent withdrawn by subject	2
Death	34
Lost to follow-up	4

Baseline characteristics

Reporting groups	
Reporting group title	Sotorasib

Reporting group description:

Participants received sotorasib 960 mg orally once daily (QD). Treatment cycles were 28 days long, with no treatment-free intervals. Participants were treated with sotorasib until disease progression, intolerance of protocol treatment, start of another anti-cancer therapy, death, withdrawal of informed consent, or for up to 6 months (if in accordance with local laws and regulations) of treatment for an individual participant after sotorasib received marketing authorization approval for the treatment of NSCLC in the participant's country, whichever occurred first. Participants with previously treated locally advanced unresectable/metastatic NSCLC with KRAS p.G12C mutation who were not eligible or did not have the opportunity to enroll in an ongoing sotorasib interventional clinical study and who met the eligibility criteria outlined in the protocol were considered for participation in this study.

Reporting group values	Sotorasib	Total	
Number of subjects	119	119	
Age Categorical Units: Subjects			
Adults (18-64 years)	45	45	
From 65-84 years	72	72	
85 years and over	2	2	
Age Continuous Units: years			
arithmetic mean	66.8		
standard deviation	± 8.5	-	
Gender Categorical Units: Participants			
Female	49	49	
Male	70	70	
Race Units: Subjects			
White	116	116	
Other races	3	3	
Ethnicity Units: Subjects			
Not Hispanic or Latino	103	103	
Hispanic or Latino	16	16	

End points

End points reporting groups

Reporting group title	Sotorasib

Reporting group description:

Participants received sotorasib 960 mg orally once daily (QD). Treatment cycles were 28 days long, with no treatment-free intervals. Participants were treated with sotorasib until disease progression, intolerance of protocol treatment, start of another anti-cancer therapy, death, withdrawal of informed consent, or for up to 6 months (if in accordance with local laws and regulations) of treatment for an individual participant after sotorasib received marketing authorization approval for the treatment of NSCLC in the participant's country, whichever occurred first. Participants with previously treated locally advanced unresectable/metastatic NSCLC with KRAS p.G12C mutation who were not eligible or did not have the opportunity to enroll in an ongoing sotorasib interventional clinical study and who met the eligibility criteria outlined in the protocol were considered for participation in this study.

Primary: Number of Participants Who Experienced a Treatment-Emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced a Treatment-Emergent Adverse Event (TEAE)[1]

End point description:

TEAEs were events categorized as Adverse Events (AEs) starting on or after first dose of investigation product. An AE was defined is any untoward medical occurrence in a clinical study participant irrespective of a causal relationship with the study treatment.

The full analysis set (FAS) included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Primary

End point timeframe:

Up to approximately 1 year

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary endpoint.

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Participants	112			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Treatment-related Treatment-emergent AE

End point title	Number of Participants Who Experienced a Treatment-related Treatment-emergent AE[2]

End point description:

Treatment-related adverse events are treatment-emergent adverse events considered related to investigational product by the investigator.

The FAS included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Primary

End point timeframe:

Up to approximately 1 year

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary endpoint.

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Participants	77			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a TEAE Leading to Discontinuation of Sotorasib

End point title	Number of Participants Who Experienced a TEAE Leading to Discontinuation of Sotorasib[3]

End point description:

The FAS included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Primary

End point timeframe:

Up to approximately 1 year

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary endpoint.

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Participants	19			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a TEAE of Interest

End point title	Number of Participants Who Experienced a TEAE of Interest[4]

End point description:

TEAEs of interest included hepatotoxicity, pneumonitis, and renal toxicity.

The FAS included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Primary

End point timeframe:

Up to approximately 1 year

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary endpoint.

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Participants	43			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Serious TEAE

End point title	Number of Participants Who Experienced a Serious TEAE[5]

End point description:

A serious adverse event is defined as any untoward medical occurrence that, meets at least 1 of the following serious criteria: results in death, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or other medically important serious event.

The FAS included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Primary

End point timeframe:

Up to approximately 1 year

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary endpoint.

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Participants	48			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with each KRAS p.G12C Testing Modality

End point title	Number of participants with each KRAS p.G12C Testing Modality

End point description:

KRAS p.G12C testing modalities used: next-generation sequencing, polymerase chain reaction, sanger sequencing, other.

The FAS included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Secondary

End point timeframe:

Screening (up to 28 days)

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Participants				
Next-generation sequencing	58			
Polymerase chain reaction	33			
Other	21			
Sanger sequencing	3			
Missing	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment of Sotorasib

End point title	Duration of Treatment of Sotorasib

End point description:

The FAS included all enrolled subjects who received at least 1 dose of sotorasib.

End point type	Secondary

End point timeframe:

Up to a maximum of 11.1 months

End point values	Sotorasib			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Months				
median (full range (min-max))	5.3 (0.1 to 11.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 1 year

Adverse event reporting additional description:

Adverse events were reported for the full analysis set, which included all enrolled subjects who received at least 1 dose of sotorasib (118 participants)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Sotorasib

Reporting group description:

Participants received sotorasib 960 mg orally once daily (QD). Treatment cycles were 28 days long, with no treatment-free intervals. Participants were treated with sotorasib until disease progression, intolerance of protocol treatment, start of another anti-cancer therapy, death, withdrawal of informed consent, or for up to 6 months (if in accordance with local laws and regulations) of treatment for an individual participant after sotorasib received marketing authorization approval for the treatment of NSCLC in the participant's country, whichever occurred first. Participants with previously treated locally advanced unresectable/metastatic NSCLC with KRAS p.G12C mutation who were not eligible or did not have the opportunity to enroll in an ongoing sotorasib interventional clinical study and who met the eligibility criteria outlined in the protocol were considered for participation in this study.

Serious adverse events	Sotorasib		
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 118 (40.68%)		
number of deaths (all causes)	33		
number of deaths resulting from adverse events	26		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-small cell lung cancer			
subjects affected / exposed	12 / 118 (10.17%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 10		
Metastases to central nervous system			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma stage IV			

subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Lung adenocarcinoma				
subjects affected / exposed	4 / 118 (3.39%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 4			
Vascular disorders				
Aortic aneurysm				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Pain management				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	2 / 118 (1.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pyrexia				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Sudden death				
subjects affected / exposed	2 / 118 (1.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Respiratory, thoracic and mediastinal disorders				
Respiratory failure				
subjects affected / exposed	2 / 118 (1.69%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pleuritic pain				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 118 (1.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchial obstruction				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Agitation				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Hallucination, visual				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Completed suicide				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Investigations				
Blood bilirubin increased				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Clavicle fracture				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardio-respiratory arrest				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	1 / 118 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Atrial fibrillation				

subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Oesophageal ulcer			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Intra-abdominal haematoma			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hypertransaminasaemia			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis of jaw			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			

subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
COVID-19			
subjects affected / exposed	2 / 118 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Respiratory tract infection			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Tumour lysis syndrome			
subjects affected / exposed	1 / 118 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Sotorasib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 118 (79.66%)		
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	16 / 118 (13.56%)		
occurrences (all)	36		
Blood bilirubin increased			
subjects affected / exposed	6 / 118 (5.08%)		
occurrences (all)	11		
Blood alkaline phosphatase increased			
subjects affected / exposed	13 / 118 (11.02%)		
occurrences (all)	23		
Aspartate aminotransferase increased			
subjects affected / exposed	17 / 118 (14.41%)		
occurrences (all)	30		
Alanine aminotransferase increased			
subjects affected / exposed	17 / 118 (14.41%)		
occurrences (all)	48		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 118 (12.71%)		
occurrences (all)	22		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	13 / 118 (11.02%)		
occurrences (all)	15		
Pain			
subjects affected / exposed	6 / 118 (5.08%)		
occurrences (all)	7		
Fatigue			
subjects affected / exposed	9 / 118 (7.63%)		
occurrences (all)	9		
Asthenia			

subjects affected / exposed occurrences (all)	24 / 118 (20.34%) 31		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 10 / 118 (8.47%) 10 6 / 118 (5.08%) 6 42 / 118 (35.59%) 77 10 / 118 (8.47%) 10 13 / 118 (11.02%) 18 19 / 118 (16.10%) 21		
Hepatobiliary disorders Hypertransaminasaemia subjects affected / exposed occurrences (all)	 6 / 118 (5.08%) 13		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 17 / 118 (14.41%) 18 7 / 118 (5.93%) 8		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 7 / 118 (5.93%) 8		

Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	6 / 118 (5.08%)		
occurrences (all)	10		
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 118 (6.78%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	15 / 118 (12.71%)		
occurrences (all)	20		
Hypokalaemia			
subjects affected / exposed	9 / 118 (7.63%)		
occurrences (all)	12		
Hypercholesterolaemia			
subjects affected / exposed	8 / 118 (6.78%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2021	The protocol was amended for the following reasons: • Removed microscopic examination from the urinalysis • Added language to address the risks/benefits assessment for COVID-19 • Added anti-programmed death-1 (PD-1)/anti-PD-1 ligand 1 (PD-L1) immunotherapy and docetaxel to inclusion criteria • Changed inclusion criteria for estimated glomerular filtration rate to ≥ 45 mL/min/1.73 m^2 • Removed dose modification guidelines for grade ≥ 3 thrombocytopenia, febrile neutropenia, and neutropenia lasting longer than 7 days, and grade 4 hemoglobin decrease
06 May 2021	The protocol was amended for the following reasons: • Added other anticancer therapies to schedule of activities to be collected at screening and safety follow-up visits • Added probability and adverse event rate to sample size determination section
11 January 2022	The protocol was amended for the following reasons: • Added interstitial lung disease/pneumonitis as key risk as determined by Amgen and for consistency with other studies within the sotorasib program • Added sotorasib dose modification guidelines for ILD/pneumonitis • Added details for reporting of serious adverse events after end of study • Added requirement for polymerase chain reaction for hepatitis C virus (HCV) ribonucleic acid (RNA) to confirm diagnosis if hepatitis C test positive • Clarified the definition of participant enrollment: when participant received first dose of sotorasib

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported