Clinical trial results:
A pilot study to assess the safety, tolerability, dose finding and efficacy ORY-1001 in combination with platinum-etoposide chemotherapy in patients with relapsed, extensive-stage disease small cell lung cancer

Summary

EudraCT number	2018-000469-35
Trial protocol	ES
Global end of trial date	11 September 2020

Results information

Result version number	v1 (current)
This version publication date	12 July 2023
First version publication date	12 July 2023

Trial information

Trial identification

Sponsor protocol code	CL03-ORY-1001SCLC

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oryzon Genomics S. A.
Sponsor organisation address	Carrer de Sant Ferran, 74, CORNELLA DE LLOBREGAT, Spain, 08940
Public contact	Douglas V. Faller, Oryzon Genomics S. A., 34 93 515 13 13, dfaller@oryzon.com
Scientific contact	Douglas V. Faller, Oryzon Genomics S. A., 34 93 515 13 13, dfaller@oryzon.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	15 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 September 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the maximum tolerated dose (MTD), schedule and recommended Phase II dose (RP2D) of ORY-1001 in combination with platinum-etoposide based chemotherapy (EP) in patients with relapsed, extensive-stage disease small cell lung cancer (ED SCLC). This will include characterization of ORY-1001 dose-limiting toxicities (DLTs) and overall safety profile in this population.

Protection of trial subjects:

In accordance with European Union RGPD 2016/679 of 27 April, 2016 the data were processed in accordance with the specifications outlined by the local law to ensure that requirements regarding personal data protection are met. If an external organization processed data on behalf of Oryzon, a contractual procedure was signed between Oryzon and the external organization to ensure compliance with the above-mentioned legislation. If applicable, the participation of patients in this study was reported to the appropriate local data protection agencies, in accordance with European Union RGPD 2016/679 of 27 April 2016 and Country-specific guidelines and laws (Spanish Organic Law 3/2018 of 5 December).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 December 2018
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	Spain: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	6
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 17 subjects were screened to obtain a total of 14 enrolled patients. Patients were assigned to any of the Cohorts by the Sponsor and the Medical Monitor according to the available data and the recruitment rate.

Pre-assignment

Screening details:

ICF for pre-screening specific procedures was obtained in order to confirm tumor biomarkers. If biomarkers positive an ICF was obtained before starting the study procedures.
A total of 17 patients signed informed consent. Three patients were screening failures and therefore only 14 patients were accrued in the study and started treatment.

Period 1

Period 1 title	Part 1 or dose-finding stage (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	1st TREATMENT SCHEME

Arm description:

Dose iadademstat = 60 µg/m2/d. For 4-6 cycles: first week etoposide/platinum + iadademstat; second and third week iadademstat.

Arm type	Experimental
Investigational medicinal product name	Iadademstat
Investigational medicinal product code	ORY-1001
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Dose iadademstat = 60 µg/m2/d. For 4-6 cycles: first week etoposide/platinum + iadademstat; second and third week iadademstat.

Investigational medicinal product name	Etoposide/platinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Platinum-etoposide was given per the SmPC

Arm title	Cohort A

Arm description:

Dose iadademstat = 60 µg/m2/d. Dosing Scheme #1

Arm type	Experimental
Investigational medicinal product name	Iadademstat
Investigational medicinal product code	ORY-1001
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Dose iadademstat = 60 µg/m2/d at second and third cycle week.

Investigational medicinal product name	Etoposide/platinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Platinum-etoposide was given per the SmPC

Arm title	Cohort B

Arm description:

Dose iadademstat = 60 µg/m2/d. Dosing Scheme #2

Arm type	Experimental
Investigational medicinal product name	Iadademstat
Investigational medicinal product code	ORY-1001
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Dose iadademstat = 60 µg/m2/d. For 4-6 cycles: first week etoposide/platinum + iadademstat; first and third cycle week

Investigational medicinal product name	Etoposide/platinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Platinum-etoposide was given per the SmPC

Arm title	Cohort C

Arm description:

Dose iadademstat = 45 µg/m2/d. Dosing Scheme #3

Arm type	Experimental
Investigational medicinal product name	Iadademstat
Investigational medicinal product code	ORY-1001
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Dose iadademstat = 45 µg/m2/d

Investigational medicinal product name	Etoposide/platinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Platinum-etoposide was given per the SmPC

Arm title	Cohort D

Arm description:

Dose iadademstat = 60 µg/m2/d. Dosing Scheme #4

Arm type	Experimental

Investigational medicinal product name	Iadademstat
Investigational medicinal product code	ORY-1001
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

Dose iadademstat = 60 µg/m2/d. For 4-6 cycles: Three weeks treatment.

Investigational medicinal product name	Etoposide/platinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Third week etoposide/platinum. Platinum-etoposide was given per the SmPC

Arm title	Cohort E

Arm description:

Dose iadademstat = 60 µg/m2/d. Dosing Scheme #5

Arm type	Experimental
Investigational medicinal product name	Iadademstat
Investigational medicinal product code	ORY-1001
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

From cycle 2 to 4 or 6: first week with etoposide/platinum and G-CSF administered on days 4, 5 and 6, starting the first dose at least 24 hours after the last dose of etoposide; second week iadademstat; no treatment in third week.

Investigational medicinal product name	Etoposide/platinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Platinum-etoposide was given per the SmPC

Number of subjects in period 1	1st TREATMENT SCHEME	Cohort A	Cohort B
Started	4	2	1
Completed	1	1	1
Not completed	3	1	0
Adverse event, serious fatal	1	-	-
Protocol deviation	2	1	-

Number of subjects in period 1	Cohort C	Cohort D	Cohort E
Started	1	3	3
Completed	1	3	2
Not completed	0	0	1
Adverse event, serious fatal	-	-	1

Protocol deviation	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Part 1 or dose-finding stage

Reporting group description: -

Reporting group values	Part 1 or dose-finding stage	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	64.79		
standard deviation	± 7.94	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	12	12	

Subject analysis sets

Subject analysis set title	Safety Analysis Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who have received at least one dose of any study treatment, whether prematurely withdrawn from the study or not, will be included in the safety analysis. Unless otherwise specified, the safety population will be the default analysis set used for this study.

Subject analysis set title	Efficacy Analysis Population
Subject analysis set type	Per protocol

Subject analysis set description:

All patients who have met all the selection criteria and have received at least one dose of study treatment. These patients will have at least screening/baseline data and one assessment of the response during the treatment.

Reporting group values	Safety Analysis Population	Efficacy Analysis Population	
Number of subjects	14	9	
Age categorical Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	64.79	64.00	
standard deviation	± 7.94	± 9.55	
Gender categorical Units: Subjects			
Female	2	1	
Male	12	8	

End points

End points reporting groups

Reporting group title	1st TREATMENT SCHEME
Reporting group description:	
Dose iadademstat = 60 µg/m2/d. For 4-6 cycles: first week etoposide/platinum + iadademstat; second and third week iadademstat.	
Reporting group title	Cohort A
Reporting group description:	
Dose iadademstat = 60 µg/m2/d. Dosing Scheme #1	
Reporting group title	Cohort B
Reporting group description:	
Dose iadademstat = 60 µg/m2/d. Dosing Scheme #2	
Reporting group title	Cohort C
Reporting group description:	
Dose iadademstat = 45 µg/m2/d. Dosing Scheme #3	
Reporting group title	Cohort D
Reporting group description:	
Dose iadademstat = 60 µg/m2/d. Dosing Scheme #4	
Reporting group title	Cohort E
Reporting group description:	
Dose iadademstat = 60 µg/m2/d. Dosing Scheme #5	
Subject analysis set title	Safety Analysis Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who have received at least one dose of any study treatment, whether prematurely withdrawn from the study or not, will be included in the safety analysis. Unless otherwise specified, the safety population will be the default analysis set used for this study.	
Subject analysis set title	Efficacy Analysis Population
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients who have met all the selection criteria and have received at least one dose of study treatment. These patients will have at least screening/baseline data and one assessment of the response during the treatment.	

Primary: Safety

End point title	Safety[1]
End point description:	
Safety	
End point type	Primary
End point timeframe:	
From ICF signature to 30 days after last dose study treatment	

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: Categorical variables were described using absolute and relative frequencies. Continuous variables were described using the mean, standard deviation, confidence interval of mean with 95%, median, percentiles 25th and 75th, minimum and maximum, including the total number of valid values.

End point values	1st TREATMENT SCHEME	Cohort A	Cohort B	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	1	1
Units: Adverse events				
Total AE	110	31	16	15
Total SAE	1	1	0	0
Total ADR	77	20	15	15
Total SADR	0	0	0	0

End point values	Cohort D	Cohort E	Safety Analysis Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	3	14	
Units: Adverse events				
Total AE	26	15	213	
Total SAE	5	2	9	
Total ADR	22	7	156	
Total SADR	4	1	5	

Statistical analyses

No statistical analyses for this end point

Primary: Tolerability

End point title	Tolerability[2]

End point description:

AE considered DLT

End point type	Primary

End point timeframe:

Firts treatment cycle

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: Categorical variables were described using absolute and relative frequencies. Continuous variables were described using the mean, standard deviation, confidence interval of mean with 95%, median, percentiles 25th and 75th, minimum and maximum, including the total number of valid values.

End point values	1st TREATMENT SCHEME	Cohort A	Cohort B	Cohort C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	1	1
Units: Number of DLTs				
Total DLT	1	0	1	0

End point values	Cohort D	Cohort E	Safety Analysis Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	3	14	
Units: Number of DLTs				
Total DLT	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor response according to RECIST version 1.1.

End point title	Tumor response according to RECIST version 1.1.

End point description:

The secondary efficacy endpoint of tumor response was assessed by the investigators following treatment with iadademstat and PE.

End point type	Secondary

End point timeframe:

Treatment period

End point values	Efficacy Analysis Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: Subjects				
Complete Response	0			
Partial Response	3			
First response not achieved	6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	1st Treatment scheme
Reporting group description: -	
Reporting group title	Cohort A
Reporting group description: -	
Reporting group title	Cohort B
Reporting group description: -	
Reporting group title	Cohort C
Reporting group description: -	
Reporting group title	Cohort D
Reporting group description: -	
Reporting group title	Cohort E
Reporting group description: -	

Serious adverse events	1st Treatment scheme	Cohort A	Cohort B
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	1	1	0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Infections and infestations			
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort C	Cohort D	Cohort E
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	1	1
Cardiac disorders			
Cardio-respiratory arrest			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Septic shock			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	1st Treatment scheme	Cohort A	Cohort B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
Investigations			
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
occurrences (all)	12	8	6
Neutrophil count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
occurrences (all)	3	3	5
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	3 / 4 (75.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
occurrences (all)	9	4	3
Neutropenia			
subjects affected / exposed	3 / 4 (75.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	9	0	0
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	9	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	7	1	0
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	1 / 1 (100.00%)
occurrences (all)	4	1	1
Constipation			
subjects affected / exposed	3 / 4 (75.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	3 / 4 (75.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	2 / 2 (100.00%)	0 / 1 (0.00%)
occurrences (all)	1	5	0
Cough			
subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	1 / 1 (100.00%)
occurrences (all)	2	1	1
Hypokalaemia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0

Non-serious adverse events	Cohort C	Cohort D	Cohort E
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Investigations			
Platelet count decreased			

subjects affected / exposed	1 / 1 (100.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	8	4	1
Neutrophil count decreased			
subjects affected / exposed	1 / 1 (100.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 1 (100.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	4	3	2
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	3 / 3 (100.00%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2019	Pre-Screening period, metastatic sample, changes inclusion criteria 2,3 and 4 and exclusion criteria 4 and 5. Discontinuation Reasons, toxicity management of platinum-based treatment exploratory Biomarkers, prophylaxis treatment with Filgrastim, Chemotherapy concentration.
25 March 2019	Change Part 1 – Finding dose stage: new dosing scheme
28 May 2019	Modifications in the v.3.0 protocol due to clarifications request from RA to substantial amendment nº 2 and include urinaltsis weekly.
15 July 2019	Change Part 1 – Finding dose stage: 2 new Cohorts and include 2 new sites
01 October 2019	Review scheme of Cohorts D and E and toxicity management. Change principal investigator IOR. Add new site. Cohorts A and B removed

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 March 2020	The sponsor decided to close the recruitment due to the slow pace of enrollment on May 2020, but closing was precipitated to February 2020 by the National health emergency situation caused by SARS-COV-2 (COVID-19).	-

Notes:

Limitations and caveats

None reported