Clinical trial results:
A randomized, blinded, placebo-controlled, Phase II trial of LEE011 in patients with relapsed, refractory, incurable teratoma with recent progression

Summary

EudraCT number	2014-000428-12
Trial protocol	ES FR NL DK IT
Global end of trial date	21 February 2018

Results information

Result version number	v1 (current)
This version publication date	06 September 2018
First version publication date	06 September 2018

Trial information

Trial identification

Sponsor protocol code	CLEE011X2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02300987
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	21 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This was a multi-center, randomized, double blind, placebo-controlled Phase II study to determine the efficacy and safety of treatment with ribociclib (LEE011) versus placebo in subjects with progressive relapsed, refractory incurable teratoma. Eligible subjects were randomized at a 2:1 ratio to ribociclib or placebo. Subjects received study drug until disease progression, unacceptable toxicity, death, or discontinuation from the study drug for any other reason (i.e. loss to follow-up or withdrawal of consent).
Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 February 2015
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	France: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	10
EEA total number of subjects	7

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were randomly assigned to Ribociclib or Placebo in a 2:1 ratio.
After 10 subjects were enrolled and treated, the recruitment was halted due to business reasons. There were no safety concerns which contributed to the decision to halt enrollment.

Pre-assignment

Screening details:

42 subjects were planned to be included (28 for the LEE011 arm and 14 for the Placebo arm). However the study was stopped prematurely with 10 patients randomized and treated in this study (8 in the ribociclib arm, 2 in the placebo arm).

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	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Blinding implementation details:

2:1 allocation ratio, LEE011 versus placebo

Arms

Are arms mutually exclusive?	Yes
Arm title	LEE011

Arm description:

600 mg daily dosing days 1-21 of a 28 day cycle

Arm type	Experimental
Investigational medicinal product name	Ribociclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

LEE011 200 mg hard gelatin capsule, 600 mg once daily on Days 1-21 of a 28-day cycle

Arm title	Placebo Arm

Arm description:

600 mg daily dosing days 1-21 of a 28 day cycle

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

Dosage and administration details:

Placebo 0 mg hard gelatin capsule, 600 mg once daily on Days 1-21 of a 28-day cycle

Number of subjects in period 1	LEE011	Placebo Arm
Started	8	2
Completed	2	0
Not completed	6	2
Physician decision	2	-
Consent withdrawn by subject	1	-
progressive disease	3	2

Baseline characteristics

Reporting groups	
Reporting group title	LEE011
Reporting group description:	
600 mg daily dosing days 1-21 of a 28 day cycle	
Reporting group title	Placebo Arm
Reporting group description:	
600 mg daily dosing days 1-21 of a 28 day cycle	

Reporting group values	LEE011	Placebo Arm	Total
Number of subjects	8	2	10
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)	8	2	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	32.3	40.5	
standard deviation	± 6.76	± 17.68	-
Sex: Female, Male Units: Subjects			
Female	0	0	0
Male	8	2	10
Race/Ethnicity, Customized Units: Subjects			
Caucasian|	4	1	5
Native American|	1	0	1
Unknown|	3	1	4

End points

End points reporting groups

Reporting group title	LEE011
Reporting group description:	
600 mg daily dosing days 1-21 of a 28 day cycle	
Reporting group title	Placebo Arm
Reporting group description:	
600 mg daily dosing days 1-21 of a 28 day cycle	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)[1]
End point description:	
Date of randomization to the date of the first documented progression or death due to any causeas per RECIST v1.1 (by local investigator assessment).	
End point type	Primary
End point timeframe:	
At 24 months	

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: After 10 subjects were enrolled and treated, the recruitment was halted due to business reasons.There were no safety concerns which contributed to the decision to halt enrollment. Limited efficacy analyses were performed. The primary endpoint of the study was PFS. The statistical analysis of PFS was conducted. Only median and 90% CI are provided (if estimable).

End point values	LEE011	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2		
Units: Days				
median (confidence interval 90%)	999 (2.9 to 999)	4.7 (1.9 to 7.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR)

End point title	Best Overall Response (BOR)
End point description:	
as per RECIST v1.1	
End point type	Secondary
End point timeframe:	
At 24 months	

End point values	LEE011	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2		
Units: Percentage of Participants				
Stable Disease (SD)|	100	50		
Progressive Disease (PD)|	0	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)
End point description: as per RECIST v1.1	
End point type	Secondary
End point timeframe: At 24 months	

End point values	LEE011	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 36.9)	0 (0.0 to 84.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description: as per RECIST v1.1	
End point type	Secondary
End point timeframe: At 24 months	

End point values	LEE011	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2		
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (63.1 to 100.0)	50.0 (1.3 to 98.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

End point type	Secondary

End point timeframe:

At 27 months

End point values	LEE011	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2[2]		
Units: Percentage of Participants				
number (confidence interval 95%)	87.5 (38.7 to 98.1)	999 (999 to 999)		

Notes:

[2] - Due to the low number of events, the confidence interval are not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Overal Survival Rate

End point title	Overal Survival Rate

End point description:

End point type	Secondary

End point timeframe:

At 27 months

End point values	LEE011	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2[3]		
Units: Percentage of Participants				
number (confidence interval 95%)	87.5 (38.7 to 98.1)	999 (999 to 999)		

Notes:

[3] - Due to the low number of events, the confidence interval are not estimable.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events that occurred within 30 days from the last dose of study drug treatment are reported in this record, from date of First Patient First Treatment until Last Patient Last Visit up to approximately 3 years.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events fields "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	LEE011

Reporting group description:

LEE011

Reporting group title	Placebo

Reporting group description:

Placebo

Reporting group title	All patients

Reporting group description:

All patients

Serious adverse events	LEE011	Placebo	All patients
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Meningitis bacterial			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	LEE011	Placebo	All patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	1 / 2 (50.00%)	9 / 10 (90.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	3	0	3
Breakthrough pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	6	0	6
Impaired healing			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Malaise			

subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Non-cardiac chest pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	3
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	4	0	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	1 / 2 (50.00%)	2 / 10 (20.00%)
occurrences (all)	2	1	3
Dysphonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	3
Pleuritic pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	3	0	3
Libido decreased			

subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Investigations			
Alpha 1 foetoprotein increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Blood creatine increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	6	0	6
Haemoglobin decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	3
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Neutrophil count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	4
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Procedural pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Thermal burn			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Congenital, familial and genetic disorders			

Dermoid cyst			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	6 / 8 (75.00%)	0 / 2 (0.00%)	6 / 10 (60.00%)
occurrences (all)	6	0	6
Neuropathy peripheral			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Leukopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Lymphopenia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Neutropenia			
subjects affected / exposed	4 / 8 (50.00%)	0 / 2 (0.00%)	4 / 10 (40.00%)
occurrences (all)	6	0	6
Thrombocytopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Tinnitus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	4	0	4
Abdominal pain upper			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	6	0	6
Diarrhoea			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	4	0	4
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	5 / 8 (62.50%)	0 / 2 (0.00%)	5 / 10 (50.00%)
occurrences (all)	10	0	10
Stomatitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Vomiting			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	7	0	7
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Night sweats			

subjects affected / exposed	2 / 8 (25.00%)	0 / 2 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Rash			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rash maculo-papular			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Skin lesion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Nocturia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Back pain			
subjects affected / exposed	3 / 8 (37.50%)	0 / 2 (0.00%)	3 / 10 (30.00%)
occurrences (all)	5	0	5
Muscle tightness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Musculoskeletal stiffness			

subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Infections and infestations			
Anal infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Fungal infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Laryngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 8 (50.00%)	0 / 2 (0.00%)	4 / 10 (40.00%)
occurrences (all)	6	0	6
Dehydration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hypercalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 2 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hyperglycaemia			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0	1 / 10 (10.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2014	• Subjects with pathologic evidence of malignant transformation were no longer included in this study • The plan to perform interim analysis was removed. • It was required to perform cardiac imaging (MUGA/ECHO) at screening and EOTvisits for all subjects to more completely evaluate underlying cardiac disease.
05 September 2015	• Updates to monitoring and dose adjustment guidelines for QTcF prolongation including additional ECG assessments. • Updates to monitoring and dose adjustment guidelines for hepatobiliary toxicities including ALT, AST, and total bilirubin.
18 August 2017	• To facilitate unblinding of subject treatment status. • On-going subjects were unblinded in order to permit crossover to ribociclib for subjects receiving placebo. • Allowed subjects receiving ribociclib to discontinue the study treatment and transfer to Novartis ribociclib rollover clinical trial.

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.

After 10 subjects were enrolled and treated, the recruitment was halted due to business reasons.There were no safety concerns which contributed to the decision to halt enrollment. Limited efficacy analyses were performed.

Notes: