Clinical trial results:
A Phase II Multicenter, Open label Study to Evaluate the Safety and Efficacy of the CD40 Agonistic Antibody APX005M With or Without Stereotactic Body Radiation Therapy in Adults with Unresectable or Metastatic Melanoma

Summary

EudraCT number	2018-003864-30
Trial protocol	ES PL
Global end of trial date	02 August 2022

Results information

Result version number	v1 (current)
This version publication date	03 February 2024
First version publication date	03 February 2024

Trial information

Trial identification

Sponsor protocol code	APX005M-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04337931
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pyxis Oncology, Inc.
Sponsor organisation address	321 Harrison Avenue, Boston, United States, MA 02118
Public contact	Clinical Operations, Pyxis Oncology, Inc., 1 (339) 545 8252, clinicaltrials@pyxisoncology.com
Scientific contact	Ken Kobayashi, Pyxis Oncology, Inc., 1 (816) 830-5408, kkobayashi@pyxisoncology.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	02 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the overall response rate (ORR) by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 in each cohort.

Protection of trial subjects:

This study was conducted in accordance with the study protocol, the ethical principles that have their origins in the Declaration of Helsinki, the International Conference on Harmonization guidelines on Good Clinical Practice, the United States Code of Federal regulations, Title 21, Part 50 (21CFR50), as well as all other applicable country and regional legal and regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2019
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	Poland: 10
Country: Number of subjects enrolled	Spain: 34
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	23
From 65 to 84 years	20
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 45 participants were enrolled in Poland and Spain between June 2019 and August 2022.

Pre-assignment

Screening details:

Forty-four participants received treatment with sotigalimab and were included in the Safety Population. One participant enrolled in Cohort 2 did not receive treatment due to withdrawal of consent and was therefore excluded from the Safety Population.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Participants received 0.3mg/kg of sotigalimab administered intravenously (IV) every 21 days (3 week) treatment cycle.

Arm type	Experimental
Investigational medicinal product name	Sotigalimab
Investigational medicinal product code	PYX-107
Other name	APX005M
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sotigalimab is a CD40 agonistic monoclonal antibody.

Arm title	Cohort 2

Arm description:

Participants received 0.3mg/kg of sotigalimab administered IV every 14 days (2 week) treatment cycle.

Arm type	Experimental
Investigational medicinal product name	Sotigalimab
Investigational medicinal product code	PYX-107
Other name	APX005M
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sotigalimab is a CD40 agonistic monoclonal antibody.

Arm title	Cohort 3 -Sotigalimab + Radiation Therapy

Arm description:

Participants received 0.3 mg/kg of sotigalimab administered in combination with stereotactic body radiation therapy (SBRT) every 2 weeks (14-day cycle) up to 16 weeks followed by sotigalimab administered IV at 0.3 mg/kg every 2 weeks (14-day cycle).

Arm type	Experimental

Investigational medicinal product name	Sotigalimab
Investigational medicinal product code	PYX-107
Other name	APX005M
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sotigalimab is a CD40 agonistic monoclonal antibody.

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy
Started	12	13	19
Safety Population	12	13	19
Efficacy Population	11	13	19
Completed	0	0	0
Not completed	12	13	19
Death	4	1	7
Initiation of subsequent anti-cancer treatment	1	-	9
Study terminated by sponsor	3	6	2
Initiated first treatment with anti-PD1/L1 therapy	3	5	1
Colorectal cancer treatment	1	-	-
Withdrawal by subject	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Participants received 0.3mg/kg of sotigalimab administered intravenously (IV) every 21 days (3 week) treatment cycle.	
Reporting group title	Cohort 2
Reporting group description:	
Participants received 0.3mg/kg of sotigalimab administered IV every 14 days (2 week) treatment cycle.	
Reporting group title	Cohort 3 -Sotigalimab + Radiation Therapy
Reporting group description:	
Participants received 0.3 mg/kg of sotigalimab administered in combination with stereotactic body radiation therapy (SBRT) every 2 weeks (14-day cycle) up to 16 weeks followed by sotigalimab administered IV at 0.3 mg/kg every 2 weeks (14-day cycle).	

Reporting group values	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy
Number of subjects	12	13	19
Age categorical Units: Subjects			
Age continuous Units: years			
median	69.00	59.00	63.00
full range (min-max)	36.00 to 80.00)	40.00 to 85.00	30.00 to 75.00
Gender categorical Units: Subjects			
Female	4	6	10
Male	8	7	9
Ethnicity Units: Subjects			
Hispanic or Latino	0	3	0
Not Hispanic or Latino	12	10	19
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	12	13	19
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Poland	1	1	8
Spain	11	12	11
Eastern Cooperative Oncology Group			

(ECOG) Performance Status			
ECOG Performance Status determines the ability of participants to tolerate therapies in serious illness. 0= Asymptomatic (no symptoms), 1= Symptomatic (exhibits symptoms) but completely ambulatory.			
Units: Subjects			
0 (asymptomatic)	7	8	7
1 (symptomatic but ambulatory)	5	5	12
Weight			
Units: kg			
median	77.20	79.00	75.00
full range (min-max)	51.00 to 96.10	58.00 to 95.10	53.00 to 104.00
Height			
Units: cm			
median	169.00	166.00	168.00
full range (min-max)	156.00 to 179.00	153.00 to 176.00	146.50 to 185.00

Reporting group values	Total		
Number of subjects	44		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	20		
Male	24		
Ethnicity			
Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	41		
Unknown or Not Reported	0		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	44		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment			
Units: Subjects			
Poland	10		
Spain	34		
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG Performance Status determines the ability of participants to tolerate therapies in serious illness. 0= Asymptomatic (no symptoms), 1= Symptomatic (exhibits symptoms) but completely ambulatory.			
Units: Subjects			

0 (asymptomatic)	22		
1 (symptomatic but ambulatory)	22		

Weight			
Units: kg			
median			
full range (min-max)	-		
Height			
Units: cm			
median			
full range (min-max)	-		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Participants received 0.3mg/kg of sotigalimab administered intravenously (IV) every 21 days (3 week) treatment cycle.	
Reporting group title	Cohort 2
Reporting group description:	
Participants received 0.3mg/kg of sotigalimab administered IV every 14 days (2 week) treatment cycle.	
Reporting group title	Cohort 3 -Sotigalimab + Radiation Therapy
Reporting group description:	
Participants received 0.3 mg/kg of sotigalimab administered in combination with stereotactic body radiation therapy (SBRT) every 2 weeks (14-day cycle) up to 16 weeks followed by sotigalimab administered IV at 0.3 mg/kg every 2 weeks (14-day cycle).	

Primary: RECIST 1.1 ORR

End point title	RECIST 1.1 ORR[1]

End point description:

The percentage of participants having reached a confirmed Complete Response (CR) or Partial Response (PR) by RECIST 1.1, relative to the number of participants belonging to the Efficacy Population. Confidence Intervals (CIs) were calculated using exact (Clopper-Pearson) method.

CR: Disappearance of all target lesions and nontarget (NT) lesions; PR: >30% decrease in the sum of the longest diameter of target lesions and no progressive disease in NT lesions or new lesions.

Participants evaluable for efficacy (tumor response) are defined as those who have measurable disease and at least one evaluable (post baseline) tumor assessment performed during the treatment period or within 30 days after the administration of the last dose of treatment.

End point type	Primary

End point timeframe:

12 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: No additional statistical analyses were pre-specified for this endpoint.

End point values	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	13	19	
Units: percentage of participants				
number (confidence interval 90%)	9.09 (0.47 to 36.44)	7.69 (0.39 to 31.63)	0.00 (0.00 to 14.59)	

Statistical analyses

No statistical analyses for this end point

Secondary: Modified RECIST 1.1 for Immune-based Therapeutics (iRECIST 1.1) Overall Response Rate (iORR)

End point title	Modified RECIST 1.1 for Immune-based Therapeutics (iRECIST 1.1) Overall Response Rate (iORR)

End point description:

The percentage of participants having reached an immune confirmed Complete Response (iCR) or Partial Response (iPR) by iRECIST 1.1, relative to the number of participants belonging to the Efficacy Population. CIs were calculated using exact (Clopper-Pearson) method.

iCR: Disappearance of all target lesions and NT lesions; iPR: >30% decrease in the sum of the longest diameter of target lesions and no progressive disease in NT lesions or new lesions.

iORR for iRECIST 1.1 by Cohort (Efficacy Population).

End point type	Secondary

End point timeframe:

12 months

End point values	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	13	19	
Units: percentage of participants				
number (confidence interval 90%)	9.09 (0.47 to 36.44)	7.69 (0.39 to 31.63)	0.00 (0.00 to 14.59)	

Statistical analyses

No statistical analyses for this end point

Secondary: RECIST 1.1 Duration of Response (DoR)

End point title	RECIST 1.1 Duration of Response (DoR)

End point description:

The DoR was defined as the time (in months) from the first evidence of confirmed objective response (CR or PR) to the event or censoring date. An event was defined as the first documentation of progression disease (PD; disease progression assessed based on tumor assessment or clinical progression) or death due to any cause, whichever occurs earlier. Median DoR was calculated using Kaplan-Meier analysis. CIs were calculated using exact (Clopper-Pearson) method.

CR: Disappearance of all target lesions and NT lesions; PR: >30% decrease in the sum of the longest diameter of target lesions and no progressive disease in NT lesions or new lesions; PD: >20% increase in the sum of the longest diameter of target lesions and an absolute increase of ≥5mm, or a measurable increase in a non-target lesion, or the appearance of new lesions. Values of "99999" indicate Median and CIs were not reached due to low number of events.

DoR for RECIST 1.1 by Cohort (Efficacy Population).

End point type	Secondary

End point timeframe:

12 months

End point values	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1[2]	1[3]	0[4]	
Units: months				
median (confidence interval 90%)	99999 (99999 to 99999)	99999 (99999 to 99999)	(to)	

Notes:

[2] - Inclusive of participants who experienced CR or PR only.

[3] - Inclusive of participants who experienced CR or PR only.

[4] - Inclusive of participants who experienced CR or PR only.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: RECIST 1.1 Progression-free Survival (PFS)

End point title	RECIST 1.1 Progression-free Survival (PFS)

End point description:

The PFS was defined as the time (in months) from the first administration of APX005M to the event or censoring date. An event was defined as the first documentation of PD (disease progression assessed based on tumor assessment or clinical progression) or death due to any cause, whichever occurs earlier. Median DoR was calculated using Kaplan-Meier analysis. CIs were calculated using exact (Clopper-Pearson) method.

PD: >20% increase in the sum of the longest diameter of target lesions and an absolute increase of ≥5mm, or a measurable increase in a non-target lesion, or the appearance of new lesions.

PFS for RECIST 1.1 by Cohort (Efficacy Population).

End point type	Other pre-specified

End point timeframe:

12 months

End point values	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	13	19	
Units: months				
median (confidence interval 90%)	1.87 (1.35 to 3.71)	3.48 (1.81 to 9.20)	1.87 (1.64 to 1.91)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to approximately 79 weeks	
Adverse event reporting additional description:	
All AE's below are reported regardless of relationship to treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Participants received 0.3mg/kg of sotigalimab administered IV every 21 days (3 week) treatment cycle.	
Reporting group title	Cohort 2
Reporting group description:	
Participants received 0.3mg/kg of sotigalimab administered IV every 14 days (2 week) treatment cycle.	
Reporting group title	Cohort 3 -Sotigalimab + Radiation Therapy
Reporting group description:	
Participants received 0.3 mg/kg of sotigalimab administered in combination with SBRT every 2 weeks (14-day cycle) up to 16 weeks followed by sotigalimab administered IV at 0.3 mg/kg every 2 weeks (14-day cycle).	

Serious adverse events	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	0 / 13 (0.00%)	3 / 19 (15.79%)
number of deaths (all causes)	4	1	7
number of deaths resulting from adverse events			
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			

subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhagic stroke			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			

subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 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	Cohort 1	Cohort 2	Cohort 3 - Sotigalimab + Radiation Therapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	12 / 13 (92.31%)	19 / 19 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)	3 / 13 (23.08%)	1 / 19 (5.26%)
occurrences (all)	1	4	1
Flushing			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 12 (33.33%)	7 / 13 (53.85%)	4 / 19 (21.05%)
occurrences (all)	4	11	4
Chills			
subjects affected / exposed	2 / 12 (16.67%)	6 / 13 (46.15%)	5 / 19 (26.32%)
occurrences (all)	2	7	6

Pyrexia			
subjects affected / exposed	7 / 12 (58.33%)	7 / 13 (53.85%)	13 / 19 (68.42%)
occurrences (all)	17	15	20
Axillary pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Discomfort			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Malaise			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	1	4	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	4 / 19 (21.05%)
occurrences (all)	1	3	5
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Epistaxis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pharyngeal erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Persistent depressive disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 12 (50.00%)	6 / 13 (46.15%)	7 / 19 (36.84%)
occurrences (all)	13	14	9
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 12 (58.33%)	6 / 13 (46.15%)	8 / 19 (42.11%)
occurrences (all)	12	10	11
Blood creatinine increased			

subjects affected / exposed	2 / 12 (16.67%)	3 / 13 (23.08%)	0 / 19 (0.00%)
occurrences (all)	3	4	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 12 (33.33%)	3 / 13 (23.08%)	1 / 19 (5.26%)
occurrences (all)	6	7	1
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
Blood glucose increased			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 12 (16.67%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	3	4	0
Blood urea increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Fibrin D dimer increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Heart rate increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Neutrophil count increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
White blood cell count increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			

Infusion related reaction			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	8 / 19 (42.11%)
occurrences (all)	1	2	11
Radiation skin injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)	3 / 13 (23.08%)	1 / 19 (5.26%)
occurrences (all)	1	4	1
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Dysaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 12 (25.00%)	2 / 13 (15.38%)	4 / 19 (21.05%)
occurrences (all)	3	2	7
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Lymphocytosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	1 / 19 (5.26%)
occurrences (all)	2	1	1
Neutropenia			

subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	2 / 12 (16.67%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	3	2	0
Eye disorders			
Eye Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	2 / 19 (10.53%)
occurrences (all)	1	2	2
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	5 / 13 (38.46%)	4 / 19 (21.05%)
occurrences (all)	2	13	6
Vomiting			
subjects affected / exposed	4 / 12 (33.33%)	6 / 13 (46.15%)	1 / 19 (5.26%)
occurrences (all)	4	10	1
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	1 / 19 (5.26%)
occurrences (all)	1	3	1
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Haematochezia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Oral pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	3 / 12 (25.00%)	4 / 13 (30.77%)	2 / 19 (10.53%)
occurrences (all)	4	5	4
Hepatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	3 / 13 (23.08%)	4 / 19 (21.05%)
occurrences (all)	1	7	4
Rash			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	3 / 19 (15.79%)
occurrences (all)	1	3	3
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Rash macular			

subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Uticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Chronic kidney			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Glycosuria			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	2 / 19 (10.53%)
occurrences (all)	0	2	3
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Groin pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	1 / 19 (5.26%)
occurrences (all)	0	1	2
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Myalgia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	2 / 19 (10.53%)
occurrences (all)	1	2	2
Hyperamylasaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2019	The protocol title was amended to reflect study design. The protocol was amended to: - edit Inclusion Criterion #2, - add Exclusion Criteria of previous participation in another clinical trial of an investigational drug (or a medical device) within 30 days of study enrollment, - update and resolve inconsistencies in sample collection schedule for correlative studies described in Section 4.4.
28 December 2020	The protocol was amended to introduce Cohort 3 combining sotigalimab with SBRT in participants with unresectable or metastatic melanoma that failed available therapies and to adjust the sample size in Cohorts 1 and 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported