Clinical trial results:
An Open-Label, Randomized, Phase 2, Umbrella Study of Various Neoadjuvant Therapies for Participants With Muscle-Invasive Urothelial Carcinoma of the Bladder Who Are Cisplatin-Ineligible or Refuse Cisplatin Therapy and Undergoing Radical Cystectomy (Optimus)

Summary

EudraCT number	2020-002244-23
Trial protocol	FR IT
Global end of trial date	29 January 2024

Results information

Result version number	v1 (current)
This version publication date	09 February 2025
First version publication date	09 February 2025

Trial information

Trial identification

Sponsor protocol code	INCB 24360-901

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 855-463-3463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 855-463-3463, medinfo@incyte.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	29 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 January 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study was conducted to determine biologic response in participants who had muscle-invasive urothelial carcinoma of the bladder and were cisplatin ineligible or refused cisplatin therapy and were awaiting radical cystectomy.

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was being conducted.

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	30
EEA total number of subjects	21

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	24

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled at 2 study centers in the United States, 2 study centers in Italy, and 1 study center in France.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W

Arm description:

Participants received oral epacadostat 600 milligrams (mg) twice daily (BID) + intravenous retifanlimab 500 mg every 4 weeks (Q4W; on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Arm type	Experimental
Investigational medicinal product name	retifanlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/milliliter (mL) liquid formulation administered intravenously over 30 minutes (+ 15 minutes) on Day 1
of each 28-day cycle

Investigational medicinal product name	epacadostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For the 600 mg BID dose, two 300-mg tablets BID. For the 400 mg BID dose reduction, one 300-mg and one 100-mg tablet. Both dose levels were administered without regard to food. Epacadostat was administered daily up to and including the day of surgery.

Arm title	Retifanlimab 500 mg Q4W

Arm description:

Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Arm type	Experimental
Investigational medicinal product name	retifanlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/mL liquid formulation administered intravenously over 30 minutes (+ 15 minutes) on Day 1

of each 28-day cycle

Arm title	Epacadostat 600 mg BID

Arm description:

Participants received oral epacadostat 600 mg BID. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

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

Dosage and administration details:

For the 600 mg BID dose, two 300-mg tablets BID. For the 400 mg BID dose reduction, one 300-mg and one 100-mg tablet. Both dose levels were administered without regard to food. Epacadostat was administered daily up to and including the day of surgery.

Arm title	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W

Arm description:

Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg every 2 weeks (Q2W). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Arm type	Experimental
Investigational medicinal product name	INCAGN02385
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/mL administered intravenously (30-minute infusion with filter followed by flush)

Investigational medicinal product name	retifanlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/mL liquid formulation administered intravenously over 30 minutes (+ 15 minutes) on Day 1 of each 28-day cycle

Arm title	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg

Arm description:

Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg Q2W + intravenous INCAGN02390 400 mg Q2W. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Arm type	Experimental
Investigational medicinal product name	retifanlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 25 mg/mL liquid formulation administered intravenously over 30 minutes (+ 15 minutes) on Day 1 of each 28-day cycle	
Investigational medicinal product name	INCAGN02390
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 50 mg/ mL administered intravenously (30-minute infusion with filter followed by flush) every 2 weeks	
Investigational medicinal product name	INCAGN02385
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 50 mg/mL administered intravenously (30-minute infusion with filter followed by flush) every 2 weeks	

Number of subjects in period 1	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID
Started	3	20	2
Completed	2	19	2
Not completed	1	1	0
Lost to follow-up	1	-	-
AE Delayed Surgery; No Follow-Up Data Collected	-	1	-

Number of subjects in period 1	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg
Started	4	1
Completed	3	1
Not completed	1	0
Lost to follow-up	1	-
AE Delayed Surgery; No Follow-Up Data Collected	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W
Reporting group description:	
Participants received oral epacadostat 600 milligrams (mg) twice daily (BID) + intravenous retifanlimab 500 mg every 4 weeks (Q4W; on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Retifanlimab 500 mg Q4W
Reporting group description:	
Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Epacadostat 600 mg BID
Reporting group description:	
Participants received oral epacadostat 600 mg BID. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Reporting group description:	
Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg every 2 weeks (Q2W). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg
Reporting group description:	
Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg Q2W + intravenous INCAGN02390 400 mg Q2W. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	

Reporting group values	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID
Number of subjects	3	20	2
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)	0	5	1
From 65-84 years	3	15	1
85 years and over	0	0	0
Age Continuous			
120=Mean (SD) age cannot be reported for a single participant due to privacy concerns.			
Units: years			
arithmetic mean	75.7	71.1	65.0
standard deviation	± 6.66	± 6.08	± 1.41
Sex/Gender, Customized Units: participants			
Female	0	2	1

Male	3	18	1
Cannot Be Reported Due to Participant Privacy	0	0	0

Race, Customized Units: Subjects			
White/Caucasian	2	16	2
Not Reported	1	4	0
Cannot Be Reported Due to Participant Privacy	0	0	0
Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	2	15	1
Not Reported	1	5	1
Cannot Be Reported Due to Participant Privacy	0	0	0

Reporting group values	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg	Total
Number of subjects	4	1	30
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)	0	0	6
From 65-84 years	4	1	24
85 years and over	0	0	0
Age Continuous			
120=Mean (SD) age cannot be reported for a single participant due to privacy concerns.			
Units: years			
arithmetic mean	69.3	120	
standard deviation	± 3.86	± 120	-
Sex/Gender, Customized Units: participants			
Female	1	0	4
Male	3	0	25
Cannot Be Reported Due to Participant Privacy	0	1	1
Race, Customized Units: Subjects			
White/Caucasian	4	0	24
Not Reported	0	0	5
Cannot Be Reported Due to Participant Privacy	0	1	1
Ethnicity, Customized Units: Subjects			

Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	0	22
Not Reported	0	0	7
Cannot Be Reported Due to Participant Privacy	0	1	1

End points

End points reporting groups

Reporting group title	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W
Reporting group description:	
Participants received oral epacadostat 600 milligrams (mg) twice daily (BID) + intravenous retifanlimab 500 mg every 4 weeks (Q4W; on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Retifanlimab 500 mg Q4W
Reporting group description:	
Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Epacadostat 600 mg BID
Reporting group description:	
Participants received oral epacadostat 600 mg BID. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Reporting group description:	
Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg every 2 weeks (Q2W). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	
Reporting group title	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg
Reporting group description:	
Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg Q2W + intravenous INCAGN02390 400 mg Q2W. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.	

Primary: Change from Baseline in CD8+ lymphocytes within the resected tumor

End point title	Change from Baseline in CD8+ lymphocytes within the resected tumor[1]
End point description:	
Fold Change from Baseline in CD8+ lymphocytes = CD8+ Lymphocytes at cystectomy divided by CD8+ lymphocytes at Screening. Analysis was conducted in members of the Translation Evaluable Population, comprised of all participants who enrolled in the study who received at least 4 weeks of neoadjuvant study treatment (needed to receive the last dose of epacadostat within 2 days prior to the day of surgery or needed to receive the last dose of retifanlimab and/or INCAGN02385 and/or INCAGN02390 within the 7 weeks prior to day of surgery) and provided evaluable paired biopsies (pretreatment core biopsy and surgical resection biopsy). Translational data in all but the retifanlimab 500 mg Q4W treatment group were limited and insufficient to assess this outcome measure.	
End point type	Primary
End point timeframe:	
up to 69 days	

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: Statistical analysis was not conducted for this endpoint.

End point values	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	6[3]	0[4]	0[5]
Units: log 2 of fold change				
arithmetic mean (standard deviation)	()	0.791 (± 0.9332)	()	()

Notes:

[2] - Translation Evaluable Population

[3] - Translation Evaluable Population

[4] - Translation Evaluable Population

[5] - Translation Evaluable Population

End point values	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: log 2 of fold change				
arithmetic mean (standard deviation)	()			

Notes:

[6] - Translation Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Number of participants with any treatment-emergent adverse event (TEAE)

End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug related. An AE could therefore have been any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study drug. Analysis was conducted in members of the Safety Population, comprised of all participants who received at least 1 dose of study treatment. Treatment groups were determined according to the actual treatment the participant received regardless of the assigned study treatment.

End point type	Secondary

End point timeframe:

up to 159 days

End point values	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[7]	20[8]	2[9]	4[10]
Units: participants	3	18	2	4

Notes:

[7] - Safety Population

[8] - Safety Population

[9] - Safety Population

[10] - Safety Population

End point values	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	1[11]			
Units: participants	1			

Notes:

[11] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any ≥Grade 3 TEAE

End point title	Number of participants with any ≥Grade 3 TEAE

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug related. A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study drug. The severity of AEs was assessed using Common Terminology Criteria for Adverse Events (CTCAE) version 5 Grades 1 through 5. Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated. Grade 2: moderate; minimal, local, or noninvasive treatment indicated; limiting age-appropriate activities of daily living. Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living. Grade 4: life-threatening consequences; urgent treatment indicated. Grade 5: fatal.

End point type	Secondary

End point timeframe:

up to 159 days

End point values	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[12]	20[13]	2[14]	4[15]
Units: participants	2	9	0	2

Notes:

[12] - Safety Population

[13] - Safety Population

[14] - Safety Population

[15] - Safety Population

End point values	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	1[16]			
Units: participants	1			

Notes:

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pathological complete response rate

End point title	Pathological complete response rate

End point description:

Pathological complete response rate was defined as the percentage of participants with ypT0N0. The 80% confidence interval was estimated using the Clopper-Pearson method. Analysis was conducted in members of the Efficacy Population, comprised of all participants with secondary efficacy endpoint data available for both Baseline and post-Baseline measurements.

End point type	Secondary

End point timeframe:

up to 69 days

End point values	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[17]	20[18]	2[19]	4[20]
Units: percentage of participants				
number (confidence interval 80%)	100 (31.62 to 100)	40 (24.91 to 56.73)	0 (0 to 68.38)	0 (0 to 43.77)

Notes:

[17] - Efficacy Population

[18] - Efficacy Population

[19] - Efficacy Population

[20] - Efficacy Population

End point values	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390			

	400 mg			
Subject group type	Reporting group			
Number of subjects analysed	1[21]			
Units: percentage of participants				
number (confidence interval 80%)	100 (10 to 100)			

Notes:

[21] - Efficacy Population

Statistical analyses

No statistical analyses for this end point

Secondary: Major pathological response

End point title	Major pathological response

End point description:

Major pathological response was defined as the percentage of participants with residual ypT0/1/a/isN0M0.

End point type	Secondary

End point timeframe:

up to 69 days

End point values	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[22]	20[23]	2[24]	4[25]
Units: percentage of participants				
number (confidence interval 80%)	100 (31.62 to 100)	50 (33.82 to 66.18)	50 (5.13 to 94.87)	50 (14.26 to 85.74)

Notes:

[22] - Efficacy Population

[23] - Efficacy Population

[24] - Efficacy Population

[25] - Efficacy Population

End point values	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	1[26]			
Units: percentage of participants				
number (confidence interval 80%)	100 (10 to 100)			

Notes:

[26] - Efficacy Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 159 days

Adverse event reporting additional description:

Adverse events have been reported for members of the Safety Population, comprised of all participants who received at least 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W

Reporting group description:

Participants received oral epacadostat 600 milligrams (mg) twice daily (BID) + intravenous retifanlimab 500 mg every 4 weeks (Q4W; on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Reporting group title	Retifanlimab 500 mg Q4W

Reporting group description:

Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Reporting group title	Epacadostat 600 mg BID

Reporting group description:

Participants received oral epacadostat 600 mg BID. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Reporting group title	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W

Reporting group description:

Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg every 2 weeks (Q2W). Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Reporting group title	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg

Reporting group description:

Participants received intravenous retifanlimab 500 mg Q4W (on Day 1 of each 28-day cycle) + intravenous INCAGN02385 350 mg Q2W + intravenous INCAGN02390 400 mg Q2W. Treatment continued for 4 to 10 weeks, as long as participants did not meet any criteria for study withdrawal.

Serious adverse events	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	4 / 20 (20.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Ileus paralytic			

subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (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
Myositis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (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
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (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
Purulent discharge			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (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
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (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

Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (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
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (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	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 1 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Ileus paralytic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purulent discharge			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Epacadostat 600 mg BID + retifanlimab 500 mg Q4W	Retifanlimab 500 mg Q4W	Epacadostat 600 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	18 / 20 (90.00%)	2 / 2 (100.00%)
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 3 (0.00%)	4 / 20 (20.00%)	0 / 2 (0.00%)
occurrences (all)	0	8	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	3 / 20 (15.00%)	0 / 2 (0.00%)
occurrences (all)	2	3	0
Asthenia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 20 (25.00%)	1 / 2 (50.00%)
occurrences (all)	0	7	1
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Hyperpyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Epididymal cyst			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Epididymal tenderness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Testicular swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vaginal prolapse			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 20 (5.00%)	1 / 2 (50.00%)
occurrences (all)	1	1	1
Blood lactate dehydrogenase			

increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Carbon dioxide increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Inflammatory marker increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Post procedural discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			

Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 3 (33.33%)	5 / 20 (25.00%)	0 / 2 (0.00%)
occurrences (all)	2	8	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Anal incontinence			

subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Aerophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 20 (15.00%)	0 / 2 (0.00%)
occurrences (all)	0	4	0
Diarrhea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 20 (5.00%)	1 / 2 (50.00%)
occurrences (all)	1	4	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 3 (33.33%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	5	1	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Bladder spasm			
subjects affected / exposed	0 / 3 (0.00%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Dysuria			
subjects affected / exposed	1 / 3 (33.33%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Nocturia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Urinary tract infection			

subjects affected / exposed	0 / 3 (0.00%)	3 / 20 (15.00%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Epididymitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	1	2	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 20 (5.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 20 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 20 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Retifanlimab 500 mg Q4W + INCAGN02385 350 mg Q2W	Retifanlimab 500 mg + INCAGN02385 350 mg + INCAGN02390 400 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	1 / 1 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperpyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Epididymal cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Epididymal tenderness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Testicular swelling			

subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Vaginal prolapse			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Blood bicarbonate decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 4 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Carbon dioxide increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Inflammatory marker increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
International normalised ratio increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Lipase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			

Post procedural discomfort subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 1 (0.00%) 0	
Head injury subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 1 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 1 (0.00%) 0	
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 1 (0.00%) 0	
Nervous system disorders Syncope subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 1 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 1 (0.00%) 0	
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 1 (0.00%) 0	
Paraesthesia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 1 (0.00%) 0	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 1 (0.00%) 0	
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 7	1 / 1 (100.00%) 1	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 1 (0.00%) 0	

Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 4 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Anal incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Aerophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Diarrhea			
subjects affected / exposed	3 / 4 (75.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Bladder spasm			

subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	2 / 4 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Nocturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	2 / 4 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Urinary retention			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	1	2	
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			

subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Herpes simplex			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Epididymitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	2	
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	7	0	
Hyperkalaemia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	4	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2020	The primary purpose of this amendment was to address regulatory comments regarding eligibility criteria, secondary objective and endpoints, withdrawal criteria, and study conduct and additional feedback from investigators to clarify several errors and omissions.
02 February 2021	The sponsor evaluated its strategy in bladder cancer and made a decision to remove pemigatinib from this study. As such, this amendment removed the 3 treatment groups that contained pemigatinib (pemigatinib monotherapy, pemigatinib plus retifanlimab, and pemigatinib followed by retifanlimab). The removal of information on fibroblast growth factor receptor was reflected throughout the protocol.
10 May 2021	The primary purpose of this amendment was to address requested comments and changes from the French Health Authority Review.
01 March 2022	The primary purpose of this amendment was to add 2 new treatment groups to the Protocol (retifanlimab plus INCAGN02385 as well as retifanlimab plus INCAGN02385 plus INCAGN02390) and to clarify the radiologic tools used for tumor imaging.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported