Clinical trial results:
A Phase 2, Open Label Study to Evaluate Safety and Clinical Activity of Avelumab (Bavencio) in Combination With Axitinib (Inlyta) in Patients With Advanced or Metastatic Previously Treated Non-Small Cell Lung Cancer or Treatment naïve cisplatin-ineligible urothelial cancer.

Summary

EudraCT number	2017-004345-24
Trial protocol	HU ES PL
Global end of trial date	09 February 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	B9991027

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03472560
WHO universal trial number (UTN)	-
Other trial identifiers	AVE/ AXI COMBO UC: Other Study ID, AVE/AXI COMBO UC/NSCLC: Other Study ID

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	14 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the Objective Response Rate (ORR) based on Investigator assessment, per Response Evaluation Criteria in Solid Tumors V1.1 (RECIST v1.1) of avelumab in combination with axitinib in subjects with advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) who have received at least one prior platinum-containing therapy and in treatment naïve subjects with advanced or metastatic Urothelial Cancer (UC), who are ineligible for cisplatin-containing chemotherapy for their advanced disease.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	56 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	61
EEA total number of subjects	20

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)	26
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects diagnosed with advanced or metastatic non- small cell lung cancer (NSCLC) and received at least 1 prior platinum-containing therapy or subjects with advanced or metastatic urothelial cancer (UC) and were treatment naive and ineligible for cisplatin-containing chemotherapy for their advanced disease were enrolled.

Pre-assignment

Screening details:

A total of 104 subjects were screened, out of which 43 subjects failed screening and 61 subjects were enrolled into the study.

Period 1

Period 1 title	Treatment (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	NSCLC Avelumab + Axitinib

Arm description:

Subjects with NSCLC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.

Arm type	Experimental
Investigational medicinal product name	Axitinib 5 mg
Investigational medicinal product code	AG-013736
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received Axitinib 5 mg twice daily orally

Investigational medicinal product name	Avelumab 800mg
Investigational medicinal product code	MSB0010718C
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Avelumab 800 mg intravenously every two weeks of each 28-day cycle

Arm title	UC Avelumab + Axitinib

Arm description:

Subjects with UC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.

Arm type	Experimental
Investigational medicinal product name	Avelumab 800mg
Investigational medicinal product code	MSB0010718C
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Avelumab 800 mg intravenously every two weeks of each 28-day cycle

Investigational medicinal product name	Axitinib 5 mg
Investigational medicinal product code	AG-013736
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received Axitinib 5 mg twice daily orally

Number of subjects in period 1	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib
Started	41	20
Completed	0	0
Not completed	41	20
Adverse event, serious fatal	7	4
Physician decision	1	-
Consent withdrawn by subject	4	-
Global deterioration of health status	-	4
Adverse event, non-fatal	5	3
Subject transfer to continuation protocol	-	1
Progressive disease	24	8

Baseline characteristics

Reporting groups	
Reporting group title	NSCLC Avelumab + Axitinib
Reporting group description:	
Subjects with NSCLC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.	
Reporting group title	UC Avelumab + Axitinib
Reporting group description:	
Subjects with UC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.	

Reporting group values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib	Total
Number of subjects	41	20	61
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)	22	4	26
From 65-84 years	19	16	35
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	64.0	70.7	
standard deviation	± 8.93	± 8.66	-
Sex: Female, Male Units: Subjects			
Female	11	8	19
Male	30	12	42
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	21	1	22
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	20	17	37
More than one race	0	1	1
Unknown or Not Reported	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	2	3
Not Hispanic or Latino	40	17	57
Unknown or Not Reported	0	1	1

End points

End points reporting groups

Reporting group title	NSCLC Avelumab + Axitinib
Reporting group description:	
Subjects with NSCLC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.	
Reporting group title	UC Avelumab + Axitinib
Reporting group description:	
Subjects with UC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.	

Primary: Percentage of Subjects With Confirmed Objective Response- Objective Response Rate (ORR)

End point title	Percentage of Subjects With Confirmed Objective Response-Objective Response Rate (ORR)[1]
End point description:	
ORR: Percentage of subjects with confirmed Complete Response (CR)/Partial Response (PR) based on investigator's assessment as per Response Evaluation Criteria in Solid Tumours (RECIST v1.1). CR and PR were confirmed by repeat assessments performed no less than 4 weeks after criteria for response first met. CR:complete disappearance of all target(T) lesions, non-target(NT) disease, with exception of nodal disease. All nodes,T and NT, must decrease to normal(short axis less than [<]10 millimeter [mm]). No new lesions. PR: greater than or equal to (>=)30% decrease under baseline of sum of diameters of all T lesions. Short axis was used in sum for T nodes, while longest diameter was used in sum for all other T lesions. No unequivocal progression of NT disease. No new lesions. Stable disease=not qualifying for CR, PR, progressive disease. Full Analysis Set=subjects who received at least one dose of avelumab and axitinib. Subjects were classified according to the study treatment received.	
End point type	Primary
End point timeframe:	
Baseline up to 56 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 statistical analysis was planned for this endpoint.

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: Percentage of subjects				
number (confidence interval 95%)	31.7 (18.1 to 48.1)	10.0 (1.2 to 31.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Hematology Test Results of Maximum National Cancer Institute; Common Terminology Criteria for Adverse Events (NCI CTCAE) Grade During the On-Treatment Period

End point title	Percentage of Subjects With Hematology Test Results of Maximum National Cancer Institute; Common Terminology Criteria for Adverse Events (NCI CTCAE) Grade During the On-Treatment Period

End point description:

The following hematology parameters were assessed: anemia, hemoglobin increased, international normalized ratio (INR) increased, lymphocyte count decreased, lymphocyte count increased, neutrophil count decreased, platelet count decreased and white blood cell decreased. Laboratory abnormality events were graded according to NCI CTCAE version 4.03 (grade 3= severe and grade 4= life-threatening). Categories with non-zero values are presented. Safety analysis set included all subjects who received at least one dose of study drug (avelumab or axitinib). Subjects were classified according to the study treatment received. Here 'Overall Number of Subjects Analyzed' signifies subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to 30 days post last dose of study treatment or start of new anti-cancer treatment -1 day (maximum up to 56 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	18		
Units: Percentage of subjects				
number (not applicable)				
Lymphocyte count decreased (Grade >=3)	12.2	5.6		
Neutrophil count decreased (Grade >=3)	2.4	0		
Platelet count decreased (Grade >=3)	0	5.6		
White blood cell decreased (Grade >=3)	2.4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs) During the On-Treatment Period

End point title	Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs) During the On-Treatment Period

End point description:

An Adverse Event (AE) was any untoward medical occurrence attributed to study drug in a subject who received avelumab or axitinib. Treatment-emergent adverse events (TEAEs) were those events with onset dates occurring during the on-treatment period (the time from the first dose of study treatment through minimum 30 days post last dose of study treatment or start day of new anti-cancer treatment - 1 day). Safety analysis set included all subjects who received at least one dose of study drug (avelumab or axitinib). Subjects were classified according to the study treatment received.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to 30 days post last dose of study treatment or start of new anti-cancer treatment -1 day (maximum up to 56 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: Percentage of subjects				
number (not applicable)	100.0	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Chemistry Test Results of Maximum CTCAE Grade During the On-Treatment Period

End point title	Percentage of Subjects With Chemistry Test Results of Maximum CTCAE Grade During the On-Treatment Period

End point description:

The following chemistry parameters were assessed: alanine aminotransferase(ALT) increased, alkaline phosphatase(ALP) increased, aspartate aminotransferase(AST) increased, blood bilirubin increased, cholesterol high, creatine phosphokinase (CPK) increased, creatinine increased, gamma-glutamyl transferase (GGT) increased, hypercalcaemia, hyperglycaemia, hyperkalaemia, hypermagnesemia, hypernatremia, hypertriglyceridemia, hypoalbuminemia, hypocalcaemia, hypoglycaemia, hypokalaemia, hypomagnesemia, hyponatremia, hypophosphatemia, lipase increased and serum amylase increased. Laboratory abnormalities were graded according CTCAE version 4.03; Grade(G) 3= severe, G4= life-threatening and G5= death related. Categories with non-zero values are presented. Safety analysis set. Subjects were classified according to the study treatment received. Overall Number of Subjects Analyzed =subjects evaluable for this outcome measure. Here n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to 30 days post last dose of study treatment or start of new anti-cancer treatment -1 day (maximum up to 56 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	18		
Units: Percentage of subjects				
number (not applicable)				
ALT increased Grade 3 (n=41,18)	7.3	5.6		
ALP increased Grade 3 (n=41,18)	2.4	11.1		
AST increased Grade 3 (n=41,18)	2.4	5.6		
Blood bilirubin increased Grade 3 (n=41,18)	2.4	0		
Creatinine increased Grade 3 (n=41,18)	2.4	5.6		
GGT increased Grade 3 (n=40,16)	7.5	18.8		
Hyperglycemia Grade 3 (n=41,18)	4.9	5.6		

Hyperglycemia Grade 4 (n=41,18)	2.4	0		
Hyperkalemia Grade 3 (n=41,18)	7.3	0		
Hypermagnesemia Grade 3 (n=41,18)	2.4	0		
Hypermagnesemia Grade 4 (n=41,18)	0	5.6		
Hypoalbuminemia Grade 3 (n=41,18)	0	5.6		
Hypocalcemia Grade 3 (n=41,18)	4.9	5.6		
Hypoglycemia Grade 4 (n=41,18)	2.4	0		
Hypokalemia Grade 3 (n=41,18)	4.9	0		
Hypomagnesemia Grade 3 (n=41,18)	2.4	0		
Hypomagnesemia Grade 4 (n=41,18)	2.4	0		
Hyponatremia Grade 3 (n=41,18)	9.8	16.7		
Hyponatremia Grade 4 (n=41,18)	2.4	0		
Hypophosphatemia Grade 3 (n=41,18)	4.9	5.6		
Lipase increased Grade 3 (n=39,16)	10.3	6.3		
Lipase increased Grade 4 (n=39,16)	2.6	6.3		
Serum amylase increase Grade 3 (n=40,16)	2.5	12.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR) in Subjects With Confirmed CR or PR

End point title	Time to Tumor Response (TTR) in Subjects With Confirmed CR or PR

End point description:

TTR was defined as the time from the first dose of study treatment to the first documentation of objective tumor response documented in subjects with confirmed objective response (CR or PR). CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must decrease to normal (short axis <10 mm). No new lesions. PR was defined as >=30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions. Analysis was performed using Kaplan-Meier method. Full Analysis Set was used. Subjects were classified according to the study treatment received. Here, 'Overall Number of subjects Analyzed = subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From date of start of treatment until date of first documentation of objective tumor response (maximum up to 56 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	2		
Units: Months				
median (confidence interval 95%)	1.9 (1.8 to 5.3)	2.8 (1.3 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response in Subjects With Confirmed CR or PR

End point title	Duration of Response in Subjects With Confirmed CR or PR

End point description:

Duration of response (DOR) was defined as time from first documentation of objective tumor response to first documentation of objective tumor progression or to death due to any cause, whichever occurred first in subjects with confirmed objective response (CR or PR). CR=complete disappearance of all target (T) lesions and non-target (NT) disease, with the exception of nodal disease. All nodes, both T and NT, must decrease to normal (short axis <10 mm). No new lesions. PR was defined as >=30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions. Analysis was performed using Kaplan-Meier method. Full analysis set was used. Subjects were classified according to the study treatment received. Overall Number of subjects Analyzed = subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From date of first documentation of objective tumor response to the first documentation of objective tumor progression or to death due to any cause, whichever occurred first (maximum up to 56 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	2		
Units: Months				
median (confidence interval 95%)	7.5 (3.7 to 15.5)	17.4 (5.6 to 29.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Avelumab

End point title	Maximum Observed Serum Concentration (Cmax) of Avelumab

End point description:

The Pharmacokinetic (PK) parameter analysis set is a subset of the safety analysis set and included all subjects who have at least one of the PK parameters of interest for avelumab or axitinib. Here, 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure. Here n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose, 1 hour post-dose on Cycle 1 Day 1, Day 15 and Cycle 2 Day 1

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	15		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1: Day 1 (n=35,12)	235.0 (± 26)	206.3 (± 27)		
Cycle 1: Day 15 (n=32,15)	264.0 (± 34)	163.9 (± 211)		
Cycle 2: Day 1 (n=29,15)	283.2 (± 24)	260.4 (± 25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from the date of first study treatment to the date of death due to any cause. Subjects last known to be alive were censored at date of last contact. Analysis was performed using Kaplan-Meier method. Full Analysis Set included all subjects who received at least one dose of avelumab and axitinib. Subjects were classified according to the study treatment actually received.

End point type	Secondary

End point timeframe:

From date of start of study treatment until date of death or censoring date (maximum up to 56 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: Months				
median (confidence interval 95%)	15.4 (8.0 to 26.9)	16.8 (2.3 to 35.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the time from first dose of study treatment (ie, start date) to the date of progression of disease (PD) by RECIST v 1.1 or death due to any cause, whichever occurred first. PFS data was censored on the date of the last adequate tumor assessment for subjects without an event (PD or death), for subjects who started new anti-cancer treatment prior to an event, or for subjects with an event after two or more missing tumor assessments. PD as per RECIST v1.1 for target lesions was defined as 20% increase in the sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm. For non-target lesions PD was defined as unequivocal progression of pre-existing lesions. Analysis was performed using Kaplan-Meier method. Full Analysis Set was used. Subjects were classified according to the study treatment received.

End point type	Secondary

End point timeframe:

From start of study treatment until first documentation of PD or death due to any cause or censoring date (maximum of 24 months)

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: Months				
median (confidence interval 95%)	5.5 (2.5 to 7.0)	2.3 (1.8 to 5.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Axitinib

End point title	Cmax of Axitinib

End point description:

PK parameter analysis set is a subset of the safety analysis set and included all subjects who have at least one of the PK parameters of interest for avelumab or axitinib. Here, 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure. Here n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose, 2 hour post-dose on Cycle 1 Day 15, Cycle 2 Day 1 and 15

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	5		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient				

of variation)				
Cycle 1: Day 15 (n=12,5)	17.29 (± 198)	14.64 (± 448)		
Cycle 2: Day 1 (n=16,3)	16.46 (± 91)	5.206 (± 448)		
Cycle 2: Day 15 (n=10,4)	10.64 (± 223)	2.868 (± 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Observed Serum Concentration (Ctrough) of Avelumab

End point title	Pre-dose Observed Serum Concentration (Ctrough) of Avelumab

End point description:

PK parameter analysis set is a subset of the safety analysis set and included all subjects who have at least one of the PK parameters of interest for avelumab or axitinib. Here, 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure. Here n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose on Cycle 1 Day 1, 15, Cycle 2 Day 1, Cycle 3 Day 15, Cycle 6 Day 15, Cycle 9 Day 15, and Cycle 12 Day 15

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	19		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1: Day 1 (n=38,19)	0 (± 0)	0 (± 0)		
Cycle 1: Day 15 (n=39,18)	19.46 (± 80)	18.84 (± 101)		
Cycle 2: Day 1 (n=32,17)	20.96 (± 119)	19.62 (± 91)		
Cycle 3: Day 15 (n=21,9)	28.22 (± 55)	39.29 (± 36)		
Cycle 6: Day 15 (n=17,6)	29.68 (± 52)	43.30 (± 57)		
Cycle 9: Day 15 (n=12,3)	32.84 (± 29)	42.41 (± 47)		
Cycle 12: Day 15 (n=6,3)	36.71 (± 50)	39.01 (± 20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough of Axitinib

End point title	Ctrough of Axitinib

End point description:

PK parameter analysis set is a subset of the safety analysis set and included all subjects who have at

least one of the PK parameters of interest for avelumab or axitinib. Here, 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure. Here n= subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose on Cycle 1 Day 15, Cycle 2 Day 1 and 15

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	14		
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1: Day 15 (n=29,12)	7.923 (± 127)	4.613 (± 231)		
Cycle 2: Day 1 (n=28,14)	8.871 (± 123)	5.247 (± 172)		
Cycle 2: Day 15 (n=23,12)	6.455 (± 129)	3.944 (± 172)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Programmed Death-Ligand 1 (PD-L1) Status

End point title	Number of Subjects With Programmed Death-Ligand 1 (PD-L1) Status

End point description:

PD-L1 status was defined as positive when PD-L1 staining of any intensity was observed in >= 1% of the tumor cells. PD-L1 status was defined as negative when PD-L1 staining of any intensity was observed in < 1% of the tumor cells. Biomarker analysis set is a subset of the safety analysis set and included subjects who had at least one baseline biomarker assessment. Analysis sets was defined separately for blood-based and tumor tissue-based biomarkers. Here 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Screening

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	16		
Units: Subjects				
PD-L1 positive	8	5		
PD-L1 negative	24	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Tumour Mutational Burden (TMB) in Tumor Tissue

End point title	Tumour Mutational Burden (TMB) in Tumor Tissue

End point description:

Mutational load within tumor tissue was defined as number per megabase of the genome, coding, base substitution, and indel mutations present in the sample. Mutational load was determined in whole blood samples using next generation deoxyribonucleic acid (DNA) sequencing followed by computational analysis. Biomarker analysis set is a subset of the safety analysis set and included subjects who had at least one baseline biomarker assessment. Analysis sets was defined separately for blood-based and tumor tissue-based biomarkers. Here 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Screening

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	15		
Units: Mutations per megabase				
arithmetic mean (standard deviation)	2.8 (± 2.97)	3.7 (± 4.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: T-cell Receptor (TCR) Sequencing to Identify Fraction Productive of Cells, Simpson Clonality, Total T Cells

End point title	T-cell Receptor (TCR) Sequencing to Identify Fraction Productive of Cells, Simpson Clonality, Total T Cells

End point description:

The immune response was measured by total TCR sequencing in peripheral blood. It is used to determine the fraction productive of cells, simpson clonality and total number of T Cells for the characterization of immune repertoires. Fraction productive of cells is defined as the number of T cells within the total nucleated cell count (T cells and non-T cells). Simpson clonality is calculated for a sample as the square root of Simpson’s diversity index for all productive rearrangements. Values for clonality range from 0 to 1. Values near 1 represent samples with one or a few predominant rearrangements (monoclonal or oligoclonal samples) dominating the observed repertoire. Clonality values near 0 represent more polyclonal samples. Biomarker analysis set was used. Here 'Overall Number of subjects Analyzed' signifies subjects evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Screening

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: Number				
arithmetic mean (standard deviation)				
Fraction Productive of Cells	0.2 (± 0.17)	0.1 (± 0.08)		
Simpson Clonality	0.1 (± 0.04)	0.1 (± 0.03)		
Total T Cells	1623.7 (± 1971.39)	1168.4 (± 1450.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-drug Antibody (ADA) and Neutralizing Antibodies (nAb) Against Avelumab

End point title	Number of Subjects With Positive Anti-drug Antibody (ADA) and Neutralizing Antibodies (nAb) Against Avelumab

End point description:

ADA and nAb positive was defined as presence of at least one positive ADA and nAb sample, respectively. NAb analysis was planned to be conducted for ADA positive samples. Immunogenicity analysis set is a subset of the safety analysis set and included subjects who had at least one ADA assessment collected for avelumab. Here, 'Number Analyzed' signifies number of subjects evaluable for the specified rows. Here, 99999 indicates due to low observed rate of the treatment-induced immunogenicity responses, none of the ADA positive samples was tested for the NAb assay.

End point type	Secondary

End point timeframe:

2 hours pre-dose on Cycle 1 Day 1,15, Cycle 2 Day 1; Day 15 of Cycle 3, 6, 9, 12, end of treatment and 30 days after last dose of study treatment

End point values	NSCLC Avelumab + Axitinib	UC Avelumab + Axitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: Subjects				
ADA ever-Positive (n=41,20)	7	0		
nAb ever-Positive (n=0,0)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment (Day 1) up to 30 days post last dose of study treatment or start of new anti-cancer treatment -1 day (maximum up to 56 months)

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE but are distinct events. An event may be categorised as serious in 1 subject and non-serious in another, or a subject may have experienced both SAE and non-SAE.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	UC Avelumab + Axitinib

Reporting group description:

Subjects with UC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.

Reporting group title	NSCLC Avelumab + Axitinib

Reporting group description:

Subjects with NSCLC received avelumab 800 mg intravenous dose every two weeks, (Day 1 and 15) of each 28-day cycle in combination with axitinib 5 mg twice daily dose on a continuous dosing schedule.

Serious adverse events	UC Avelumab + Axitinib	NSCLC Avelumab + Axitinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	21 / 41 (51.22%)	
number of deaths (all causes)	11	27	
number of deaths resulting from adverse events	1	5	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypertension			

subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	3 / 20 (15.00%)	4 / 41 (9.76%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac dysfunction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			

subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness unilateral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal perforation			

subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hepatobiliary disorders			
Hepatobiliary disease			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Endocrine disorders			
Cushing's syndrome			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infectious pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (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	1 / 20 (5.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	UC Avelumab + Axitinib	NSCLC Avelumab + Axitinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)	41 / 41 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 20 (10.00%)	2 / 41 (4.88%)	
occurrences (all)	2	2	
Hypertensive crisis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	4	
Hypertension			
subjects affected / exposed	4 / 20 (20.00%)	17 / 41 (41.46%)	
occurrences (all)	7	32	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	5 / 20 (25.00%)	9 / 41 (21.95%)	
occurrences (all)	8	17	
General physical health deterioration			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Mucosal inflammation			
subjects affected / exposed	2 / 20 (10.00%)	4 / 41 (9.76%)	
occurrences (all)	2	4	
Asthenia			
subjects affected / exposed	5 / 20 (25.00%)	7 / 41 (17.07%)	
occurrences (all)	6	7	
Chills			
subjects affected / exposed	1 / 20 (5.00%)	7 / 41 (17.07%)	
occurrences (all)	1	8	
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	6 / 41 (14.63%)	
occurrences (all)	0	8	
Oedema peripheral			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 20 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	4	
Pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	4	
Dysphonia			
subjects affected / exposed	3 / 20 (15.00%)	6 / 41 (14.63%)	
occurrences (all)	5	6	
Cough			

subjects affected / exposed	1 / 20 (5.00%)	5 / 41 (12.20%)	
occurrences (all)	3	6	
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 20 (10.00%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Anxiety			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 20 (10.00%)	2 / 41 (4.88%)	
occurrences (all)	2	2	
Blood corticotrophin increased			
subjects affected / exposed	0 / 20 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	5	
Blood bilirubin increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 20 (15.00%)	1 / 41 (2.44%)	
occurrences (all)	5	1	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 20 (20.00%)	8 / 41 (19.51%)	
occurrences (all)	6	15	
Amylase increased			
subjects affected / exposed	2 / 20 (10.00%)	3 / 41 (7.32%)	
occurrences (all)	5	3	
Alanine aminotransferase increased			
subjects affected / exposed	3 / 20 (15.00%)	9 / 41 (21.95%)	
occurrences (all)	4	15	
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 20 (5.00%)	3 / 41 (7.32%)	
occurrences (all)	1	3	
Weight decreased			

subjects affected / exposed	6 / 20 (30.00%)	9 / 41 (21.95%)	
occurrences (all)	7	17	
Lipase increased			
subjects affected / exposed	2 / 20 (10.00%)	3 / 41 (7.32%)	
occurrences (all)	7	3	
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 20 (20.00%)	3 / 41 (7.32%)	
occurrences (all)	6	5	
C-reactive protein increased			
subjects affected / exposed	1 / 20 (5.00%)	3 / 41 (7.32%)	
occurrences (all)	1	6	
Blood triglycerides increased			
subjects affected / exposed	0 / 20 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	4	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 20 (0.00%)	6 / 41 (14.63%)	
occurrences (all)	0	7	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	2 / 41 (4.88%)	
occurrences (all)	2	2	
Headache			
subjects affected / exposed	1 / 20 (5.00%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 20 (15.00%)	4 / 41 (9.76%)	
occurrences (all)	4	7	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)	3 / 41 (7.32%)	
occurrences (all)	1	4	
Dysphagia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 41 (2.44%)	
occurrences (all)	2	1	

Nausea			
subjects affected / exposed	4 / 20 (20.00%)	8 / 41 (19.51%)	
occurrences (all)	6	8	
Stomatitis			
subjects affected / exposed	1 / 20 (5.00%)	4 / 41 (9.76%)	
occurrences (all)	2	5	
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)	12 / 41 (29.27%)	
occurrences (all)	7	43	
Constipation			
subjects affected / exposed	2 / 20 (10.00%)	7 / 41 (17.07%)	
occurrences (all)	2	7	
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)	4 / 41 (9.76%)	
occurrences (all)	1	5	
Abdominal pain			
subjects affected / exposed	2 / 20 (10.00%)	1 / 41 (2.44%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)	4 / 41 (9.76%)	
occurrences (all)	3	6	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 20 (5.00%)	7 / 41 (17.07%)	
occurrences (all)	1	10	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 20 (10.00%)	6 / 41 (14.63%)	
occurrences (all)	11	15	
Dry skin			
subjects affected / exposed	2 / 20 (10.00%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	2 / 20 (10.00%)	4 / 41 (9.76%)	
occurrences (all)	4	31	
Haematuria			

subjects affected / exposed	3 / 20 (15.00%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 20 (5.00%)	5 / 41 (12.20%)	
occurrences (all)	1	6	
Hypothyroidism			
subjects affected / exposed	1 / 20 (5.00%)	13 / 41 (31.71%)	
occurrences (all)	1	15	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 20 (10.00%)	2 / 41 (4.88%)	
occurrences (all)	3	4	
Arthralgia			
subjects affected / exposed	3 / 20 (15.00%)	6 / 41 (14.63%)	
occurrences (all)	6	9	
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	4	
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	3 / 41 (7.32%)	
occurrences (all)	4	4	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 20 (15.00%)	1 / 41 (2.44%)	
occurrences (all)	9	1	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 41 (2.44%)	
occurrences (all)	9	1	
Hypoalbuminaemia			
subjects affected / exposed	3 / 20 (15.00%)	0 / 41 (0.00%)	
occurrences (all)	8	0	
Hypertriglyceridaemia			
subjects affected / exposed	2 / 20 (10.00%)	4 / 41 (9.76%)	
occurrences (all)	4	5	

Hypermagnesaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Hyperkalaemia			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	6	
Decreased appetite			
subjects affected / exposed	5 / 20 (25.00%)	14 / 41 (34.15%)	
occurrences (all)	6	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported