



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 (\geq)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, hypermagnesaemia, hyponatremia, hypertriglyceridemia, hypoalbuminemia, hypocalcaemia, hypoglycaemia, hypokalaemia, hypomagnesaemia, 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 $\geq 30\%$ 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 $\geq 30\%$ 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

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|-----------------|---|
| 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 (Ctough) of Avelumab

| | |
|-----------------|--|
| End point title | Pre-dose Observed Serum Concentration (Ctough) 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: Ctough of Axitinib

| | |
|-----------------|--------------------|
| End point title | Ctough 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 $\geq 1\%$ 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 occurrences (all) | 1 / 20 (5.00%) 3 | 5 / 41 (12.20%) 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 occurrences (all) | 3 / 20 (15.00%) 3 | 0 / 41 (0.00%) 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