Clinical trial results:
A RANDOMIZED, OPEN-LABEL, MULTICENTER, PHASE 3 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF AVELUMAB (MSB0010718C) IN COMBINATION WITH AND/OR FOLLOWING CHEMOTHERAPY IN PATIENTS WITH PREVIOUSLY UNTREATED EPITHELIAL OVARIAN CANCER

Summary

EudraCT number	2015-003239-36
Trial protocol	SK NL BG HU EE IE GB LV DE PL HR IT
Global end of trial date	16 May 2019

Results information

Result version number	v1 (current)
This version publication date	29 May 2020
First version publication date	29 May 2020

Trial information

Trial identification

Sponsor protocol code	B9991010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02718417
WHO universal trial number (UTN)	-
Other trial identifiers	Alias Study Number: JAVELIN OVARIAN 100

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	03 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that avelumab in combination with platinum-based chemotherapy followed by avelumab maintenance (Arm C) is superior to platinum-based chemotherapy alone followed by observation (Arm A) in prolonging progression free survival (PFS) in subjects with previously untreated epithelial ovarian cancer (EOC). Also, to demonstrate that platinum-based chemotherapy alone followed by avelumab maintenance (Arm B) is superior to platinum-based chemotherapy alone followed by observation (Arm A) in prolonging PFS in patients with previously untreated EOC.

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 trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 May 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 41
Country: Number of subjects enrolled	United States: 240
Country: Number of subjects enrolled	Hong Kong: 12
Country: Number of subjects enrolled	Japan: 100
Country: Number of subjects enrolled	Korea, Republic of: 88
Country: Number of subjects enrolled	Singapore: 13
Country: Number of subjects enrolled	Taiwan: 34
Country: Number of subjects enrolled	European Union: 103
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	Russian Federation: 101
Country: Number of subjects enrolled	Ukraine: 61
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Ireland: 10
Country: Number of subjects enrolled	Italy: 79
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Switzerland: 2

Country: Number of subjects enrolled	United Kingdom: 62
Worldwide total number of subjects	998
EEA total number of subjects	168

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)	687
From 65 to 84 years	310
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted at 25 countries between 19 May 2016 and 16 May 2019.

Period 1

Period 1 title	Chemotherapy Phase (CP)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemotherapy followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Arm title	Chemotherapy + Avelumab followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 3 weeks on Day 1 for Cycle 1 to 6 in chemotherapy phase. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Arm title	Chemotherapy followed by Observation

Arm description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Arm type	Control
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Number of subjects in period 1	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation
Started	332	331	335
Safety population	328	329	334
Completed	280	294	289
Not completed	52	37	46
Adverse event, serious fatal	5	4	1
Consent withdrawn by subject	13	8	15
Physician decision	5	-	4
Global deterioration of health status	3	2	1
Adverse event, non-fatal	9	14	13
No longer met eligibility criteria	4	2	1
Unspecified	2	-	1
Progressive disease	11	7	10

Period 2

Period 2 title	Maintenance (MP), Observation Phase (OP)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemotherapy followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression,

received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Arm title	Chemotherapy + Avelumab followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 3 weeks on Day 1 for Cycle 1 to 6 in chemotherapy phase. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Arm title	Chemotherapy followed by Observation

Arm description:

In chemotherapy phase, based on investigator's decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Arm type	Control

No investigational medicinal product assigned in this arm

Number of subjects in period 2[1]	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation
Started	267	288	284
Completed	1	1	2
Not completed	266	287	282
Adverse event, serious fatal	1	1	2
Consent withdrawn by subject	17	20	34
Physician decision	6	7	9
Global deterioration of health status	5	3	1
Adverse event, non-fatal	21	26	1
No longer met eligibility criteria	-	1	-
Study terminated by sponsor	114	140	135
Unspecified	2	1	7
Progressive disease	100	88	92
Lost to follow-up	-	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects not completing chemotherapy phase could also start this phase.

Period 3

Period 3 title	Follow-up Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemotherapy followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Arm title	Chemotherapy + Avelumab followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle

of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 3 weeks on Day 1 for Cycle 1 to 6 in chemotherapy phase. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Arm title	Chemotherapy followed by Observation

Arm description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Arm type	Control
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Number of subjects in period 3[2]	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation
Started	1	1	1
Completed	103	91	20
Not completed	135	172	19
Adverse event, serious fatal	7	7	3
Consent withdrawn by subject	19	17	5
Adverse event, non-fatal	3	1	1
Study terminated by sponsor	100	138	6
Unspecified	4	6	4
Lost to follow-up	2	3	-
Joined	237	262	38
Not completing MP or OP who started	237	262	38

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects not completing maintenance, observation phase could also start this phase.

Period 4

Period 4 title	Long-term follow-up Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemotherapy followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Arm title	Chemotherapy + Avelumab followed by Avelumab

Arm description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg, over 1 hour IV infusion, once every 3 weeks on Day 1 for Cycle 1 to 6 in chemotherapy phase. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase,

Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Arm title	Chemotherapy followed by Observation

Arm description:

In chemotherapy phase, based on investigator's decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Arm type	Control
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m2, IV infusion on Day 1 of Cycles 1 to 6 or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15 of Cycles 1 to 6.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6.

Number of subjects in period 4[3]	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation
Started	89	82	19
Completed	0	0	0
Not completed	139	112	135
Adverse event, serious fatal	20	17	11
Consent withdrawn by subject	6	9	9
Study terminated by sponsor	105	80	112
Unspecified	-	2	-
Lost to follow-up	8	4	3
Joined	50	30	116

Not completing follow-up phase who started	50	30	116

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects not completing follow-up phase could also start this phase.

Baseline characteristics

Reporting groups

Reporting group title	Chemotherapy followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy + Avelumab followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy followed by Observation

Reporting group description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Reporting group values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation
Number of subjects	332	331	335
Age categorical Units: Subjects			
Adults (18-64 years)	224	224	239
From 65-84 years	107	107	96
85 years and over	1	0	0
Age Continuous Units: Years			
arithmetic mean	58.34	58.16	57.10
standard deviation	± 11.00	± 10.85	± 11.27
Sex: Female, Male Units: Subjects			
Female	332	331	335

Male	0	0	0

Race/Ethnicity, Customized Units: Subjects			
Black or African American	2	4	1
American Indian or Alaska Native	1	0	0
Asian	86	82	95
White	236	238	236
Other	7	7	3

Reporting group values	Total		
Number of subjects	998		
Age categorical Units: Subjects			
Adults (18-64 years)	687		
From 65-84 years	310		
85 years and over	1		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	998		
Male	0		
Race/Ethnicity, Customized Units: Subjects			
Black or African American	7		
American Indian or Alaska Native	1		
Asian	263		
White	710		
Other	17		

End points reporting groups

Reporting group title	Chemotherapy followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy + Avelumab followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy followed by Observation

Reporting group description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Reporting group title	Chemotherapy followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy + Avelumab followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of

of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy followed by Observation

Reporting group description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Reporting group title	Chemotherapy followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy + Avelumab followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy followed by Observation

Reporting group description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Reporting group title	Chemotherapy followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy + Avelumab followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy followed by Observation

Reporting group description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation (long-term follow up phase).

Subject analysis set title	PK: Chemotherapy followed by Avelumab
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel once every three weeks (Q3W) (or once weekly [QW] on Days 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles. During the maintenance phase, subjects received avelumab once every 2 weeks (Q2W) on Days 1, 15 and 29 of each 42 day cycle.

Subject analysis set title	PK: Chemotherapy + Avelumab followed by Avelumab
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Days 1, 8 and 15), followed by carboplatin Q3W along with avelumab Q3W on Day 1 of each 21 day cycle for 6 cycles. During the maintenance phase, subjects received avelumab Q2W (on Days 1, 15 and 29 of each 42 day cycle).

Subject analysis set title	PK: Chemotherapy followed by Observation
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Day 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles.

Subject analysis set title	PK: Chemotherapy followed by Avelumab
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Days 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles. During the maintenance phase, subjects received avelumab Q2W on Days 1, 15 and 29 of each 42 day cycle.

Subject analysis set title	PK: Chemotherapy + Avelumab followed by Avelumab
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Days 1, 8 and 15), followed by carboplatin Q3W along with avelumab Q3W on Day 1 of each 21 day cycle for 6 cycles. During the maintenance phase, subjects received avelumab Q2W (on Days 1, 15 and 29 of each 42 day cycle).

Subject analysis set title	PK: Chemotherapy followed by Observation
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Day 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles.

Subject analysis set title	PK: Chemotherapy followed by Avelumab
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Days 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles. During the maintenance phase, subjects received avelumab Q2W on Days 1, 15 and 29 of each 42 day cycle.

Subject analysis set title	PK: Chemotherapy followed by Observation
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Day 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles.

Subject analysis set title	PK: Chemotherapy + Avelumab followed by Avelumab
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Days 1, 8 and 15), followed by carboplatin Q3W along with avelumab Q3W on Day 1 of each 21 day cycle for 6 cycles. During the maintenance phase, subjects received avelumab Q2W (on Days 1, 15 and 29 of each 42 day cycle).

Subject analysis set title	PK: Chemotherapy followed by Observation
Subject analysis set type	Per protocol

Subject analysis set description:

In chemotherapy phase, subjects received paclitaxel Q3W (or QW on Day 1, 8 and 15), followed by carboplatin Q3W on Day 1 of each 21 day cycle for 6 cycles.

Primary: Progression-Free Survival (PFS) as Assessed by Blinded Independent Central Review (BICR)

End point title	Progression-Free Survival (PFS) as Assessed by Blinded Independent Central Review (BICR)

End point description:

BICR assessed PFS: Duration from randomization until disease progression or death. PFS data censored on date of last adequate tumor assessment for subjects who did not have an event (progression of disease or death),who started new anti-cancer therapy prior to an event or subjects with an event after 2 or more missing tumor assessments. Progression as per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1:at least a 20% increase in sum of diameters of target lesions, taking as reference smallest sum on study (this includes the baseline sum if that is smallest on study). In addition to relative increase of 20%, the sum must have also demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered progression. Analysis was performed using Kaplan-Meier method. Median and upper limit of 95% CI was not estimable due to limited number of events and has been denoted by '99999'. Full analysis set: all randomized subjects

End point type	Primary

End point timeframe:

Baseline to progression of disease or discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	331	335	
Units: months				
median (confidence interval 95%)	16.8 (13.5 to 99999)	18.1 (14.8 to 99999)	99999 (18.2 to 99999)	

Statistical analyses

Statistical analysis title	Chemotherapy by Avelumab Vs. Chemo by Observation

Statistical analysis description:

Analysis was performed using a Cox's Proportional Hazard model stratified by the randomization strata and a stratified log-rank test.

Comparison groups	Chemotherapy followed by Avelumab v Chemotherapy followed by Observation
Number of subjects included in analysis	667
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.989 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.051
upper limit	1.946

Notes:

[1] - One-sided log-rank test was used.

Statistical analysis title	Chemo + Avel by Avel Vs. Chemo by Observation

Statistical analysis description:

Analysis was performed using a Cox's Proportional Hazard model stratified by the randomization strata and a stratified log-rank test.

Comparison groups	Chemotherapy + Avelumab followed by Avelumab v Chemotherapy followed by Observation
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7935 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.832
upper limit	1.565

Notes:

[2] - One-sided log-rank test was used.

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time (in months) from the date of randomization 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. Median and 95% CI were not estimable due to limited number of events and has been denoted by '99999'. The full analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline to discontinuation from the study or death, whichever occurred first (maximum duration of 27

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	331	335	
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

Statistical analysis title	Chemotherapy by Avelumab Vs. Chemo by Observation

Statistical analysis description:

Analysis was performed using a Cox’s Proportional Hazard model stratified by the randomization strata and a stratified log-rank test.

Comparison groups	Chemotherapy followed by Avelumab v Chemotherapy followed by Observation
Number of subjects included in analysis	667
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8848 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	3.08

Notes:

[3] - One-sided log-rank test was used.

Statistical analysis title	Chemo + Avel by Avel Vs. Chemo by Observation

Statistical analysis description:

Analysis was performed using a Cox’s Proportional Hazard model stratified by the randomization strata and a stratified log-rank test.

Comparison groups	Chemotherapy + Avelumab followed by Avelumab v Chemotherapy followed by Observation
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8953 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.776
upper limit	3.111

Notes:

[4] - One-sided log-rank test was used.

Secondary: Progression-Free Survival (PFS) as Assessed by Investigator

End point title	Progression-Free Survival (PFS) as Assessed by Investigator

End point description:

Investigator assessed PFS was defined as time (in months) from date of randomization to the first documentation of disease progression or death (due to any cause), whichever occurred first. Progression as per RECIST 1.1, was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must have also demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered progression. Analysis was performed using a Cox's Proportional Hazard model stratified by the randomization strata and a stratified log-rank test. The full analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline to progression of disease or discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	331	335	
Units: months				
median (confidence interval 95%)	13.8 (12.1 to 15.9)	16.1 (13.9 to 19.4)	15.0 (13.2 to 18.7)	

Statistical analyses

Statistical analysis title	Chemotherapy by Avelumab Vs. Chemo by Observation
Comparison groups	Chemotherapy followed by Avelumab v Chemotherapy followed by Observation
Number of subjects included in analysis	667
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9278 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.935
upper limit	1.578

Notes:

[5] - One-sided log-rank test was used.

Statistical analysis title	Chemo + Avel by Avel Vs. Chemo by Observation
Comparison groups	Chemotherapy + Avelumab followed by Avelumab v Chemotherapy followed by Observation
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2367 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.688
upper limit	1.189

Notes:

[6] - One-sided log-rank test was used.

Secondary: Percentage of Subjects With Objective Response as Assessed by Investigator

End point title	Percentage of Subjects With Objective Response as Assessed by Investigator

End point description:

Investigator assessed objective response according to RECIST version 1.1, was defined as subjects with confirmed best overall response of complete response (CR) or partial response (PR). CR was defined as disappearance of all target and non-target lesions, and sustained for at least 4 weeks. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<) 10 mm. PR was defined as at least 30% decrease in the sum of the longest dimensions of target lesions taking as reference the baseline sum longest dimensions. The full analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline to progression of disease, start of new anti-cancer therapy or discontinuation from study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	331	335	
Units: percentage of subjects				
number (confidence interval 95%)	25.9 (21.3 to 31.0)	31.1 (26.2 to 36.4)	27.8 (23.0 to 32.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Objective Response as Assessed by Blinded Independent Central Review (BICR)

End point title	Percentage of Subjects With Objective Response as Assessed by Blinded Independent Central Review (BICR)

End point description:

BICR assessed objective response according to RECIST version 1.1, was defined as subjects with confirmed best overall response of CR or PR. CR was defined as disappearance of all target and non-target lesions, and sustained for at least 4 weeks. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as at least 30% decrease in the sum of the longest dimensions of target lesions taking as reference the baseline sum longest dimensions. The full analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline to progression of disease, start of new anti-cancer therapy or discontinuation from study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	331	335	
Units: percentage of subjects				
number (confidence interval 95%)	30.4 (25.5 to 35.7)	36.0 (30.8 to 41.4)	30.4 (25.6 to 35.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Assessed by Investigator

End point title	Duration of Response (DOR) as Assessed by Investigator

End point description:

Investigator assessed DOR: time in months from first documentation of objective response to date of first documentation of PD or death due to any cause. RECIST version 1.1, CR:disappearance of all target and non-target lesions,sustained for at least 4 weeks. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR: at least 30% decrease in sum of longest dimensions of target lesions taking as reference baseline sum longest dimensions. PD:at least 20% increase in sum of diameters of target lesions, taking as reference smallest sum on study (included baseline sum if that is smallest). In addition, sum must have an absolute increase of at least 5 mm. Appearance of one or more new lesions was also considered progression. Analysis was performed using Kaplan-Meier method

on subset of randomized subjects, who had objective response, as assessed by Investigator. Median and upper limit of 95% CI was not estimable due to limited number of events and denoted by '99999'

End point type	Secondary

End point timeframe:

First response subsequently confirmed to progression of disease or start of new anti-cancer therapy or discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	103	93	
Units: months				
median (confidence interval 95%)	10.6 (8.3 to 20.2)	99999 (11.7 to 99999)	15.4 (8.3 to 18.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Assessed by Blinded Independent Central Review (BICR)

End point title	Duration of Response (DOR) as Assessed by Blinded Independent Central Review (BICR)

End point description:

BICR assessed DOR: time from first documentation of objective response to date of first documentation of PD or death due to any cause. RECIST version 1.1, CR:disappearance of all target and non-target lesions, and sustained for at least 4 weeks. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR:at least 30% decrease in sum of longest dimensions of target lesions taking as reference baseline sum longest dimensions. PD:at least a 20% increase in sum of diameters of target lesions, taking as reference smallest sum on study (this included baseline sum if that is smallest on study). In addition, sum must havean absolute increase of at least 5 mm. Appearance of one or more new lesions was also considered progression. Analysis was performed using Kaplan-Meier method on subset of randomized subjects, who had objective response, as assessed by BICR. Median and upper limit of 95% CI was not estimable due to limited number of events and denoted by '99999'.

End point type	Secondary

End point timeframe:

First response subsequently confirmed to progression of disease or start of new anti-cancer therapy or discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	119	102	
Units: months				
median (confidence interval 95%)	11.9 (8.9 to 99999)	14.5 (11.7 to 99999)	99999 (16.1 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maintenance Progression-Free Survival as Assessed by Blinded Independent Central Review (BICR)

End point title	Maintenance Progression-Free Survival as Assessed by Blinded Independent Central Review (BICR)

End point description:

BICR assessed maintenance PFS: defined as time from Cycle 1 Day 1 of maintenance phase to date of first documentation of PD or death due to any cause, whichever occurs first. Defined, for subjects who proceeded to maintenance phase and who did not have disease progression by BICR during chemotherapy phase. RECIST version 1.1, PD: at least a 20% increase in sum of diameters of target lesions, taking as reference smallest sum on study (this included baseline sum if that is smallest on study). In addition, sum must have an absolute increase of at least 5 mm. Appearance of one or more new lesions was also considered progression. Analysis was performed using Kaplan-Meier method. Analysis set: randomized subjects who proceeded to maintenance phase and who did not have PD by BICR assessment during chemotherapy phase. Median and upper limit of 95% CI was not estimable due to limited number of events and is denoted by '99999'.

End point type	Secondary

End point timeframe:

From Day 1 of Cycle 1 (42 days) of maintenance phase to progression of disease or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	248	267	247	
Units: months				
median (confidence interval 95%)	13.6 (9.3 to 99999)	13.8 (11.1 to 99999)	99999 (13.8 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maintenance Progression-Free Survival (PFS) as Assessed by Investigator

End point title	Maintenance Progression-Free Survival (PFS) as Assessed by Investigator

End point description:

Investigator assessed maintenance PFS: time from Cycle 1 Day 1 of maintenance phase to date of first documentation of PD or death due to any cause, whichever occurs first. Defined, for subjects who

proceeded to maintenance phase and who did not have disease progression by investigator during chemotherapy phase.RECIST version 1.1, PD:at least a 20% increase in sum of diameters of target lesions, taking as reference smallest sum on study (this included baseline sum if that is smallest on study). In addition,sum must have also demonstrated an absolute increase of at least 5 mm. Appearance of one or more new lesions was also considered progression. Analysis was performed using Kaplan-Meier method. Analysis set:randomized subjects who proceeded to maintenance phase and who did not have PD by investigator assessment during chemotherapy phase. Upper limit of 95% CI was not estimable due to limited number of events and denoted by '99999'.

End point type	Secondary

End point timeframe:

From Day 1 of Cycle 1 (42 days) of maintenance phase to progression of disease or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	252	271	252	
Units: months				
median (confidence interval 95%)	10.4 (8.2 to 13.6)	11.6 (9.9 to 13.8)	12.7 (9.5 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Pathological Complete Response (pCR)

End point title	Percentage of Subjects with Pathological Complete Response (pCR)

End point description:

pCR was defined (for neoadjuvant subjects who underwent interval debulking surgery [IDS]), as the chemotherapy response score 3 (CSR3), based on a study by Bohm et al, 2015. CSR3 was defined as complete or near-complete response with no residual tumor or minimal irregularly scattered tumor foci seen as individual cells, cell groups, or nodules up to 2 mm. Complete or near-complete response was defined as complete or near-complete microscopic disappearance of invasive tumor/ residual disease. Analysis was performed on a subset of randomized subjects which included neoadjuvant subjects who underwent IDS.

End point type	Secondary

End point timeframe:

Baseline to progression of disease or discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	115	116	
Units: percentage of subjects				
number (not applicable)	15.7	17.4	25.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival 2 (PFS2)

End point title	Progression-Free Survival 2 (PFS2)

End point description:

PFS2 was defined as time (in months) from the date of randomization to the start of second subsequent treatment after first documentation of PD, or death from any cause, whichever occurred first. Progression as per RECIST version 1.1, was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this included the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must have also demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered progression. Analysis was performed using Kaplan-Meier method. The trial was terminated due to crossing of futility boundaries for both experimental arms as compared to the control arm at the pre-specified interim analysis for PFS based on BICR assessment. Subsequently, the data for this endpoint was not collected and analyzed.

End point type	Secondary

End point timeframe:

Baseline up to start of second subsequent treatment after first PD or discontinuation from study or death, which ever occured first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[7]	0[8]	0[9]	
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[7] - The data for this endpoint was not collected and analyzed due to futility reasons.

[8] - The data for this endpoint was not collected and analyzed due to futility reasons.

[9] - The data for this endpoint was not collected and analyzed due to futility reasons.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) as Assessed by Gynecological Cancer Intergroup (GCIG) Criteria

End point title	Progression-Free Survival (PFS) as Assessed by Gynecological

	Cancer Intergroup (GCIG) Criteria

End point description:

PFS by GCIG was assessed by both RECIST 1.1 and cancer antigen 125 (CA-125). Defined as time from randomization to first documentation of disease progression (PD) or death, whichever occurred first. PD defined as per RECIST 1.1. PD based on serum CA-125 was defined as (i) subjects with elevated CA-125 pretreatment and normalization of CA-125, (ii) CA-125 in reference range before treatment; (i) and (ii) must have showed CA-125 >= 2 times upper limit of reference range on 2 occasions >= 1 week apart, or (iii) elevated CA-125 before treatment, which never normalized, showed CA-125 >= 2 times the nadir value on 2 occasions >= 1 week apart. Censoring date for PFS by GCIG was latest of censoring dates for PFS by RECIST 1.1 and PFS by CA-125. Trial was terminated due to crossing of futility boundaries for both experimental arms as compared to the control arm at pre-specified interim analysis for PFS based on BICR assessment. Data for this endpoint was not collected and analyzed.

End point type	Secondary

End point timeframe:

Baseline until disease progression by GCIG criteria or start of new anti-cancer therapy or discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[10]	0[11]	0[12]	
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[10] - The data for this endpoint was not collected and analyzed due to futility reasons.

[11] - The data for this endpoint was not collected and analyzed due to futility reasons.

[12] - The data for this endpoint was not collected and analyzed due to futility reasons.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (AEs) Graded Based on, National Cancer Institute Common Terminology Criteria (NCI-CTCAE), Version 4.03

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) Graded Based on, National Cancer Institute Common Terminology Criteria (NCI-CTCAE), Version 4.03

End point description:

AE:any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship.NCI-CTCAE version 4.03,Grade 1:asymptomatic or mild symptoms,clinical or diagnostic observations only,intervention not indicated;Grade 2:moderate,minimal,local or noninvasive intervention indicated,limiting age-appropriate instrumental activities of daily life(ADL); Grade 3:severe or medically significant but not immediately life-threatening,hospitalization or prolongation of existing hospitalization indicated,disabling,limiting self-care ADL; Grade 4:life-threatening consequence,urgent intervention indicated; Grade 5:death related to AE. Treatment-emergent events: events between first dose of study drug and up to 36 months that were absent before treatment or worsened relative to pretreatment state. Safety analysis set:all subjects who had received at least one dose of study drug. Here,'number of subjects analysed'=subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to discontinuation from the study or death, whichever occurred first (maximum duration of 36 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	323	328	321	
Units: subjects				
Grade 1	11	13	15	
Grade 2	89	77	96	
Grade 3	151	148	131	
Grade 4	67	84	76	
Grade 5	5	6	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities Greater Than or Equal to (>=) Grade 3, Based on National Cancer Institute Common Terminology Criteria (NCI-CTCAE), Version 4.03

End point title	Number of Subjects With Laboratory Abnormalities Greater Than or Equal to (>=) Grade 3, Based on National Cancer Institute Common Terminology Criteria (NCI-CTCAE), Version 4.03

End point description:

NCI-CTCAE v 4.03,Grade 3 and above criteria; Hematology [Anemia - Grade 3: hemoglobin <8.0 grams per deciliter (g/dL), <4.9 millimoles per liter (mmol/L),<80 grams per liter (g/L), transfusion indicated, Grade 4: life-threatening consequences, urgent intervention indicated, Grade 5:death; platelet count decreased- Grade 3:<50.0 to 25.0*10^9/Liters(L),Grade 4: <25.0*10^9/L;lymphocyte count decreased-Grade 3: <0.5-0.2*10^9/L, Grade 4: <0.2*10^9/L; neutrophil count decreased-Grade 3: <1.0 to 0.5*10^9 /L, Grade 4: <0.5*10^9/L]. Chemistry[creatinine increased-Grade 3: >3.0 to 6.0*upper limit of normal (ULN), Grade 4: >6.0*ULN; serum amylase increased, lipase increased-Grade 3: >2.0 - 5.0*ULN, Grade 4: >5.0*ULN]. Liver function [aspartate aminotransferase(AST) and alanine aminotransferase(ALT)-Grade 3: >5.0 to 20.0*ULN, Grade 4: >20.0*ULN]. Safety analysis set:all subjects who had received at least one dose of study drug. Here,'n' = Subjects evaluable for this end point at specified rows.

End point type	Secondary

End point timeframe:

Baseline to discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	328	329	334	
Units: subjects				
Anemia(n=326,326,328)	73	68	63	

Platelet Count Decreased(n=326,326,328)	20	35	38	
Lymphocyte Count Decreased(n=326,326,328)	35	63	29	
Neutrophil Count Decreased(n=326,326,328)	144	159	156	
Creatinine Increased(n=324,326,327)	2	7	0	
Serum Amylase Increased(n=321,322,326)	5	9	10	
Lipase Increased(n=323,323,325)	19	24	11	
ALT or AST(n=324,326,327)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs - Blood Pressure at Day 1 of Cycles 2, 3, 4 in Chemotherapy Phase; Days 1, 15 and 29 of Cycles 1 and 2 in Maintenance Phase and at End of Treatment

End point title	Change from Baseline in Vital Signs - Blood Pressure at Day 1 of Cycles 2, 3, 4 in Chemotherapy Phase; Days 1, 15 and 29 of Cycles 1 and 2 in Maintenance Phase and at End of Treatment

End point description:

Vital signs included blood pressure and pulse rate. Blood pressure included sitting diastolic blood pressure (DBP) and sitting systolic blood pressure (SBP). Safety analysis set:all subjects who had received at least one dose of study drug. Here, 'number of subjects analysed' = subjects who were evaluable for this endpoint and 'n' = subjects evaluable for this end point at specified rows.

End point type	Secondary

End point timeframe:

Baseline, first 3 months of Chemotherapy Phase (CP): Day 1 of Cycles 2, 3 and 4 (each cycle 21 days); Maintenance Phase (MP): Days 1, 15 and 29 of Cycles 1 and 2 (each cycle 42 days) and at end of treatment (up to 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	318	317	316	
Units: millimeters of mercury				
arithmetic mean (standard deviation)				
CP:ChangeatDay1,Cycle2:SittingDBP(n=310,305,301)	0.00 (± 9.28)	0.10 (± 9.86)	0.70 (± 9.33)	
CP:ChangeatDay 1,Cycle 3:SittingDBP(n=305,299,295)	-0.50 (± 10.18)	0.50 (± 10.84)	1.00 (± 9.69)	
CP:ChangeatDay1,Cycle4:SittingDBP(n=287,291,289)	-0.10 (± 10.48)	-0.50 (± 10.89)	-0.40 (± 10.19)	
MP:ChangeatDay1,Cycle1:SittingDBP(n=253,266,253)	-2.20 (± 10.36)	-1.30 (± 10.74)	-0.90 (± 10.54)	
MP:ChangeatDay15,Cycle1:SittingDBP(n=241,249,3)	-2.10 (± 10.04)	-1.80 (± 10.57)	-9.70 (± 5.69)	
MP:ChangeatDay29,Cycle1:SittingDBP(n=233,249,3)	-1.70 (± 10.29)	-1.80 (± 11.24)	-8.30 (± 6.03)	

MP:ChangeatDay1,Cycle2:SittingDBP(n=229,247,226)	-2.30 (± 10.26)	-1.70 (± 10.63)	-0.70 (± 10.67)	
MP:ChangeatDay15,Cycle2:SittingDBP(n=219,236,0)	-2.00 (± 10.71)	-2.40 (± 10.82)	99999 (± 99999)	
MP:ChangeatDay29,Cycle2:SittingDBP(n=215,225,0)	-2.60 (± 10.86)	-1.90 (± 10.16)	99999 (± 99999)	
ChangeatEOT:SittingDBP(n=137,116,120)	-0.70 (± 11.36)	0.00 (± 12.45)	0.70 (± 10.00)	
CP:ChangeatDay1,Cycle2:SittingSBP(n=310,305,301)	2.30 (± 14.91)	0.70 (± 15.32)	1.00 (± 14.00)	
CP:ChangeatDay1,Cycle3:SittingSBP(n=305,299,295)	1.50 (± 14.00)	-0.30 (± 15.48)	1.70 (± 14.80)	
CP:ChangeatDay1,Cycle4:SittingSBP(n=287,291,289)	1.00 (± 14.60)	0.10 (± 16.75)	0.60 (± 15.61)	
MP:ChangeatDay1,Cycle1:SittingSBP(n=253,266,253)	-1.80 (± 15.12)	-1.60 (± 16.64)	0.00 (± 14.81)	
MP:ChangeatDay15,Cycle1:SittingSBP(n=241,249,3)	-1.10 (± 14.37)	-3.20 (± 16.44)	-4.70 (± 10.21)	
MP:ChangeatDay29,Cycle1:SittingSBP(n=233,249,3)	-2.20 (± 15.81)	-2.80 (± 15.93)	-9.30 (± 8.14)	
MP:Changeat Day1,Cycle2:SittingSBP(n=229,247,226	-1.20 (± 15.16)	-0.60 (± 15.46)	-0.50 (± 14.43)	
MP:ChangeatDay15,Cycle 2:SittingSBP(n=219,236,0)	-2.10 (± 14.44)	-3.90 (± 16.20)	99999 (± 99999)	
MP:Changeat Day29,Cycle2:SittingSBP(n=215,225,0)	-2.70 (± 13.79)	-2.90 (± 15.28)	99999 (± 99999)	
Changeat EOT:Sitting SBP(n=137,116,120)	1.70 (± 16.96)	-1.00 (± 17.56)	2.90 (± 16.69)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs - Pulse Rate at Day 1 of Cycles 2, 3, 4 in Chemotherapy Phase; Days 1, 15 and 29 of Cycles 1 and 2 in Maintenance Phase and at End of Treatment

End point title	Change from Baseline in Vital Signs - Pulse Rate at Day 1 of Cycles 2, 3, 4 in Chemotherapy Phase; Days 1, 15 and 29 of Cycles 1 and 2 in Maintenance Phase and at End of Treatment

End point description:

Vital signs included blood pressure and pulse rate. Changes from baseline in sitting pulse rate were summarized. Safety analysis set:all subjects who had received at least one dose of study drug. Here, 'number of subjects analysed' = subjects who were evaluable for this endpoint and 'n' = subjects evaluable for this end point at specified rows.

End point type	Secondary

End point timeframe:

Baseline, first 3 months of Chemotherapy Phase (CP): Day 1 of Cycles 2, 3 and 4 (each cycle 21 days); Maintenance Phase (MP): Days 1, 15 and 29 of Cycles 1 and 2 (each cycle 42 days) and at end of treatment (up to 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	318	317	316	
Units: beats per minute				
arithmetic mean (standard deviation)				
CP:Change at Day 1, Cycle 2(n=310,304,301)	-0.5 (± 12.34)	1.80 (± 12.04)	-0.70 (± 11.42)	
CP: Change at Day 1, Cycle 3(n=305,298,295)	-0.20 (± 12.71)	2.90 (± 13.64)	-0.0 (± 12.29)	
CP: Change at Day 1, Cycle 4(n=287,290,289)	-0.30 (± 13.49)	1.90 (± 13.86)	-0.30 (± 14.02)	
MP: Change at Day 1, Cycle 1(n=253,266,253)	-1.90 (± 13.70)	-0.10 (± 13.99)	-0.70 (± 13.02)	
MP: Change at Day 15, Cycle 1(n=241,249,3)	-2.90 (± 12.94)	-2.40 (± 13.57)	-11.70 (± 15.14)	
MP: Change at Day 29, Cycle 1(n=233,249,3)	-3.10 (± 12.48)	-3.60 (± 13.48)	-4.00 (± 7.55)	
MP: Change at Day 1, Cycle 2(n=228,247,226)	-3.50 (± 13.71)	-4.70 (± 13.09)	-3.40 (± 13.11)	
MP: Change at Day 15, Cycle 2(n=219,236,0)	-5.10 (± 13.73)	-4.90 (± 13.67)	99999 (± 99999)	
MP: Change at Day 29, Cycle 2(n=215,225,0)	-5.60 (± 13.71)	-5.20 (± 12.79)	99999 (± 99999)	
Change at EOT(n=136,116,119)	-1.60 (± 14.47)	-1.50 (± 15.22)	-3.70 (± 15.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Electrocardiogram (ECG) Abnormalities

End point title	Number of Subjects With Electrocardiogram (ECG) Abnormalities

End point description:

ECG abnormalities included: 1) QT interval, QT interval corrected using Bazett's formula (QTcB) and QT interval corrected using Fridericia's formula (QTcF): increase from baseline greater than (>) 30 millisecond (ms) or 60 ms; absolute value > 450 ms, >480 ms and > 500 ms; 2) heart rate (HR) : absolute value <=50 bpm and decrease from baseline >=20 bpm; absolute value >=120 beats per minute (bpm) and increase from baseline >=20 bpm; 3) PR interval: absolute value >=220 ms and increase from baseline >=20 ms; 4) QRS interval: absolute value >= 120 ms. Safety analysis set:all subjects who had received at least one dose of study drug. Here, 'number of subjects analysed' = subjects who were evaluable for this endpoint and 'n' = subjects in safety analysis set who had at least one baseline and post-baseline ECG assessment.

End point type	Secondary

End point timeframe:

Baseline to discontinuation from the study or death, whichever occurred first (maximum duration of 27 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	321	320	
Units: subjects				
QT increase from baseline >30 ms(n=314,314,314)	128	152	106	
QT increase from baseline >60 ms(n=314,314,314)	31	60	35	
QT >450 ms (n=317,321,320)	12	30	20	
QT >480 ms (n=317,321,320)	2	10	7	
QT >500 ms (n=317,321,320)	1	6	5	
QTcB increase from baseline >30 ms (n=300,303,306)	107	137	116	
QTcB increase from baseline >60 ms (n=300,303,306)	19	38	25	
QTcB >450 ms (n=303,312,313)	135	185	165	
QTcB >480 ms (n=303,312,313)	29	63	32	
QTcB >500 ms (n=303,312,313)	16	29	17	
QTcF increase from baseline >30 ms (n=300,303,306)	90	125	89	
QTcF increase from baseline >60 ms (n=300,303,306)	14	34	17	
QTcF >450 ms (n=303,312,313)	44	83	53	
QTcF >480 ms (n=303,312,313)	10	25	15	
QTcF >500 ms (n=303,312,313)	6	11	11	
Heartrate<=50 bpm&decrease>= 20bpm(n=300,303,306)	1	1	3	
Heartrate>=120bpm&increase>=20bpm (n=300,303,306)	7	10	6	
PR>=220msincreasefrombaseline>=20 ms(n=312,311,313)	7	6	6	
QRS >=120 ms (n=317,321,320)	7	9	16	

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Assessment of Ovarian Symptom Index- 18 (FOSI-18) Score

End point title	Functional Assessment of Ovarian Symptom Index- 18 (FOSI-18) Score

End point description:

The National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy (NCCN-FACT) Ovarian Symptom Index-18 (FOSI-18) is an 18-itemed questionnaire, completed by patients, designed to assess the impact of cancer therapy on ovarian cancer-related symptoms. It is based on numerical point scoring of symptoms. It includes three subscales: disease-related symptoms (10 items), treatment-related side effects (5 items) and general function/well-being (3 items). Subjects rated their level of symptoms for each of the 18 items using 5-point scale from 0 (not at all) to 4 (very much). For items that were negatively framed, scores were reversed for analysis so that higher scores equated to good quality of life. The total symptom index was calculated as the total of 18 scores, ranging from 0 ("severely symptomatic") to 72 ("asymptomatic"). Higher FOSI-18 scores indicated better functioning or lower symptom burden. The full analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

CP: Pre-dose on Day 1 of Cycles 2 to 6 (1 cycle= 21 days); MP:Day 1 of Cycles 1 to 12 (1 cycle= 42 days), End of treatment (any time up to at Month 27)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	331	335	
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
CP: Day 1, Cycle 2	54.33 (53.5 to 55.2)	53.88 (53.0 to 54.7)	54.27 (53.4 to 55.1)	
CP: Day 1, Cycle 3	54.61 (53.8 to 55.5)	54.10 (53.2 to 54.9)	54.51 (53.6 to 55.4)	
CP: Day 1, Cycle 4	54.88 (54.0 to 55.7)	54.31 (53.5 to 55.1)	54.75 (53.9 to 55.6)	
CP: Day 1, Cycle 5	55.16 (54.3 to 56.0)	54.53 (53.7 to 55.4)	54.99 (54.1 to 55.8)	
CP: Day 1, Cycle 6	55.43 (54.6 to 56.3)	54.74 (53.9 to 55.6)	55.23 (54.4 to 56.1)	
MP: Day 1, Cycle 1	55.70 (54.9 to 56.5)	54.96 (54.1 to 55.8)	55.47 (54.6 to 56.3)	
MP: Day 1, Cycle 2	56.25 (55.4 to 57.1)	55.39 (54.6 to 56.2)	55.95 (55.1 to 56.8)	
MP: Day 1, Cycle 3	56.80 (55.9 to 57.7)	55.82 (55.0 to 56.7)	56.43 (55.6 to 57.3)	
MP: Day 1, Cycle 4	57.35 (56.5 to 58.2)	56.25 (55.4 to 57.1)	56.91 (56.0 to 57.8)	
MP: Day 1, Cycle 5	57.90 (57.0 to 58.8)	56.69 (55.8 to 57.6)	57.39 (56.4 to 58.3)	
MP: Day 1, Cycle 6	58.45 (57.5 to 59.4)	57.12 (56.1 to 58.1)	57.87 (56.9 to 58.9)	
MP: Day 1, Cycle 7	59.00 (57.9 to 60.1)	57.55 (56.5 to 58.6)	58.36 (57.3 to 59.4)	
MP: Day 1, Cycle 8	59.55 (58.4 to 60.7)	57.98 (56.9 to 59.1)	58.84 (57.7 to 60.0)	
MP: Day 1, Cycle 9	60.09 (58.9 to 61.3)	58.41 (57.2 to 59.6)	59.32 (58.1 to 60.5)	
MP: Day 1, Cycle 10	60.64 (59.4 to 61.9)	58.84 (57.6 to 60.1)	59.80 (58.5 to 61.1)	
MP: Day 1, Cycle 11	61.19 (59.8 to 62.6)	59.28 (57.9 to 60.6)	60.28 (58.9 to 61.7)	
MP: Day 1, Cycle 12	61.74 (60.3 to 63.2)	59.71 (58.3 to 61.1)	60.76 (59.3 to 62.2)	
End of treatment	57.04 (56.2 to 57.9)	56.01 (55.1 to 56.9)	56.64 (55.8 to 57.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) Score

End point title	European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) Score

End point description:

EQ-5D-5L:standardized subject completed questionnaire that measures health-related quality of life and translates that score into an index value or utility score. EQ-5D-5L consists of two components: a health state profile and an optional visual analogue scale (VAS). In VAS, subjects rated their overall health status from 0 (worst imaginable) to 100 (best imaginable). EQ-5D health state profile has 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems, and 5=extreme problems. 57 overall scores ranged from 0 to 1, with low scores representing a higher level of dysfunction. Trial was terminated due to crossing of futility boundaries for both experimental arms as compared to the control arm at the pre-specified interim analysis for PFS based on BICR assessment. Data for this outcome measure was not collected and analyzed.

End point type	Secondary

End point timeframe:

Baseline to discontinuation from the study or death, whichever occurred first (maximum duration of 36 months)

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[13]	0[14]	0[15]	
Units: units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[13] - Data for this outcome measure was not collected and analyzed due to futility reasons.

[14] - Data for this outcome measure was not collected and analyzed due to futility reasons.

[15] - Data for this outcome measure was not collected and analyzed due to futility reasons.

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Paclitaxel (Once a Week [QW] Regimen)

End point title	Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Paclitaxel (Once a Week [QW] Regimen)

End point description:

Cmax is maximum plasma concentration of paclitaxel. The LLQ of paclitaxel was 10.0 ng/mL. Paclitaxel PK parameter analysis set: all subjects who received at least one dose of study drug and who had at least one of the PK parameters of interest for paclitaxel. Here ‘number of subjects analysed’ signifies subjects who received Paclitaxel infusion on QW regimen and had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose and at 1, 3, 4, 5, 6, 10, and 24 hours post paclitaxel infusion on Day 1 of Cycle 2

End point values	PK: Chemotherapy followed by Avelumab	PK: Chemotherapy + Avelumab followed by Avelumab	PK: Chemotherapy followed by Observation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	4	9	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	2880 (± 44)	2678 (± 22)	2649 (± 35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Paclitaxel (Once Every Three Weeks [Q3W] Regimen)

End point title	Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Paclitaxel (Once Every Three Weeks [Q3W] Regimen)

End point description:

Cmax is maximum plasma concentration of paclitaxel. The LLQ of paclitaxel was 10.0 ng/mL. Paclitaxel PK parameter analysis set: all subjects who received at least one dose of study drug and who had at least one of the PK parameters of interest for paclitaxel. Here 'number of subjects analysed' signifies subjects who received Paclitaxel infusion on Q3W regimen and had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose and at 1, 3, 4, 5, 6, 10, and 24 hours post paclitaxel infusion on Day 1 of Cycle 2

End point values	PK: Chemotherapy followed by Avelumab	PK: Chemotherapy + Avelumab followed by Avelumab	PK: Chemotherapy followed by Observation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	5	9	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	5646 (± 68)	4775 (± 24)	4694 (± 28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Carboplatin (Total and Free)

End point title	Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Carboplatin (Total and Free)

End point description:

Cmax is maximum plasma concentration of carboplatin. The LLQ of carboplatin was 100.0 ng/mL.

Carboplatin PK parameter analysis set included all subjects who had received at least one dose of study drug and who had at least one of the PK parameters of interest for carboplatin. Here 'number of subjects analysed' signifies subjects who had data available for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose and at 0.5, 1, 5, 6, 10, and 24 hours post carboplatin infusion on Day 1 of Cycle 2

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	7	13	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Total Carboplatin	23580 (± 34)	18350 (± 44)	18990 (± 31)	
Free Carboplatin	21740 (± 39)	15350 (± 65)	17090 (± 33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUCinf) of Paclitaxel (QW Regimen)

End point title	Chemotherapy Phase: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUCinf) of Paclitaxel (QW Regimen)

End point description:

AUCinf is the plasma area under the plasma concentration-time profile from time 0 extrapolated to infinite time.Paclitaxel PK parameter analysis set: all subjects who received at least one dose of study drug and who had at least one of the PK parameters of interest for paclitaxel. Here 'number of subjects analysed' signifies subjects who received Paclitaxel infusion on QW regimen and had data available for this endpoint

End point type	Secondary

End point timeframe:

Pre-dose and at 1, 3, 4, 5, 6, 10, and 24 hours post paclitaxel infusion on Day 1 of Cycle 2

End point values	PK: Chemotherapy + Avelumab followed by Avelumab	PK: Chemotherapy followed by Avelumab	PK: Chemotherapy followed by Observation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	5	7	
Units: nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	4997 (± 15)	5138 (± 39)	4921 (± 18)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUCinf) of Paclitaxel (Q3W Regimen)

End point title	Chemotherapy Phase: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUCinf) of Paclitaxel (Q3W Regimen)

End point description:

AUCinf is the plasma area under the plasma concentration-time profile from time 0 extrapolated to infinite time. Paclitaxel PK parameter analysis set: all subjects who received at least one dose of study drug and who had at least one of the PK parameters of interest for paclitaxel. Here 'number of subjects analysed' signifies subjects who received Paclitaxel infusion on Q3W regimen and had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose and at 1, 3, 4, 5, 6, 10, and 24 hours post paclitaxel infusion on Day 1 of Cycle 2

End point values	PK: Chemotherapy followed by Avelumab	PK: Chemotherapy + Avelumab followed by Avelumab	PK: Chemotherapy followed by Observation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	4	8	
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	18070 (± 58)	16190 (± 25)	17470 (± 26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUCinf) of Carboplatin (Total and Free)

End point title	Chemotherapy Phase: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUCinf) of Carboplatin (Total and Free)

End point description:

AUCinf is the plasma area under the plasma concentration-time profile from time 0 extrapolated to infinite time. Carboplatin PK parameter analysis set included all subjects who had received at least one dose of study drug and who had at least one of the PK parameters of interest for carboplatin. Here, 'n' = Subjects evaluable for this end point at specified rows. For the chemotherapy followed by Avelumab group, the geometric coefficient of variation value cannot be calculated when there is only one subject

and is denoted as "0" in this field.

End point type	Secondary

End point timeframe:

Pre-dose and at 0.5, 1, 5, 6, 10, and 24 hours post carboplatin infusion on Day 1 of Cycle 2

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	9	18	
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Total Carboplatin (n=1,5,5)	87600 (± 0)	100500 (± 13)	90430 (± 18)	
Free Carboplatin (n=11,6,13)	55840 (± 25)	52000 (± 29)	52300 (± 25)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Area Under the Concentration Time Curve From Time Zero to 24 Hours (AUC24) of Paclitaxel (QW Regimen) When Given With Avelumab

End point title	Chemotherapy Phase: Area Under the Concentration Time Curve From Time Zero to 24 Hours (AUC24) of Paclitaxel (QW Regimen) When Given With Avelumab

End point description:

AUC24 is the area under the plasma concentration versus time curve from time zero (pre-dose) to 24 hours post-dose (0 to 24). Paclitaxel PK parameter analysis set: all subjects who received at least one dose of study drug and who had at least one of the PK parameters of interest for paclitaxel. Here 'number of subjects analysed' signifies subjects who received Paclitaxel infusion on QW regimen and had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose (0 hour), 1, 3, 4, 5, 6, 10, and 24 hours post paclitaxel infusion on Day 1 of Cycle 2

End point values	PK: Chemotherapy followed by Avelumab	PK: Chemotherapy + Avelumab followed by Avelumab	PK: Chemotherapy followed by Observation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	4	9	
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	4960 (± 38)	4572 (± 16)	4304 (± 24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Area Under the Concentration Time Curve From Time Zero to 24 Hours (AUC24) of Paclitaxel (Q3W Regimen) When Given With Avelumab

End point title	Chemotherapy Phase: Area Under the Concentration Time Curve From Time Zero to 24 Hours (AUC24) of Paclitaxel (Q3W Regimen) When Given With Avelumab

End point description:

AUC24 is the area under the plasma concentration versus time curve from time zero (pre-dose) to 24 hours post-dose (0 to 24). Paclitaxel PK parameter analysis set: all subjects who received at least one dose of study drug and who had at least one of the PK parameters of interest for paclitaxel. Here 'number of subjects analysed' signifies subjects who received Paclitaxel infusion on Q3W regimen and had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose (0 hour), 1, 3, 4, 5, 6, 10, and 24 hours post paclitaxel infusion on Day 1 of Cycle 2

End point values	PK: Chemotherapy followed by Avelumab	PK: Chemotherapy + Avelumab followed by Avelumab	PK: Chemotherapy followed by Observation	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	5	9	
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	17540 (± 60)	15870 (± 21)	16390 (± 26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Area Under the Concentration Time Curve From Time Zero to 24 Hours (AUC24) of Carboplatin (Total and Free) When Given With Avelumab

End point title	Chemotherapy Phase: Area Under the Concentration Time Curve From Time Zero to 24 Hours (AUC24) of Carboplatin (Total and Free) When Given With Avelumab

End point description:

AUC24 is the area under the plasma concentration versus time curve from time zero (pre-dose) to 24 hours post-dose. Carboplatin PK parameter analysis set included all subjects who had received at least one dose of study drug and who had at least one of the PK parameters of interest for carboplatin. Here

'number of subjects analysed' signifies subjects who had data available for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose (0 hour), 0.5, 1, 5, 6, 10, and 24 hours post carboplatin infusion on Day 1 of Cycle 2

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	7	13	
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Total Carboplatin	84380 (± 22)	84100 (± 12)	80960 (± 17)	
Free Carboplatin	56880 (± 25)	52100 (± 26)	52590 (± 24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maintenance Phase: Predose Plasma Concentration (Ctrough) of Avelumab

End point title	Maintenance Phase: Predose Plasma Concentration (Ctrough) of Avelumab[16]

End point description:

Ctrough=concentration at the end of the dosing interval when avelumab was given as a Q2W regimen in the absence of carboplatin and paclitaxel following 1 cycle of avelumab dosing, i.e. before administration of drug on Day 1 of cycle 2. The LLQ of avelumab was 0.20 micro-gram per milliliter (mcg/mL). Data for this endpoint was not reported for reporting arms "Chemotherapy + Avelumab followed by Avelumab" (since data was not planned to be collected 1 cycle after the initiation of avelumab dosing) and "Chemotherapy followed by Observation" (since avelumab was not administered in this arm and therefore data collection was not planned). Avelumab PK concentration analysis set:all subjects who had received at least one dose of study drug and who had at least one post-dose concentration measurement above the LLQ for avelumab. Here 'number of subjects analysed' signifies subjects who had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose (0 hour) on Day 1 of Cycle 2

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for reporting arm: Chemotherapy followed by Avelumab

End point values	Chemotherapy followed by Avelumab			
Subject group type	Reporting group			
Number of subjects analysed	209			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	29.18 (± 57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maintenance Phase: Maximum Plasma Concentration (Cmax) of Avelumab

End point title	Maintenance Phase: Maximum Plasma Concentration (Cmax) of Avelumab[17]

End point description:

Cmax is the concentration at the end of a 1 hour infusion, corresponding to the maximum plasma concentration of avelumab. The LLQ of avelumab was 0.20 mcg/mL. Data for this endpoint was not reported for reporting arms "Chemotherapy + Avelumab followed by Avelumab" (since data was not planned to be collected 1 cycle after the initiation of avelumab dosing) and "Chemotherapy followed by Observation" (since avelumab was not administered in this arm and therefore data collection was not planned). Avelumab PK concentration analysis set included all subjects who had received at least one dose of study drug and who had at least one post-dose concentration measurement above the LLQ for avelumab. Here 'number of subjects analysed' signifies subjects who had data available for this endpoint.

End point type	Secondary

End point timeframe:

End of avelumab infusion on Day 1 of Cycle 2

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for reporting arm: Chemotherapy followed by Avelumab

End point values	Chemotherapy followed by Avelumab			
Subject group type	Reporting group			
Number of subjects analysed	174			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	205.6 (± 50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Maximum Plasma Concentration (Cmax) of Avelumab When Given With Paclitaxel and Carboplatin

End point title	Chemotherapy Phase: Maximum Plasma Concentration (Cmax)

	of Avelumab When Given With Paclitaxel and Carboplatin[18]

End point description:

Cmax is the concentration at the end of a 1 hour infusion, corresponding to the maximum plasma concentration of avelumab. The LLQ of avelumab was 0.20 mcg/mL. Data for this endpoint was not reported for reporting arms "Chemotherapy followed by Avelumab" (data not available for this OM as avelumab was not given along with paclitaxel and carboplatin in this arm) and "Chemotherapy followed by Observation" (since avelumab was not administered in this arm and therefore data collection was not planned). PK concentration analysis set included all subjects who had received at least one dose of study drug and who had at least one post-dose concentration measurement above the LLQ for avelumab. Here 'number of subjects analysed' signifies subjects who had data available for this endpoint.

End point type	Secondary

End point timeframe:

End of infusion on Day 1 of Cycle 2

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for reporting arm: Chemotherapy + Avelumab followed by Avelumab

End point values	Chemotherapy + Avelumab followed by Avelumab			
Subject group type	Reporting group			
Number of subjects analysed	220			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	162.9 (± 139)			

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy Phase: Predose Plasma Concentration (Ctrough) of Avelumab When Given With Paclitaxel and Carboplatin

End point title	Chemotherapy Phase: Predose Plasma Concentration (Ctrough) of Avelumab When Given With Paclitaxel and Carboplatin[19]

End point description:

Ctrough is the concentration at the end of the dosing interval when avelumab was given as a Q2W regimen in the absence of carboplatin and paclitaxel following 1 cycle of avelumab dosing, i.e. before administration of drug on Day 1 of cycle 2. The LLQ of avelumab was 0.20 mcg/mL. Data for this endpoint was not reported for reporting arms "Chemotherapy followed by Avelumab" (data not available for this OM as avelumab was not given along with paclitaxel and carboplatin in this arm) and "Chemotherapy followed by Observation" (since avelumab was not administered in this arm and therefore data collection was not planned). Avelumab PK concentration analysis set included all subjects who had received at least one dose of study drug and who had at least one post-dose concentration measurement above the LLQ for avelumab. Here 'number of subjects analysed' signifies subjects who had data available for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose (0 hour) on Day 1 of Cycle 2

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for reporting arm: Chemotherapy + Avelumab followed by

End point values	Chemotherapy + Avelumab followed by Avelumab			
Subject group type	Reporting group			
Number of subjects analysed	251			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	3.607 (± 113)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Drug Antibodies (ADA) Against Avelumab by Never and Ever Positive Status

End point title	Number of Subjects With Anti-Drug Antibodies (ADA) Against Avelumab by Never and Ever Positive Status[20]

End point description:

ADA against avelumab in serum samples was determined and reported separately for ADA never-positive and ADA ever-positive subjects. Subjects were considered ADA ever-positive if they had at least one positive (ADA titer greater than or equal to 60 with assay cut point of 1.12) ADA result at any time point and were otherwise considered negative. The immunogenicity analysis set included all subjects who had received at least one dose of study drug and who had at least one ADA sample collected for avelumab in the avelumab containing arms. Here 'number of subjects analysed' signifies subjects who had data available for this endpoint.

End point type	Secondary

End point timeframe:

Up to 36 months

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for reporting arms: Chemotherapy followed by Avelumab and Chemotherapy + Avelumab followed by Avelumab

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	328		
Units: subjects				
Never-positive	231	197		
Ever-positve	41	131		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Neutralizing Antibodies (nAb) Against Avelumab by Never and Ever Positive Status

End point title	Number of Subjects With Neutralizing Antibodies (nAb) Against Avelumab by Never and Ever Positive Status[21]

End point description:

nAb against avelumab in serum samples was determined and reported separately for nAb never-positive and nAb ever-positive subjects. Subjects were considered nAb ever-positive if they had at least one positive nAb results (less than or equal to cut point of 0.710 in qualitative competitive ligand binding assay) at any time point. nAb never-positive subjects were those who had at least one negative nAb results (greater than cut point of 0.710 in qualitative competitive ligand binding assay) at any time point. The immunogenicity analysis set included all subjects who had received at least one dose of study drug and who had at least one nAb sample collected for avelumab in the avelumab containing arms. Here 'number of subjects analysed' signifies subjects who had data available for this endpoint.

End point type	Secondary

End point timeframe:

Up to 36 months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for reporting arms: Chemotherapy followed by Avelumab and Chemotherapy + Avelumab followed by Avelumab

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	328		
Units: subjects				
Never-positive	256	282		
Ever-positve	16	46		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Programmed Death Receptor-1 Ligand-1 (PD-L1) Biomarker Expression in Tumor Tissue as Assessed by Immunohistochemistry (IHC)

End point title	Number of Subjects With Positive Programmed Death Receptor-1 Ligand-1 (PD-L1) Biomarker Expression in Tumor Tissue as Assessed by Immunohistochemistry (IHC)

End point description:

PD-L1 assessment was performed using immunohistochemistry. Subjects were considered positive if their pretreatment tumor tissue sample demonstrated cell surface PD-L1 expression on greater than or equal to (>=) 1 percentage (%) tumor cells or >= 5% immune cells and were otherwise considered negative. PD-L1 biomarker analysis set included all subjects who had received at least one dose of study drug and who had at least one screening biomarker assessment for PD-L1.

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	270	263	280	
Units: subjects	158	160	169	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Tumor-Infiltrating Cluster of Differentiation 8 (CD8+) T Lymphocytes Expression in Tumor Tissue as Assessed by Immunohistochemistry (IHC)

End point title	Number of Subjects With Positive Tumor-Infiltrating Cluster of Differentiation 8 (CD8+) T Lymphocytes Expression in Tumor Tissue as Assessed by Immunohistochemistry (IHC)

End point description:

CD8 assessment was performed using immunohistochemistry. Subjects were considered positive if their pretreatment tumor tissue sample demonstrated >= 1% CD8 positive cells and were otherwise considered negative. CD8 biomarker analysis set included all subjects who had received at least one dose of study drug and who had at least one screening biomarker assessment for CD8.

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Chemotherapy followed by Avelumab	Chemotherapy + Avelumab followed by Avelumab	Chemotherapy followed by Observation	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	250	257	
Units: subjects	107	107	118	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to maximum duration of 36 months

Adverse event reporting additional description:

Same event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event. Analysis performed on safety set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Chemotherapy followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 milligrams per square meter (mg/m2) intravenous (IV) infusion,followed by carboplatin dose at area under curve (AUC) 5 or 6,IV infusion (carboplatin dose (mg) = Target AUC (mg*min/mL) x (glomerular filtration rate[GFR] mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6.Each cycle was of 21 days.After completion of chemotherapy phase, subjects without evidence of disease progression, received avelumab 10 mg/kg, over 1 hour IV infusion,once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease,unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Reporting group title	Chemotherapy followed by Observation

Reporting group description:

In chemotherapy phase, based on investigator’s decision, subjects received either: paclitaxel 175 mg/m2, IV infusion, followed by carboplatin dose at AUC 5 or 6, IV infusion (carboplatin dose [milligrams](mg) = Target AUC [milligrams*minute per milliliter] (mg*min/mL) x GFR mL/min + 25), and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6; or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6. Each cycle was of 21 days (3 weeks). After completion of chemotherapy phase, subjects were followed every 12 weeks for survival status until death or until study completion, whichever was earlier or a maximum duration of 24 months in observation phase. Subjects were then followed up to Month 36 for safety evaluation.

Reporting group title	Chemotherapy + Avelumab followed by Avelumab

Reporting group description:

In chemotherapy phase,based on investigator’s decision,subjects received either:paclitaxel 175 mg/m2,IV,followed by carboplatin dose at AUC 5 or 6,IV (carboplatin dose [milligrams](mg) = Target AUC (mg*min/mL) x GFR mL/min + 25),and maximum carboplatin dose = target AUC x (150 mL/min) on Day 1 of Cycles 1 to 6;or Paclitaxel 80 mg/m2 IV infusion over 1 hour on Days 1, 8, and 15, along with carboplatin dose at AUC 5 or 6, IV infusion over 1 hour on Day 1 of Cycle 1 to 6 along with Avelumab 10 mg/kg administered as a 1-hour IV infusion once every 3 weeks for Cycle 1 to 6. Each cycle was of 21 days (3 weeks).After completion of chemotherapy phase, subjects without evidence of disease progression, received Avelumab IV, 10 mg/kg, once every 2 weeks on Days 1, 15, and 29 of each cycle of 42 days in maintenance phase until confirmed progressive disease (PD), unacceptable toxicity, or withdrawal of consent, or a maximum duration of 24 months. Safety evaluation followed up to Month 36.

Serious adverse events	Chemotherapy followed by Avelumab	Chemotherapy followed by Observation	Chemotherapy + Avelumab followed by Avelumab
Total subjects affected by serious adverse events			
subjects affected / exposed	92 / 328 (28.05%)	64 / 334 (19.16%)	118 / 329 (35.87%)
number of deaths (all causes)	34	20	31
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer stage I			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Flushing			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocele			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein occlusion			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Essential hypertension			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	3 / 328 (0.91%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Disease progression			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	3 / 329 (0.91%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperpyrexia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated hernia			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			

subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-cardiac chest pain			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	6 / 328 (1.83%)	1 / 334 (0.30%)	10 / 329 (3.04%)
occurrences causally related to treatment / all	5 / 8	0 / 1	4 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal perforation			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 328 (0.91%)	1 / 334 (0.30%)	3 / 329 (0.91%)
occurrences causally related to treatment / all	2 / 3	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pleural effusion			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	7 / 328 (2.13%)	3 / 334 (0.90%)	3 / 329 (0.91%)
occurrences causally related to treatment / all	1 / 7	1 / 4	2 / 3
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Pulmonary infarction			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Persistent depressive disorder			

subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocyte count decreased			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anastomotic leak			

subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	4 / 329 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural intestinal perforation			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal cuff dehiscence			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial infarction			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial nerve disorder			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	6 / 328 (1.83%)	6 / 334 (1.80%)	8 / 329 (2.43%)
occurrences causally related to treatment / all	6 / 7	5 / 6	9 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	10 / 328 (3.05%)	7 / 334 (2.10%)	8 / 329 (2.43%)
occurrences causally related to treatment / all	11 / 11	7 / 7	7 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 328 (0.61%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 328 (0.61%)	1 / 334 (0.30%)	5 / 329 (1.52%)
occurrences causally related to treatment / all	2 / 2	1 / 1	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	3 / 328 (0.91%)	4 / 334 (1.20%)	3 / 329 (0.91%)
occurrences causally related to treatment / all	0 / 3	1 / 4	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal haemorrhage			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	5 / 328 (1.52%)	1 / 334 (0.30%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	3 / 328 (0.91%)	3 / 334 (0.90%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 3	2 / 4	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic hernia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	4 / 328 (1.22%)	1 / 334 (0.30%)	3 / 329 (0.91%)
occurrences causally related to treatment / all	4 / 4	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal obstruction			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	3 / 328 (0.91%)	9 / 334 (2.69%)	4 / 329 (1.22%)
occurrences causally related to treatment / all	0 / 3	1 / 12	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal dilatation			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	4 / 328 (1.22%)	6 / 334 (1.80%)	6 / 329 (1.82%)
occurrences causally related to treatment / all	0 / 8	1 / 8	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	4 / 328 (1.22%)	2 / 334 (0.60%)	5 / 329 (1.52%)
occurrences causally related to treatment / all	2 / 4	2 / 2	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	3 / 328 (0.91%)	1 / 334 (0.30%)	7 / 329 (2.13%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subileus			

subjects affected / exposed	0 / 328 (0.00%)	2 / 334 (0.60%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	6 / 328 (1.83%)	6 / 334 (1.80%)	7 / 329 (2.13%)
occurrences causally related to treatment / all	5 / 6	4 / 7	8 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal mucosal disorder			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Drug eruption			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urogenital fistula			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymyositis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Abdominal wall abscess			

subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			

subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected lymphocele			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph gland infection			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			

subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic infection			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic inflammatory disease			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 328 (0.91%)	1 / 334 (0.30%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	1 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	2 / 329 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	7 / 328 (2.13%)	2 / 334 (0.60%)	7 / 329 (2.13%)
occurrences causally related to treatment / all	3 / 7	0 / 2	3 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval abscess			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 328 (0.00%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	3 / 329 (0.91%)
occurrences causally related to treatment / all	2 / 2	1 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 328 (0.30%)	1 / 334 (0.30%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	1 / 1	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 328 (0.00%)	0 / 334 (0.00%)	1 / 329 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	2 / 328 (0.61%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			

subjects affected / exposed	1 / 328 (0.30%)	0 / 334 (0.00%)	0 / 329 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Chemotherapy followed by Avelumab	Chemotherapy followed by Observation	Chemotherapy + Avelumab followed by Avelumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	320 / 328 (97.56%)	317 / 334 (94.91%)	325 / 329 (98.78%)
Vascular disorders			
Hot flush			
subjects affected / exposed	23 / 328 (7.01%)	16 / 334 (4.79%)	18 / 329 (5.47%)
occurrences (all)	26	18	23
Hypertension			
subjects affected / exposed	16 / 328 (4.88%)	13 / 334 (3.89%)	19 / 329 (5.78%)
occurrences (all)	20	20	32
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	35 / 328 (10.67%)	22 / 334 (6.59%)	46 / 329 (13.98%)
occurrences (all)	53	36	83
Fatigue			
subjects affected / exposed	123 / 328 (37.50%)	110 / 334 (32.93%)	115 / 329 (34.95%)
occurrences (all)	244	206	250
Malaise			
subjects affected / exposed	22 / 328 (6.71%)	14 / 334 (4.19%)	17 / 329 (5.17%)
occurrences (all)	29	19	17
Oedema peripheral			
subjects affected / exposed	27 / 328 (8.23%)	23 / 334 (6.89%)	29 / 329 (8.81%)
occurrences (all)	33	28	34
Pain			
subjects affected / exposed	21 / 328 (6.40%)	14 / 334 (4.19%)	23 / 329 (6.99%)
occurrences (all)	26	16	29
Pyrexia			

subjects affected / exposed	33 / 328 (10.06%)	23 / 334 (6.89%)	42 / 329 (12.77%)
occurrences (all)	48	25	60
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	36 / 328 (10.98%)	22 / 334 (6.59%)	55 / 329 (16.72%)
occurrences (all)	51	27	68
Dyspnoea			
subjects affected / exposed	38 / 328 (11.59%)	29 / 334 (8.68%)	47 / 329 (14.29%)
occurrences (all)	51	37	69
Epistaxis			
subjects affected / exposed	22 / 328 (6.71%)	12 / 334 (3.59%)	12 / 329 (3.65%)
occurrences (all)	22	15	14
Psychiatric disorders			
Anxiety			
subjects affected / exposed	14 / 328 (4.27%)	15 / 334 (4.49%)	18 / 329 (5.47%)
occurrences (all)	15	16	18
Insomnia			
subjects affected / exposed	52 / 328 (15.85%)	32 / 334 (9.58%)	39 / 329 (11.85%)
occurrences (all)	68	37	48
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	28 / 328 (8.54%)	20 / 334 (5.99%)	33 / 329 (10.03%)
occurrences (all)	54	37	49
Aspartate aminotransferase increased			
subjects affected / exposed	18 / 328 (5.49%)	21 / 334 (6.29%)	28 / 329 (8.51%)
occurrences (all)	34	28	36
Neutrophil count decreased			
subjects affected / exposed	60 / 328 (18.29%)	75 / 334 (22.46%)	54 / 329 (16.41%)
occurrences (all)	267	255	223
Platelet count decreased			
subjects affected / exposed	25 / 328 (7.62%)	44 / 334 (13.17%)	39 / 329 (11.85%)
occurrences (all)	79	96	103
White blood cell count decreased			
subjects affected / exposed	32 / 328 (9.76%)	34 / 334 (10.18%)	31 / 329 (9.42%)
occurrences (all)	173	150	156
Weight decreased			

subjects affected / exposed	15 / 328 (4.57%)	13 / 334 (3.89%)	17 / 329 (5.17%)
occurrences (all)	19	18	20
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	26 / 328 (7.93%)	19 / 334 (5.69%)	30 / 329 (9.12%)
occurrences (all)	35	27	48
Procedural pain			
subjects affected / exposed	27 / 328 (8.23%)	12 / 334 (3.59%)	22 / 329 (6.69%)
occurrences (all)	33	15	31
Nervous system disorders			
Dizziness			
subjects affected / exposed	45 / 328 (13.72%)	28 / 334 (8.38%)	38 / 329 (11.55%)
occurrences (all)	61	33	49
Dysgeusia			
subjects affected / exposed	22 / 328 (6.71%)	18 / 334 (5.39%)	20 / 329 (6.08%)
occurrences (all)	25	21	21
Headache			
subjects affected / exposed	55 / 328 (16.77%)	30 / 334 (8.98%)	51 / 329 (15.50%)
occurrences (all)	72	34	88
Hypoaesthesia			
subjects affected / exposed	12 / 328 (3.66%)	13 / 334 (3.89%)	21 / 329 (6.38%)
occurrences (all)	13	19	27
Neuropathy peripheral			
subjects affected / exposed	63 / 328 (19.21%)	65 / 334 (19.46%)	77 / 329 (23.40%)
occurrences (all)	93	103	114
Paraesthesia			
subjects affected / exposed	18 / 328 (5.49%)	10 / 334 (2.99%)	26 / 329 (7.90%)
occurrences (all)	21	14	29
Peripheral sensory neuropathy			
subjects affected / exposed	91 / 328 (27.74%)	82 / 334 (24.55%)	76 / 329 (23.10%)
occurrences (all)	114	120	121
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	148 / 328 (45.12%)	140 / 334 (41.92%)	151 / 329 (45.90%)
occurrences (all)	465	415	424
Leukopenia			

subjects affected / exposed	27 / 328 (8.23%)	20 / 334 (5.99%)	28 / 329 (8.51%)
occurrences (all)	53	50	73
Neutropenia			
subjects affected / exposed	112 / 328 (34.15%)	113 / 334 (33.83%)	125 / 329 (37.99%)
occurrences (all)	324	376	343
Thrombocytopenia			
subjects affected / exposed	46 / 328 (14.02%)	59 / 334 (17.66%)	62 / 329 (18.84%)
occurrences (all)	79	128	165
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	22 / 328 (6.71%)	18 / 334 (5.39%)	17 / 329 (5.17%)
occurrences (all)	27	22	26
Abdominal pain			
subjects affected / exposed	69 / 328 (21.04%)	58 / 334 (17.37%)	68 / 329 (20.67%)
occurrences (all)	99	88	82
Abdominal pain upper			
subjects affected / exposed	32 / 328 (9.76%)	24 / 334 (7.19%)	39 / 329 (11.85%)
occurrences (all)	38	29	51
Constipation			
subjects affected / exposed	113 / 328 (34.45%)	95 / 334 (28.44%)	100 / 329 (30.40%)
occurrences (all)	164	135	141
Diarrhoea			
subjects affected / exposed	84 / 328 (25.61%)	63 / 334 (18.86%)	101 / 329 (30.70%)
occurrences (all)	142	92	158
Dyspepsia			
subjects affected / exposed	31 / 328 (9.45%)	22 / 334 (6.59%)	24 / 329 (7.29%)
occurrences (all)	38	27	29
Gastrooesophageal reflux disease			
subjects affected / exposed	11 / 328 (3.35%)	11 / 334 (3.29%)	18 / 329 (5.47%)
occurrences (all)	13	12	20
Nausea			
subjects affected / exposed	153 / 328 (46.65%)	152 / 334 (45.51%)	149 / 329 (45.29%)
occurrences (all)	288	308	318
Stomatitis			
subjects affected / exposed	28 / 328 (8.54%)	20 / 334 (5.99%)	24 / 329 (7.29%)
occurrences (all)	41	23	43

Vomiting			
subjects affected / exposed	86 / 328 (26.22%)	66 / 334 (19.76%)	74 / 329 (22.49%)
occurrences (all)	133	86	111
Dry mouth			
subjects affected / exposed	17 / 328 (5.18%)	5 / 334 (1.50%)	10 / 329 (3.04%)
occurrences (all)	18	5	12
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	167 / 328 (50.91%)	177 / 334 (52.99%)	169 / 329 (51.37%)
occurrences (all)	220	220	215
Pruritus			
subjects affected / exposed	38 / 328 (11.59%)	19 / 334 (5.69%)	37 / 329 (11.25%)
occurrences (all)	53	20	60
Rash			
subjects affected / exposed	59 / 328 (17.99%)	25 / 334 (7.49%)	66 / 329 (20.06%)
occurrences (all)	107	36	104
Rash maculo-papular			
subjects affected / exposed	13 / 328 (3.96%)	5 / 334 (1.50%)	21 / 329 (6.38%)
occurrences (all)	23	6	43
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	34 / 328 (10.37%)	5 / 334 (1.50%)	33 / 329 (10.03%)
occurrences (all)	43	5	36
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	76 / 328 (23.17%)	57 / 334 (17.07%)	85 / 329 (25.84%)
occurrences (all)	102	76	136
Back pain			
subjects affected / exposed	31 / 328 (9.45%)	31 / 334 (9.28%)	36 / 329 (10.94%)
occurrences (all)	45	37	47
Musculoskeletal pain			
subjects affected / exposed	20 / 328 (6.10%)	13 / 334 (3.89%)	15 / 329 (4.56%)
occurrences (all)	28	19	17
Myalgia			
subjects affected / exposed	67 / 328 (20.43%)	43 / 334 (12.87%)	53 / 329 (16.11%)
occurrences (all)	112	81	89

Pain in extremity			
subjects affected / exposed	30 / 328 (9.15%)	37 / 334 (11.08%)	32 / 329 (9.73%)
occurrences (all)	50	62	46
Infections and infestations			
Cystitis			
subjects affected / exposed	19 / 328 (5.79%)	8 / 334 (2.40%)	7 / 329 (2.13%)
occurrences (all)	32	8	9
Upper respiratory tract infection			
subjects affected / exposed	27 / 328 (8.23%)	14 / 334 (4.19%)	28 / 329 (8.51%)
occurrences (all)	32	18	34
Urinary tract infection			
subjects affected / exposed	36 / 328 (10.98%)	28 / 334 (8.38%)	46 / 329 (13.98%)
occurrences (all)	49	35	65
Nasopharyngitis			
subjects affected / exposed	18 / 328 (5.49%)	10 / 334 (2.99%)	16 / 329 (4.86%)
occurrences (all)	24	10	21
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	64 / 328 (19.51%)	37 / 334 (11.08%)	55 / 329 (16.72%)
occurrences (all)	86	54	68
Hypokalaemia			
subjects affected / exposed	22 / 328 (6.71%)	20 / 334 (5.99%)	27 / 329 (8.21%)
occurrences (all)	32	27	62
Hypomagnesaemia			
subjects affected / exposed	32 / 328 (9.76%)	27 / 334 (8.08%)	42 / 329 (12.77%)
occurrences (all)	63	34	88

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