

**Clinical trial results:****A Phase 3, Multicenter, Randomized, Open-Label Study of Avelumab (MSB0010718C) Alone or in Combination With Pegylated Liposomal Doxorubicin Versus Pegylated Liposomal Doxorubicin Alone in Patients With Platinum Resistant/Refractory Ovarian Cancer****Summary**

EudraCT number	2015-003091-77
Trial protocol	BE GB HU AT ES GR IE NL FR PL DK CZ
Global end of trial date	12 July 2022

Results information

Result version number	v1 (current)
This version publication date	07 July 2023
First version publication date	07 July 2023

Trial information**Trial identification**

Sponsor protocol code	B9991009
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02580058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	ClinicalTrial.gov, Call Center, Pfizer Inc., ClinicalTrial.gov, Call Center, Pfizer Inc., 001 18667181021, ClinicalTrials.gov.inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, 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	12 July 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this trial is to demonstrate that avelumab given alone or in combination with pegylated liposomal doxorubicin (PLD) is superior to PLD alone in prolonging overall survival (OS) in patients with platinum resistant/platinum refractory ovarian cancer; and to demonstrate that avelumab given alone or in combination with PLD is superior to PLD alone in prolonging PFS in patients with platinum resistant/platinum-refractory ovarian cancer.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 28
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Canada: 64
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Japan: 52
Country: Number of subjects enrolled	Korea, Republic of: 40
Country: Number of subjects enrolled	Netherlands: 10

Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Russian Federation: 28
Country: Number of subjects enrolled	Singapore: 11
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Switzerland: 18
Country: Number of subjects enrolled	Taiwan: 13
Country: Number of subjects enrolled	United Kingdom: 78
Country: Number of subjects enrolled	United States: 80
Worldwide total number of subjects	566
EEA total number of subjects	152

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)	349
From 65 to 84 years	215
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 717 subjects screened, a total of 566 randomized subjects were enrolled at 199 centers in 24 countries.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Avelumab

Arm description:

Avelumab 10 milligram (mg)/kilogram (kg) given as a 1-hour intravenous (IV) infusion every 2 weeks (Q2W) in 4-week cycles.

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

Dosage and administration details:

Avelumab 10 mg/kg given as a 1-hour intravenous (IV) infusion every 2 weeks (Q2W) in 4-week cycles.

Arm title	Avelumab + PLD
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Arm description:

Avelumab 10 mg/kg given as a 1-hour IV Q2W in 4-week cycles + pegylated liposomal doxorubicin (PLD) 40 mg/square meter given as a 1-hour IV infusion every 4 weeks (Q4W) in 4-week cycles.

Arm type	Experimental
Investigational medicinal product name	Avelumab and PLD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab 10 mg/kg given as a 1-hour IV Q2W + PLD 40mg/m² given as a 1-hour IV infusion every 4 weeks (Q4W) in 4-week cycles.

Arm title	Pegylated Liposomal Doxorubicin (PLD)
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Arm description:

PLD 40 mg/square meter given as a 1-hour IV infusion Q4W in 4-week cycles.

Arm type	Active comparator
Investigational medicinal product name	PLD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

PLD 40mg/m² given as a 1-hour IV infusion Q4W in 4-week cycles.

Number of subjects in period 1	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)
Started	188	188	190
Treated	187	182	177
Completed	0	0	0
Not completed	188	188	190
Adverse event, serious fatal	4	4	5
Physician decision	1	3	11
Consent withdrawn by subject	4	7	31
Adverse event, non-fatal	16	30	20
Progressive Disease	137	125	94
Not Specified	5	1	3
Non-Compliance With Study Drug	1	-	-
No Longer Meets Eligibility Criteria	1	-	2
Global Deterioration of Health Status	19	18	24

Baseline characteristics

Reporting groups

Reporting group title	Avelumab
Reporting group description: Avelumab 10 milligram (mg)/kilogram (kg) given as a 1-hour intravenous (IV) infusion every 2 weeks (Q2W) in 4-week cycles.	
Reporting group title	Avelumab + PLD
Reporting group description: Avelumab 10 mg/kg given as a 1-hour IV Q2W in 4-week cycles + pegylated liposomal doxorubicin (PLD) 40 mg/square meter given as a 1-hour IV infusion every 4 weeks (Q4W) in 4-week cycles.	
Reporting group title	Pegylated Liposomal Doxorubicin (PLD)
Reporting group description: PLD 40 mg/square meter given as a 1-hour IV infusion Q4W in 4-week cycles.	

Reporting group values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)
Number of subjects	188	188	190
Age Categorical			
Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	111	124	114
>=65 years	77	64	76
Age Continuous			
Units: years			
arithmetic mean	61.0	59.5	60.4
standard deviation	± 10.26	± 10.05	± 10.64
Sex: Female, Male			
Units: Subjects			
Female	188	188	190
Male	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	3	1
Not Hispanic or Latino	176	176	183
Unknown or Not Reported	10	9	6
Race (NIH/OMB)			
Units: Subjects			
Black or African American	2	2	6
American Indian or Alaska Native	0	0	1
Asian	34	53	46
Native Hawaiian or Other Pacific Islander	1	0	0
White	148	133	135
Other	1	0	2
Unknown or Not Reported	2	0	0
Region of Enrollment			
Units: Subjects			
North America	49	45	50
Western Europe	78	68	63

Eastern Europe	21	20	26
Middle East	0	0	1
Australasia	10	6	12
Asia	30	49	38

Reporting group values	Total		
Number of subjects	566		
Age Categorical Units: Subjects			
<=18 years	0		
Between 18 and 65 years	349		
>=65 years	217		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	566		
Male	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6		
Not Hispanic or Latino	535		
Unknown or Not Reported	25		
Race (NIH/OMB) Units: Subjects			
Black or African American	10		
American Indian or Alaska Native	1		
Asian	133		
Native Hawaiian or Other Pacific Islander	1		
White	416		
Other	3		
Unknown or Not Reported	2		
Region of Enrollment Units: Subjects			
North America	144		
Western Europe	209		
Eastern Europe	67		
Middle East	1		
Australasia	28		
Asia	117		

End points

End points reporting groups

Reporting group title	Avelumab
Reporting group description:	Avelumab 10 milligram (mg)/kilogram (kg) given as a 1-hour intravenous (IV) infusion every 2 weeks (Q2W) in 4-week cycles.
Reporting group title	Avelumab + PLD
Reporting group description:	Avelumab 10 mg/kg given as a 1-hour IV Q2W in 4-week cycles + pegylated liposomal doxorubicin (PLD) 40 mg/square meter given as a 1-hour IV infusion every 4 weeks (Q4W) in 4-week cycles.
Reporting group title	Pegylated Liposomal Doxorubicin (PLD)
Reporting group description:	PLD 40 mg/square meter given as a 1-hour IV infusion Q4W in 4-week cycles.

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	OS is defined as the time from the date of randomization to the date of death due to any cause. OS time was summarized by treatment arm using the Kaplan-Meier method.
End point type	Primary
End point timeframe:	From randomization until the date of first documented progression or date of deaths from any cause, whichever came first, assessed up to 30 months (based on cutoff date: 19 September 2018).

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: months				
median (confidence interval 95%)	11.8 (8.9 to 14.1)	15.7 (12.7 to 18.7)	13.1 (11.8 to 15.5)	

Statistical analyses

Statistical analysis title	Overall survival comparison versus PLD
Comparison groups	Avelumab v Pegylated Liposomal Doxorubicin (PLD)
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8253
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.867
upper limit	1.497

Statistical analysis title	Overall survival comparison versus PLD
Comparison groups	Avelumab + PLD v Pegylated Liposomal Doxorubicin (PLD)
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2082
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.672
upper limit	1.179

Primary: Progression Free Survival (PFS) Based on Blinded Independent Central Review (BICR) According to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1

End point title	Progression Free Survival (PFS) Based on Blinded Independent Central Review (BICR) According to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
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End point description:

PFS is defined as the time from date of randomization to the date of the first documentation of progression of disease (PD) or death due to any cause, whichever occurs first. PFS time was summarized by treatment arm using the Kaplan-Meier method. PFS based on BICR assessment was evaluated for this endpoint.

End point type	Primary
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End point timeframe:

From randomization to date of first documentation of PD or death due to any cause whichever was first (up to 30 months); based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: months				
median (confidence interval 95%)	1.9 (1.8 to 1.9)	3.7 (3.3 to 5.1)	3.5 (2.1 to 4.0)	

Statistical analyses

Statistical analysis title	PFS comparison versus PLD
Comparison groups	Avelumab + PLD v Pegylated Liposomal Doxorubicin (PLD)
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0301
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.607
upper limit	1.011

Statistical analysis title	PFS comparison versus PLD
Comparison groups	Avelumab v Pegylated Liposomal Doxorubicin (PLD)
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.9999
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2.16

Secondary: Objective Response Rate (ORR) Based on BICR Assessment

End point title	Objective Response Rate (ORR) Based on BICR Assessment
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End point description:

Percentage of subjects achieved objective response (OR) based on BICR assessment is presented for this endpoint. OR is defined as a complete response (CR, disappearance of all target lesions) or partial response (PR, $\geq 30\%$ decrease under the baseline of the sum of diameters of all target measurable lesions) according to the RECIST (version 1.1) recorded from randomization until disease progression or death due to any cause. Both CR and PR must be confirmed by repeat assessments performed no less than 4 weeks after the criteria for response are first met and before the first documentation of disease progression. Only tumor assessments performed on or before the start date of any further anti-cancer

therapies are considered in the assessment of best overall response.

End point type	Secondary
End point timeframe:	
Tumor assessments as assessed by BICR were conducted at every 8 weeks from screening until documented disease progression (approximately up to 30 months); based on cutoff date: 19 September 2018.	

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: percentage of subjects				
number (confidence interval 95%)	3.7 (1.5 to 7.5)	13.3 (8.8 to 19.0)	4.2 (1.8 to 8.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: ORR Based on Investigator Assessment

End point title	ORR Based on Investigator Assessment
End point description:	
Percentage of subjects achieved OR based on investigator assessment is presented for this endpoint. OR is defined as a CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease under the baseline of the sum of diameters of all target measurable lesions) according to the RECIST (version 1.1) recorded from randomization until disease progression or death due to any cause. The ORR on each randomized treatment arm were estimated by dividing the number of subjects with OR (CR or PR) by number of subjects randomized to the respective treatment arm.	
End point type	Secondary
End point timeframe:	
Tumor assessments as assessed by investigator were conducted at every 8 weeks from screening until documented disease progression, up to 30 months; based on cutoff date: 19 September 2018.	

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: percentage of subjects				
number (confidence interval 95%)	5.3 (2.6 to 9.6)	18.6 (13.3 to 24.9)	9.5 (5.7 to 14.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DR) Based on BICR Assessment

End point title	Duration of Response (DR) Based on BICR Assessment
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End point description:

DR is defined, for subjects with an OR per RECIST version 1.1, as the time from the first documentation of objective tumor response (CR [disappearance of all target lesions] or PR [$\geq 30\%$ decrease under the baseline of the sum of diameters of all target measurable lesions]) to the first documentation of objective tumor progression or death due to any cause, whichever occurs first.

End point type	Secondary
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End point timeframe:

Tumor assessments as assessed by investigator were conducted at every 8 weeks from screening until documented disease progression, up to 30 months; based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	25	8	
Units: months				
median (confidence interval 95%)	9.2 (6.4 to 99999)	8.5 (6.1 to 99999)	13.1 (5.5 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: PFS Based on Investigator Assessment According to RECIST version 1.1

End point title	PFS Based on Investigator Assessment According to RECIST version 1.1
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End point description:

PFS is defined as the time from date of randomization to the date of the first documentation of PD or death due to any cause, whichever occurs first. PFS time was summarized by treatment arm using the Kaplan-Meier method.

End point type	Secondary
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End point timeframe:

From randomization to date of first documentation of PD or death due to any cause whichever was first (up to 30 months); based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: month				
median (confidence interval 95%)	1.9 (1.8 to 1.9)	4.7 (3.7 to 6.0)	3.7 (3.5 to 5.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: DR Based on Investigator Assessment

End point title	DR Based on Investigator Assessment
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End point description:

DR is defined, for subjects with an OR per RECIST version 1.1, as the time from the first documentation of objective tumor response (CR [disappearance of all target lesions] or PR [$\geq 30\%$ decrease under the baseline of the sum of diameters of all target measurable lesions]) to the first documentation of objective tumor progression or death due to any cause, whichever occurs first.

End point type	Secondary
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End point timeframe:

Tumor assessments as assessed by investigator were conducted at every 8 weeks from screening until documented disease progression, up to 30 months; based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	35	18	
Units: months				
median (confidence interval 95%)	10.4 (3.7 to 99999)	7.6 (5.6 to 9.1)	7.4 (3.6 to 11.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control (DC) Rate Based on BICR Assessment

End point title	Disease Control (DC) Rate Based on BICR Assessment
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End point description:

Percentage of subjects achieving DC based on BICR assessment is presented in this endpoint. DC is a best overall response of CR (disappearance of all target lesions), PR ($\geq 30\%$ decrease under the baseline of the sum of diameters of all target measurable lesions), non-complete response/non-progressive disease or stable disease (SD) according to the RECIST version 1.1.

End point type	Secondary
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End point timeframe:

Tumor assessments as assessed by investigator were conducted at every 8 weeks from screening until documented disease progression, up to 30 months; based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: percentage of subjects				
number (confidence interval 95%)	33.0 (26.3 to 40.2)	57.4 (50.0 to 64.6)	48.9 (41.6 to 56.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: DC Rate Based on Investigator Assessment

End point title	DC Rate Based on Investigator Assessment
End point description:	Percentage of subjects achieving DC based on investigator assessment is presented in this endpoint. DC is a best overall response of CR (disappearance of all target lesions), PR ($\geq 30\%$ decrease under the baseline of the sum of diameters of all target measurable lesions), non-complete response/non-progressive disease or SD according to the RECIST version 1.1.
End point type	Secondary
End point timeframe:	Tumor assessments as assessed by investigator were conducted at every 8 weeks from screening until documented disease progression, up to 30 months; based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: percentage of subjects				
number (confidence interval 95%)	34.0 (27.3 to 41.3)	61.7 (54.3 to 68.7)	54.7 (47.4 to 62.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)
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End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical investigation patient administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; life-threatening; initial or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect; progression of the malignancy under study. Treatment emergent AEs are those events with onset dates occurring during the on-treatment period for the first time, or if the worsening of an event is during the on-treatment period.

End point type	Secondary
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End point timeframe:

From the time of the first dose of study treatment through a minimum of 30 days + last dose of study treatment, start day of new anti-cancer therapy -1 day (up to 70 months); based on cutoff date: 13 July 2022.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	182	177	
Units: Subjects				
TEAE	180	180	173	
Treatment emergent SAEs	72	74	51	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Abnormalities

End point title	Number of Subjects with Laboratory Abnormalities
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End point description:

The number of subjects with following laboratory abnormalities meeting any of the Grades 1 to 4 classified according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) toxicity grading version 4.03 were summarized: hematology (anemia, lymphocyte count decreased, neutrophil count decreased; and platelet count decreased) and chemistry laboratory tests (creatinine increased; serum amylase increased and lipase increased).

End point type	Secondary
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End point timeframe:

From screening to the end of treatment/withdrawal visit, up to 2.7 years, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	182	177	
Units: Subjects				
Anemia Any grade >=1	135	155	144	
Lymphocyte count decreased Any grade >=1	89	148	107	
Neutrophil count decreased Any grade >=1	26	80	62	
Platelet count decreased Any grade >=1	33	48	50	
Creatinine increased Any grade >=1	154	151	120	
Serum amylase increased Any grade >=1	43	35	27	
Lipase increased Any grade >=1	27	33	21	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Vital Signs - Blood Pressure

End point title	Change From Baseline in Vital Signs - Blood Pressure
End point description:	Vital signs included blood pressure and pulse rate. Changes from baseline in sitting diastolic blood pressure (DBP) and systolic blood pressure (SBP) were summarized.
End point type	Secondary
End point timeframe:	From screening to the end of treatment/withdrawal visit, up to 2.7 years, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	182	177	
Units: mm Hg				
arithmetic mean (standard deviation)				
DBP Cycle 1 Day 15	0.1 (± 9.79)	-2.2 (± 9.12)	0.7 (± 8.89)	
DBP Cycle 2 Day 1	-1.1 (± 9.61)	-2.8 (± 8.01)	-0.1 (± 9.34)	
DBP Cycle 2 Day 15	0.1 (± 10.05)	-2.8 (± 9.19)	-0.1 (± 8.83)	
DBP Cycle 3 Day 1	0 (± 10.81)	-2.7 (± 8.95)	-0.2 (± 8.96)	
DBP Cycle 3 Day 15	-0.6 (± 9.25)	-2.3 (± 8.56)	-0.5 (± 8.67)	
DBP End of Treatment	1.1 (± 10.87)	-0.3 (± 11.08)	0.8 (± 10.40)	
SBP Cycle 1 Day 15	-0.9 (± 14.35)	-2.3 (± 13.12)	-1.0 (± 13.94)	
SBP Cycle 2 Day 1	-2.2 (± 14.44)	-3.4 (± 13.70)	-2.8 (± 13.39)	
SBP Cycle 2 Day 15	-0.6 (± 14.11)	-3.7 (± 14.78)	-1.8 (± 14.98)	
SBP Cycle 3 Day 1	-0.2 (± 15.59)	-2.7 (± 14.36)	-1.5 (± 14.14)	

SBP Cycle 3 Day 15	-0.2 (± 13.78)	-2.1 (± 15.30)	-2.2 (± 13.96)	
SBP End of Treatment	-0.9 (± 17.21)	-1.0 (± 16.83)	-3.2 (± 15.92)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Vital Signs - Pulse Rate

End point title	Change From Baseline in Vital Signs - Pulse Rate
End point description:	Vital signs included blood pressure and pulse rate. Changes from baseline in sitting pulse rate were summarized.
End point type	Secondary
End point timeframe:	From screening to the end of treatment/withdrawal visit, up to 2.7 years, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	182	177	
Units: bpm				
arithmetic mean (standard deviation)				
Cycle 1 Day 15	2.9 (± 9.95)	1.8 (± 12.10)	3.5 (± 10.70)	
Cycle 2 Day 1	2.6 (± 10.92)	2.9 (± 11.18)	1.7 (± 9.71)	
Cycle 2 Day 15	2.9 (± 11.19)	3.5 (± 11.79)	3.2 (± 11.54)	
Cycle 3 Day 1	2.4 (± 10.00)	2.1 (± 11.78)	1.4 (± 11.14)	
Cycle 3 Day 15	3.0 (± 12.23)	1.4 (± 11.44)	2.4 (± 10.41)	
End of Treatment	7.7 (± 14.27)	7.4 (± 13.70)	5.7 (± 14.10)	

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:	Categorical summarization ECG criteria were as follows: 1) QT interval, QTcB, QTcF and QTcP: increase from baseline >30 ms or 60 ms; absolute value > 450 ms, >480 ms and > 500 ms; 2) heart rate (HR): change from baseline >=20 bpm and absolute value <=50 bpm or >=120 bpm; 3) PR interval: absolute value >=220 ms and increase from baseline >=20 ms; 4) QRS: >= 120 ms.
End point type	Secondary

End point timeframe:

From screening to the end of treatment/withdrawal visit, up to 2.7 years, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	182	177	
Units: Subjects				
QT increase from baseline >30 ms	26	40	47	
QT increase from baseline >60 ms	5	9	4	
QT >450 ms	6	10	5	
QT >480 ms	1	2	2	
QT >500 ms	1	1	1	
QTcB increase from baseline >30 ms	33	36	22	
QTcB increase from baseline >60 ms	9	7	8	
QTcB >450 ms	56	63	45	
QTcB >480 ms	9	19	9	
QTcB >500 ms	5	9	5	
QTcF increase from baseline >30 ms	19	24	13	
QTcF increase from baseline >60 ms	6	5	5	
QTcF >450 ms	18	27	14	
QTcF >480 ms	4	8	5	
QTcF >500 ms	3	2	4	
QTcP increase from baseline >30 ms	17	23	12	
QTcP increase from baseline >60 ms	6	5	4	
QTcP >450 ms	19	29	17	
QTcP >480 ms	2	7	2	
QTcP >500 ms	1	2	2	
Heart rate <=50 bpm and decrease >= 20 bpm	0	1	0	
Heart rate >=120 bpm and increase >= 20 bpm	5	5	3	
PR >=220 ms and increase from baseline >=20 ms	3	4	2	
QRS >=120 ms	7	9	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with % Left Ventricular Ejection Fraction (LVEF) Decrease from Baseline

End point title	Number of Subjects with % Left Ventricular Ejection Fraction (LVEF) Decrease from Baseline
-----------------	--

End point description:

LVEF decrease was summarized by multiple-gated acquisition (MUGA)/ echocardiogram (ECHO)

parameter. Subjects with a LVEF% ≥ 10 points and ≥ 15 points decrease from baseline during the on-treatment period were summarized.

End point type	Secondary
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End point timeframe:

Screening, Cycle 3 Day 1 (repeated every 2 cycles) to the end of treatment/withdrawal visit, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	129	154	132	
Units: Subjects				
≥ 10 point decrease from baseline MUGA/ECHO	8	22	13	
≥ 15 point decrease from baseline MUGA/ECHO	3	8	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CD8 Expression for PFS (Based on BICR Assessment) and for OS

End point title	Number of Subjects with CD8 Expression for PFS (Based on BICR Assessment) and for OS
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End point description:

Tumor infiltrating CD8 positive (CD8+) T lymphocytes was assessed by immunohistochemistry. Subjects were considered positive for CD8 T cells if their baseline tissue sample demonstrated presence of $\geq 1\%$ CD8+ cells across the area of the tumor.

End point type	Secondary
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End point timeframe:

Biomarkers are measured only at screening.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	165	171	164	
Units: Subjects				
Positive	76	80	72	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Improved, Stable and Deterioration Based on 10-Point Change for EORTC QLQ-C30 Global QoL

End point title	Number of Subjects with Improved, Stable and Deterioration Based on 10-Point Change for EORTC QLQ-C30 Global QoL
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End point description:

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30) is a 30 question survey and includes 5 functional domain subscales, global health status/quality of life, disease/treatment related symptoms, and the perceived financial impact of disease. Higher scores are reflective of a greater presence of symptoms.

End point type	Secondary
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End point timeframe:

Day 1 of Cycle 1, Day 1 of each subsequent cycle, end of treatment/withdrawal visit and the 30, 60 and 90 days safety follow up visits, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	166	148	
Units: Subjects				
Deterioration	46	65	46	
Improved	23	20	26	
Stable	83	81	76	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with PD-L1 Expression for PFS (Based on BICR Assessment) and for OS

End point title	Number of Subjects with PD-L1 Expression for PFS (Based on BICR Assessment) and for OS
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End point description:

PD-L1 expression was assessed by immunohistochemistry. Subjects were considered positive for PD-L1 if their baseline tissue sample demonstrated PD-L1 expression on $\geq 1\%$ of tumor cells or $\geq 5\%$ of immune cells.

End point type	Secondary
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End point timeframe:

Biomarkers are measured only at screening.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	170	173	165	
Units: Subjects				
Positive	100	100	88	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Deterioration in Abdominal/GI Symptom Subscale of EORTC QLQ-OV28

End point title	Time to Deterioration in Abdominal/GI Symptom Subscale of EORTC QLQ-OV28
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End point description:

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer 28 (EORTC QLQ-OV28) is a 28 item instrument with 7 functional domain subscales. Time to deterioration was defined as the time from randomization to the first time the subject's score showed a 15-point or higher increase in the score of the abdominal/GI symptom subscale of the EORTC QLQ-OV28.

End point type	Secondary
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End point timeframe:

From Day 1 of Cycle 1 to prior to end of treatment/withdrawal visit, based on cutoff date: 19 September 2018.

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	188	190	
Units: months				
median (confidence interval 95%)	00000 (00000 to 99999)	11.1 (6.5 to 99999)	10.6 (9.2 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Trough Concentration (Ctough) For Avelumab Following Cycle 2 Day 1 Pegylated Liposomal Doxorubicin (PLD) Dose

End point title	Serum Trough Concentration (Ctough) For Avelumab Following Cycle 2 Day 1 Pegylated Liposomal Doxorubicin (PLD) Dose ^[1]
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End point description:

Ctough was defined as predose concentration during multiple dosing, and can be observed directly from data.

End point type	Secondary
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End point timeframe:

At predose (0 H) on Cycle 2 Day 1.

Notes:

[1] - 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: Statistics are reported for the arms specified

End point values	Avelumab	Avelumab + PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	139		
Units: microgram per milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)	21.1 (± 89)	23.19 (± 74)		

Statistical analyses

Statistical analysis title	Ctrough comparison
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Statistical analysis description:

Avelumab was the Reference treatment and Avelumab + PLD was the Test treatment

Comparison groups	Avelumab v Avelumab + PLD
Number of subjects included in analysis	275
Analysis specification	Pre-specified
Analysis type	other ^[2]
Parameter estimate	Geometric Mean Ratio (Test/Reference, %)
Point estimate	110
Confidence interval	
level	90 %
sides	2-sided
lower limit	95.4
upper limit	126.7

Notes:

[2] - The ratios (and 90% CIs) are expressed as percentages.

Secondary: Change from Baseline in EQ-VAS Score at End of Treatment

End point title	Change from Baseline in EQ-VAS Score at End of Treatment
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End point description:

The EuroQol- 5 Dimensions- 5 Levels (EQ-5D-5L) questionnaire consists of the EQ-5D-5L descriptive system and a visual analogue scale (the EuroQol-visual analogue scale [EQ-VAS]). The respondent's self-rated health is assessed on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state) by the EQ-VAS.

End point type	Secondary
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End point timeframe:

Baseline and end of treatment/withdrawal visit

End point values	Avelumab	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	116	111	
Units: scores on a scale				
arithmetic mean (standard deviation)	-13.6 (± 20.56)	-11.2 (± 19.79)	-7.7 (± 22.26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Maximum Concentration (Cmax) For Avelumab Following Cycle 2 Day 1 PLD Dose

End point title	Serum Maximum Concentration (Cmax) For Avelumab Following Cycle 2 Day 1 PLD Dose ^[3]
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End point description:

Cmax was defined as maximum observed serum concentration, and can be observed directly from data.

End point type	Secondary
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End point timeframe:

At postdose (end of infusion, 1H) on Cycle 2 Day 1.

Notes:

[3] - 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: Statistics are reported for the arms specified

End point values	Avelumab	Avelumab + PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	110		
Units: µg/mL				
geometric mean (geometric coefficient of variation)	231.6 (± 43)	207.9 (± 71)		

Statistical analyses

Statistical analysis title	Cmax comparison
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Statistical analysis description:

Avelumab was the Reference treatment and Avelumab + PLD was the Test treatment

Comparison groups	Avelumab v Avelumab + PLD
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	other ^[4]
Parameter estimate	Geometric Mean Ratio (Test/Reference, %)
Point estimate	90

Confidence interval	
level	90 %
sides	2-sided
lower limit	79.5
upper limit	101.5

Notes:

[4] - The ratios (and 90% CIs) are expressed as percentages.

Secondary: Cmax For Doxorubicin Following Cycle 2 Day 1 PLD Dose

End point title	Cmax For Doxorubicin Following Cycle 2 Day 1 PLD Dose ^[5]
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End point description:

Cmax was defined as maximum observed serum concentration, and can be observed directly from data.

End point type	Secondary
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End point timeframe:

From predose (0 H) of Cycle 2 Day 1 through 336 hours postdose.

Notes:

[5] - 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: Statistics are reported for the arms specified

End point values	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	25850 (± 17)	26810 (± 14)		

Statistical analyses

Statistical analysis title	Cmax comparison
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Statistical analysis description:

PLD was the Reference treatment and Avelumab + PLD was the Test treatment.

Comparison groups	Pegylated Liposomal Doxorubicin (PLD) v Avelumab + PLD
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other ^[6]
Parameter estimate	Geometric Mean Ratio (Test/Reference, %)
Point estimate	96
Confidence interval	
level	90 %
sides	2-sided
lower limit	87
upper limit	106

Notes:

[6] - The ratios (and 90% CIs) are expressed as percentages. There were 29 subjects in this analysis.

Secondary: Area Under The Concentration Time Profile From Time Zero to The Last Quantifiable Concentration (AUClast) For Doxorubicin Following Cycle 2 Day 1 PLD Dose

End point title	Area Under The Concentration Time Profile From Time Zero to The Last Quantifiable Concentration (AUClast) For Doxorubicin Following Cycle 2 Day 1 PLD Dose ^[7]
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End point description:

AUClast was defined as area under the concentration time profile from time zero to the time of the last quantifiable concentration (Clast).

End point type	Secondary
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End point timeframe:

From predose (0 H) of Cycle 2 Day 1 through 336 hours postdose.

Notes:

[7] - 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: Statistics are reported for the arms specified

End point values	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	2052000 (\pm 71)	2043000 (\pm 119)		

Statistical analyses

Statistical analysis title	AUClast comparison
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Statistical analysis description:

PLD was the Reference treatment and Avelumab + PLD was the Test treatment.

Comparison groups	Pegylated Liposomal Doxorubicin (PLD) v Avelumab + PLD
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other ^[8]
Parameter estimate	Geometric Mean Ratio (Test/Reference, %)
Point estimate	100
Confidence interval	
level	90 %
sides	2-sided
lower limit	60
upper limit	168

Notes:

[8] - The ratios (and 90% CIs) are expressed as percentages. There were 29 subjects in this analysis.

Secondary: Area Under The Concentration Time Profile From Time Zero to 336 Hours (AUC336) For Doxorubicin Following Cycle 2 Day 1 PLD Dose

End point title	Area Under The Concentration Time Profile From Time Zero to 336 Hours (AUC336) For Doxorubicin Following Cycle 2 Day 1 PLD Dose ^[9]
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End point description:

AUC336 was defined as area under the concentration time profile from time zero to 336 hours.

End point type Secondary

End point timeframe:

From predose (0 H) of Cycle 2 Day 1 through 336 hours postdose.

Notes:

[9] - 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: Statistics are reported for the arms specified

End point values	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	2571000 (\pm 30)	2848000 (\pm 20)		

Statistical analyses

Statistical analysis title AUC336 comparison

Statistical analysis description:

PLD was the Reference treatment and Avelumab + PLD was the Test treatment.

Comparison groups Pegylated Liposomal Doxorubicin (PLD) v Avelumab + PLD

Number of subjects included in analysis 25

Analysis specification Pre-specified

Analysis type other^[10]

Parameter estimate Geometric Mean Ratio (Test/Reference, %)

Point estimate 90

Confidence interval

level 90 %

sides 2-sided

lower limit 76

upper limit 107

Notes:

[10] - The ratios (and 90% CIs) are expressed as percentages.

Secondary: Area Under The Concentration Time Profile From Time Zero to 24 Hours (AUC24) For Doxorubicin Following Cycle 2 Day 1 PLD Dose

End point title Area Under The Concentration Time Profile From Time Zero to 24 Hours (AUC24) For Doxorubicin Following Cycle 2 Day 1 PLD Dose^[11]

End point description:

AUC24 was defined as area under the concentration time profile from time zero to 24 hours.

End point type Secondary

End point timeframe:

From 0 through 24 hours postdose.

Notes:

[11] - 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: Statistics are reported for the arms specified

End point values	Avelumab + PLD	Pegylated Liposomal Doxorubicin (PLD)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	541700 (\pm 14)	567600 (\pm 11)		

Statistical analyses

Statistical analysis title	AUC24 comparison
Statistical analysis description: PLD was the Reference treatment and Avelumab + PLD was the Test treatment.	
Comparison groups	Pegylated Liposomal Doxorubicin (PLD) v Avelumab + PLD
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio (Test/Reference, %)
Point estimate	95
Confidence interval	
level	90 %
sides	2-sided
lower limit	88
upper limit	104

Secondary: Number of Subjects With Treatment-Induced ADA

End point title	Number of Subjects With Treatment-Induced ADA ^[12]
End point description: Treatment-induced ADA was defined as patient who was ADA-negative at baseline and has at least one positive post-baseline ADA result; or if patient did not have a baseline sample, the patient had at least one positive past-baseline ADA result.	
End point type	Secondary
End point timeframe: At predose (0 H) of select cycles starting from Cycle 1 through Cycle 24, at end of treatment and 30 days after the last dose of avelumab.	

Notes:

[12] - 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: Statistics are reported for the arms specified

End point values	Avelumab	Avelumab + PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	167		
Units: Subjects	27	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Boosted Anti-Drug Antibody (ADA)

End point title	Number of Subjects With Treatment-Boosted Anti-Drug Antibody (ADA) ^[13]
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End point description:

Treatment-boosted ADA was defined as a positive ADA result at baseline and the titer $\geq 8 \times$ baseline titer at least once after treatment with avelumab.

End point type	Secondary
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End point timeframe:

At predose (0 H) of select cycles starting from Cycle 1 through Cycle 24, at end of treatment and 30 days after the last dose of avelumab.

Notes:

[13] - 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: Statistics are reported for the arms specified

End point values	Avelumab	Avelumab + PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	167		
Units: Subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Induced Neutralizing Antibody (nAb)

End point title	Number of Subjects With Treatment-Induced Neutralizing Antibody (nAb) ^[14]
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End point description:

Treatment-induced nAb was defined as patient who was not nAb positive at baseline and had at least one positive post-baseline nAb result; or if patient did not have a baseline sample, the patient had at least one positive past-baseline ADA result.

End point type	Secondary
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End point timeframe:

At predose (0 H) of select cycles starting from Cycle 1 through Cycle 24, at end of treatment and 30 days after the last dose of avelumab.

Notes:

[14] - 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: Statistics are reported for the arms specified

End point values	Avelumab	Avelumab + PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	169		
Units: Subjects	5	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study treatment through a minimum of 30 days + last dose of study treatment, start day of new anti-cancer therapy -1 day (up to 70 months). Based on the cutoff: 13 July 2022.

Adverse event reporting additional description:

The same event may appear as both an AE and an SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as non-serious in another subject, or 1 subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Avelumab
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Reporting group description:

Avelumab 10 milligram (mg)/kilogram (kg) given as a 1-hour intravenous (IV) infusion every 2 weeks (Q2W) in 4-week cycles.

Reporting group title	Pegylated Liposomal Doxorubicin (PLD)
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Reporting group description:

PLD 40 mg/square meter given as a 1-hour IV infusion Q4W in 4-week cycles.

Reporting group title	Avelumab + PLD
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Reporting group description:

Avelumab 10 mg/kg given as a 1-hour IV Q2W in 4-week cycles + pegylated liposomal doxorubicin (PLD) 40 mg/square meter given as a 1-hour IV infusion every 4 weeks (Q4W) in 4-week cycles.

Serious adverse events	Avelumab	Pegylated Liposomal Doxorubicin (PLD)	Avelumab + PLD
Total subjects affected by serious adverse events			
subjects affected / exposed	72 / 187 (38.50%)	51 / 177 (28.81%)	74 / 182 (40.66%)
number of deaths (all causes)	122	116	107
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Embolism			
subjects affected / exposed	0 / 187 (0.00%)	3 / 177 (1.69%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism venous			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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 / 187 (0.00%)	0 / 177 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Chills			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Administration site extravasation			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Complication associated with device			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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

Fatigue			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	10 / 187 (5.35%)	2 / 177 (1.13%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 10	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	2 / 187 (1.07%)	0 / 177 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 3
Influenza like illness			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Localised oedema			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	7 / 187 (3.74%)	1 / 177 (0.56%)	8 / 182 (4.40%)
occurrences causally related to treatment / all	5 / 8	0 / 3	6 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated adverse reaction			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Anaphylactic reaction			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 187 (1.60%)	0 / 177 (0.00%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 3	0 / 0	3 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Oropharyngeal pain			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 187 (1.07%)	0 / 177 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 187 (0.53%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Pulmonary embolism			
subjects affected / exposed	2 / 187 (1.07%)	2 / 177 (1.13%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Respiratory failure			

subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Product issues			
Device dislocation			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Investigations			
White blood cell count decreased			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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

Urine output decreased			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
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			
Infusion related reaction			
subjects affected / exposed	1 / 187 (0.53%)	1 / 177 (0.56%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	1 / 1	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Stoma complication			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Upper limb fracture			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Myocardial infarction			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tremor			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Aphasia			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Clonic convulsion			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Anaemia			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Febrile neutropenia			
subjects affected / exposed	0 / 187 (0.00%)	3 / 177 (1.69%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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 disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 187 (0.53%)	1 / 177 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	9 / 187 (4.81%)	6 / 177 (3.39%)	6 / 182 (3.30%)
occurrences causally related to treatment / all	1 / 10	1 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	3 / 187 (1.60%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	2 / 187 (1.07%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 187 (1.07%)	1 / 177 (0.56%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			

subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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 obstruction			
subjects affected / exposed	11 / 187 (5.88%)	6 / 177 (3.39%)	9 / 182 (4.95%)
occurrences causally related to treatment / all	2 / 16	0 / 6	0 / 9
deaths causally related to treatment / all	1 / 3	0 / 1	0 / 1
Ileus			
subjects affected / exposed	1 / 187 (0.53%)	2 / 177 (1.13%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Faecaloma			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
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 / 187 (2.14%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	2 / 4	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	7 / 187 (3.74%)	3 / 177 (1.69%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	1 / 8	3 / 5	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			

subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Subileus			
subjects affected / exposed	1 / 187 (0.53%)	2 / 177 (1.13%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	5 / 187 (2.67%)	2 / 177 (1.13%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Obstruction gastric			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Nausea			
subjects affected / exposed	7 / 187 (3.74%)	1 / 177 (0.56%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 7	0 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			

subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Pancreatitis acute			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Malignant gastrointestinal obstruction			
subjects affected / exposed	1 / 187 (0.53%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Drug-induced liver injury			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Autoimmune hepatitis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Skin and subcutaneous tissue disorders			
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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

Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitic ulcer			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	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	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive nephropathy			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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

Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basedow's disease			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glucocorticoid deficiency			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 187 (0.00%)	2 / 177 (1.13%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Cholangitis infective			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Cystitis			

subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Device related infection			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Erysipelas			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Gastroenteritis			
subjects affected / exposed	1 / 187 (0.53%)	1 / 177 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Influenza			
subjects affected / exposed	0 / 187 (0.00%)	2 / 177 (1.13%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph gland infection			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site infection			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			

subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nail infection			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Oral fungal infection			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (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
Peritonitis bacterial			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 187 (1.60%)	0 / 177 (0.00%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 187 (0.53%)	1 / 177 (0.56%)	0 / 182 (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
Respiratory tract infection			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Sepsis			

subjects affected / exposed	0 / 187 (0.00%)	2 / 177 (1.13%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 187 (0.53%)	2 / 177 (1.13%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 187 (0.53%)	0 / 177 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular device infection			

subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic pulmonary embolism			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	0 / 182 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
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 bacteraemia			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 187 (1.60%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 3	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 187 (1.07%)	1 / 177 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 187 (0.00%)	1 / 177 (0.56%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 0	0 / 3	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 187 (0.00%)	0 / 177 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 187 (0.00%)	2 / 177 (1.13%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	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	Avelumab	Pegylated Liposomal Doxorubicin (PLD)	Avelumab + PLD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	173 / 187 (92.51%)	167 / 177 (94.35%)	176 / 182 (96.70%)
General disorders and administration site conditions			
Chills			
subjects affected / exposed	18 / 187 (9.63%)	3 / 177 (1.69%)	14 / 182 (7.69%)
occurrences (all)	20	3	15
Fatigue			
subjects affected / exposed	63 / 187 (33.69%)	55 / 177 (31.07%)	77 / 182 (42.31%)
occurrences (all)	88	78	147
Influenza like illness			
subjects affected / exposed	6 / 187 (3.21%)	1 / 177 (0.56%)	10 / 182 (5.49%)
occurrences (all)	7	1	13
Asthenia			
subjects affected / exposed	18 / 187 (9.63%)	14 / 177 (7.91%)	30 / 182 (16.48%)
occurrences (all)	27	18	68
Malaise			
subjects affected / exposed	5 / 187 (2.67%)	6 / 177 (3.39%)	11 / 182 (6.04%)
occurrences (all)	5	6	14
Mucosal inflammation			
subjects affected / exposed	4 / 187 (2.14%)	19 / 177 (10.73%)	24 / 182 (13.19%)
occurrences (all)	7	29	45
Oedema peripheral			

subjects affected / exposed occurrences (all)	13 / 187 (6.95%) 16	14 / 177 (7.91%) 16	24 / 182 (13.19%) 32
Pyrexia subjects affected / exposed occurrences (all)	27 / 187 (14.44%) 32	16 / 177 (9.04%) 20	36 / 182 (19.78%) 61
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 187 (1.07%) 2	8 / 177 (4.52%) 8	12 / 182 (6.59%) 12
Dyspnoea subjects affected / exposed occurrences (all)	34 / 187 (18.18%) 45	25 / 177 (14.12%) 32	32 / 182 (17.58%) 44
Cough subjects affected / exposed occurrences (all)	17 / 187 (9.09%) 17	24 / 177 (13.56%) 27	28 / 182 (15.38%) 45
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	7 / 187 (3.74%) 7	6 / 177 (3.39%) 7	10 / 182 (5.49%) 11
Investigations			
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	13 / 187 (6.95%) 16	6 / 177 (3.39%) 9	13 / 182 (7.14%) 30
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	4 / 187 (2.14%) 5	2 / 177 (1.13%) 4	11 / 182 (6.04%) 20
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	4 / 187 (2.14%) 7	2 / 177 (1.13%) 2	18 / 182 (9.89%) 30
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	4 / 187 (2.14%) 8	2 / 177 (1.13%) 3	16 / 182 (8.79%) 22
Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 187 (0.53%) 1	4 / 177 (2.26%) 4	13 / 182 (7.14%) 54

White blood cell count decreased subjects affected / exposed occurrences (all)	6 / 187 (3.21%) 7	15 / 177 (8.47%) 41	15 / 182 (8.24%) 70
Weight decreased subjects affected / exposed occurrences (all)	10 / 187 (5.35%) 11	13 / 177 (7.34%) 19	13 / 182 (7.14%) 19
Platelet count decreased subjects affected / exposed occurrences (all)	5 / 187 (2.67%) 8	7 / 177 (3.95%) 16	10 / 182 (5.49%) 22
Neutrophil count decreased subjects affected / exposed occurrences (all)	4 / 187 (2.14%) 10	9 / 177 (5.08%) 33	17 / 182 (9.34%) 84
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 187 (0.00%) 0	3 / 177 (1.69%) 3	10 / 182 (5.49%) 13
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	13 / 187 (6.95%) 17	14 / 177 (7.91%) 14	17 / 182 (9.34%) 20
Nervous system disorders Headache subjects affected / exposed occurrences (all)	15 / 187 (8.02%) 16	11 / 177 (6.21%) 12	29 / 182 (15.93%) 34
Dizziness subjects affected / exposed occurrences (all)	5 / 187 (2.67%) 5	8 / 177 (4.52%) 8	17 / 182 (9.34%) 19
Neuropathy peripheral subjects affected / exposed occurrences (all)	2 / 187 (1.07%) 2	4 / 177 (2.26%) 4	10 / 182 (5.49%) 12
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	32 / 187 (17.11%) 68	42 / 177 (23.73%) 77	56 / 182 (30.77%) 131
Neutropenia subjects affected / exposed occurrences (all)	1 / 187 (0.53%) 2	25 / 177 (14.12%) 52	27 / 182 (14.84%) 58

Gastrointestinal disorders			
Ascites			
subjects affected / exposed	12 / 187 (6.42%)	4 / 177 (2.26%)	5 / 182 (2.75%)
occurrences (all)	16	7	9
Abdominal pain upper			
subjects affected / exposed	10 / 187 (5.35%)	13 / 177 (7.34%)	17 / 182 (9.34%)
occurrences (all)	10	13	22
Abdominal pain			
subjects affected / exposed	54 / 187 (28.88%)	38 / 177 (21.47%)	47 / 182 (25.82%)
occurrences (all)	69	48	67
Constipation			
subjects affected / exposed	35 / 187 (18.72%)	46 / 177 (25.99%)	48 / 182 (26.37%)
occurrences (all)	47	58	69
Abdominal distension			
subjects affected / exposed	14 / 187 (7.49%)	18 / 177 (10.17%)	18 / 182 (9.89%)
occurrences (all)	19	20	21
Vomiting			
subjects affected / exposed	43 / 187 (22.99%)	44 / 177 (24.86%)	43 / 182 (23.63%)
occurrences (all)	63	58	65
Stomatitis			
subjects affected / exposed	8 / 187 (4.28%)	35 / 177 (19.77%)	53 / 182 (29.12%)
occurrences (all)	13	73	125
Nausea			
subjects affected / exposed	53 / 187 (28.34%)	76 / 177 (42.94%)	87 / 182 (47.80%)
occurrences (all)	66	117	131
Gastrooesophageal reflux disease			
subjects affected / exposed	9 / 187 (4.81%)	14 / 177 (7.91%)	9 / 182 (4.95%)
occurrences (all)	9	17	11
Dyspepsia			
subjects affected / exposed	7 / 187 (3.74%)	14 / 177 (7.91%)	18 / 182 (9.89%)
occurrences (all)	7	15	25
Diarrhoea			
subjects affected / exposed	42 / 187 (22.46%)	32 / 177 (18.08%)	36 / 182 (19.78%)
occurrences (all)	61	45	57
Skin and subcutaneous tissue disorders			

Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 187 (0.53%)	40 / 177 (22.60%)	61 / 182 (33.52%)
occurrences (all)	1	74	163
Dry skin			
subjects affected / exposed	5 / 187 (2.67%)	8 / 177 (4.52%)	23 / 182 (12.64%)
occurrences (all)	5	9	25
Alopecia			
subjects affected / exposed	3 / 187 (1.60%)	7 / 177 (3.95%)	18 / 182 (9.89%)
occurrences (all)	3	7	18
Skin hyperpigmentation			
subjects affected / exposed	0 / 187 (0.00%)	10 / 177 (5.65%)	10 / 182 (5.49%)
occurrences (all)	0	10	10
Erythema			
subjects affected / exposed	4 / 187 (2.14%)	5 / 177 (2.82%)	10 / 182 (5.49%)
occurrences (all)	4	7	15
Rash maculo-papular			
subjects affected / exposed	4 / 187 (2.14%)	11 / 177 (6.21%)	14 / 182 (7.69%)
occurrences (all)	5	19	40
Rash			
subjects affected / exposed	12 / 187 (6.42%)	21 / 177 (11.86%)	51 / 182 (28.02%)
occurrences (all)	21	26	126
Pruritus			
subjects affected / exposed	13 / 187 (6.95%)	8 / 177 (4.52%)	21 / 182 (11.54%)
occurrences (all)	14	9	34
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	9 / 187 (4.81%)	2 / 177 (1.13%)	20 / 182 (10.99%)
occurrences (all)	11	2	22
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	19 / 187 (10.16%)	10 / 177 (5.65%)	17 / 182 (9.34%)
occurrences (all)	22	12	20
Back pain			
subjects affected / exposed	22 / 187 (11.76%)	21 / 177 (11.86%)	18 / 182 (9.89%)
occurrences (all)	25	25	28
Myalgia			

subjects affected / exposed occurrences (all)	9 / 187 (4.81%) 11	10 / 177 (5.65%) 10	14 / 182 (7.69%) 21
Pain in extremity subjects affected / exposed occurrences (all)	4 / 187 (2.14%) 4	13 / 177 (7.34%) 14	18 / 182 (9.89%) 20
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	15 / 187 (8.02%) 22	12 / 177 (6.78%) 21	20 / 182 (10.99%) 29
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	36 / 187 (19.25%) 41	37 / 177 (20.90%) 45	51 / 182 (28.02%) 69
Hypoalbuminaemia subjects affected / exposed occurrences (all)	8 / 187 (4.28%) 16	6 / 177 (3.39%) 8	13 / 182 (7.14%) 24
Hypokalaemia subjects affected / exposed occurrences (all)	5 / 187 (2.67%) 12	11 / 177 (6.21%) 19	12 / 182 (6.59%) 17
Hypomagnesaemia subjects affected / exposed occurrences (all)	10 / 187 (5.35%) 12	7 / 177 (3.95%) 7	8 / 182 (4.40%) 15

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2016	The protocol amendment 1 included PFS as assessed by blinded independent central review (BICR) as a additional primary objective/endpoint.
04 March 2019	The protocol amendment 2 explained that the final analysis of the study was completed and the study was planned to remain open to allow the remaining patients currently enrolled in Arm A or B to continue receiving avelumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported