



Clinical trial results:

A randomized, open-label, multicentric phase II trial of PEMBROLIZUMAB (Ketruda®) with chemotherapy versus chemotherapy alone (standard of care) as neo adjuvant treatment of ovarian cancer not amenable to front line debulking surgery.

Summary

EudraCT number	2016-004163-39
Trial protocol	FR
Global end of trial date	02 June 2023

Results information

Result version number	v1 (current)
This version publication date	27 September 2024
First version publication date	27 September 2024

Trial information

Trial identification

Sponsor protocol code	OV126b
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ARCAGY-GINECO
Sponsor organisation address	8 rue Lamennais , Paris, France, 75008
Public contact	France Binet, ARCAGY-GINECO, neopembrov-study@arcagy.org
Scientific contact	France Binet, ARCAGY-GINECO, neopembrov-study@arcagy.org

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	27 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2022
Global end of trial reached?	Yes
Global end of trial date	02 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of neoadjuvant pembrolizumab and chemo-therapy or chemotherapy alone measured by the complete resection rate after interval debulking surgery. Complete resection will be defined as the removal of all macroscopic residual tumor (Complete Cytoreduction score = 0).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki. The trial was conducted in agreement with the International Conference on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP).

As this clinical study will be carried out in France only, the study was conducted in accordance with the "Code de la Santé Publique" and data collection and recording was done in accordance with the "Méthodologie de Référence MR-001" of the Commission Nationale Informatique et Libertés.

Written informed consent (ICF) were obtained from each participant after the study protocol was explained to them and before any study-specific procedures were performed.

Background therapy:

In ovarian carcinoma patients, the anti-PD1 compound nivolumab has been reported to achieve 3 objectives responses out of 13 (23%) heavily pre-treated patients (Hamanishi J, ASCO 2014). Response was prolonged over 1 year in 2 out of the 3 responders (Hamanishi J, ASCO 2015). Similarly, the anti-PD1 pembrolizumab achieved 3 confirmed responses (11.5% [(95% CI, 2.4-30.2)]) in 26 patients treated in a phase IB study and 3 additional patients had a tumor reduction of at least 30%. Most common AEs were fatigue (42.3%), anemia (30.8%), and decreased appetite (30.8%). Drugrelated AEs occurred in 69.2% of pts (grade \geq 3, 1/26 pts) (Varga A et al, 2015).

Kryczek et al compared the PD-1 expression level at the surface of intra-tumoral CD4+ FOXP3+ Tregs among many cancer types. Interestingly, the higher level of PD-1 expression (around 20%) was found on Tregs of ovarian cancers whereas it was much lower (<10%) in other cancer types (Colon cancer, Hepatic cancer, Melanoma, Pancreatic carcinoma, Renal cell carcinoma) (Arkadiusz et al 2014). PD-L1 expression has also been detected in ovarian cancer tissue analysis by Immuno-histochemistry staining and its level of expression has been correlated to a bad outcome of patients (Kryczek et al 2009). Together with the aforementioned data on immune infiltration, these results provide rationale for a therapeutic PD-1/PD-L1 pathway blockade in ovarian cancer. In the published trials on such compounds, addition of pembrolizumab to chemotherapy or using alone has been shown to improve the response rates with a median time to response at 8 weeks (Hamanishi et al 2007, Weber et al 2014).

Evidence for comparator:

Ovarian cancer (OC) is the fifth most common cause of death from cancer in women (Gatta et al 2011). Currently, the five-year survival is close to 80-90% for stage I of 50-60% for stage II, 30% for stage III and 10% for stage IV. The 5-years survival, all stages combined, is approximately 45%. Ovarian cancer is often asymptomatic in its early stages and the majority of epithelial ovarian cancers remain clinically undetected until patients have developed late-stage disease (Cannistra 2004).

The standard procedure for initial diagnosis recommends the realization of laparoscopy first for all suspicious advanced ovarian carcinoma. This procedure should be able to confirm histological diagnosis and to describe all abdominal extension of the disease. For advanced stages, complete primary cytoreductive surgery followed by 6 cycles of chemotherapy based remains the standard of care as first

treatment in ovarian cancer. It is part of a large surgery including total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, lymphadenectomy and removal of all peritoneal carcinomatosis (Vergote et al 2010).

Complete resection of all macroscopic disease at primary debulking surgery has been shown to be the single most important independent prognostic factor in advanced ovarian carcinoma (Du Bois Cancer 2009), and this was confirmed for interval debulking surgery (IDS) after neo adjuvant chemotherapy in the EORTC-GCG study (Vergote et al., 2010). These results suggest that neo-adjuvant chemotherapy followed by surgical cytoreduction is an acceptable management strategy for patients with advanced ovarian cancer and is more and more frequently used in Europe in OC patients with high burden of tumor (2012 French national guidelines Saint Paul de Vence & ESMO guidelines). Due to these confirmed results, the rate of patients receiving neo adjuvant chemotherapy increased over time compared to up front surgery (E Stoeckle et al 2014 and Luyk EJSO 2012).

Actual start date of recruitment	03 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 91
Worldwide total number of subjects	91
EEA total number of subjects	91

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)	51
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 26/02/2018 and 17/04/2019

Pre-assignment

Screening details:

102 patients were eligible in which 11 were excluded, 91 were enrolled and treated (30 in Arm A-Paclitaxel/Carboplatin and 61 in Arm B-Paclitaxel/Carboplatin + Pembrolizumab)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A - Paclitaxel/Carboplatin
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin and paclitaxel should be taken on day 1 of each 3 weeks cycle at the dose of AUC 5 or 6 in a 15–60-minute intravenous infusion and 175 mg/m² in a 3-hour intravenous infusion respectively. One cycle is D1 to D21 and D1C2 = D22C1.

Pre-medication should be implemented according to local practices. Premedication with corticosteroids is allowed.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin and paclitaxel should be taken on day 1 of each 3 weeks cycle at the dose of AUC 5 or 6 in a 15–60-minute intravenous infusion and 175 mg/m² in a 3-hour intravenous infusion respectively. One cycle is D1 to D21 and D1C2 = D22C1.

Pre-medication should be implemented according to local practices. Premedication with corticosteroids is allowed.

Arm title	Arm B - Paclitaxel/Carboplatin with Pembrolizumab
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin and paclitaxel should be taken on day 1 of each 3 weeks cycle at the dose of AUC 5 or 6 in a 15–60-minute intravenous infusion and 175 mg/m² in a 3-hour intravenous infusion respectively. One cycle is D1 to D21 and D1C2 = D22C1.

Pre-medication should be implemented according to local practices. Premedication with corticosteroids is allowed.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin and paclitaxel should be taken on day 1 of each 3 weeks cycle at the dose of AUC 5 or 6 in a 15–60-minute intravenous infusion and 175 mg/m² in a 3-hour intravenous infusion respectively. One cycle is D1 to D21 and D1C2 = D22C1.

Pre-medication should be implemented according to local practices. Premedication with corticosteroids is allowed.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

For randomized patients in Arm B without bevacizumab, Pembrolizumab 200 mg will be administered as 30-minute IV infusion every 3 weeks. Sites should make every effort to target infusion timing to be as close to 30 minutes as possible. However, given the variability of infusion pumps from site to site, a window of -5 minutes and +10 minutes is permitted (i.e., infusion time is 30 minutes: -5 min/+10 min).

For randomized patients in Arm B with bevacizumab, pembrolizumab was administered first, followed by bevacizumab, with a minimum of 5 minutes between dosing. The initial dose of bevacizumab was delivered over 90 (±15) minutes. If the first infusion is tolerated without infusion-associated adverse events (fever and/or chills), the second infusion may be delivered over 60 (±10) minutes.

Number of subjects in period 1	Arm A - Paclitaxel/Carboplatin	Arm B - Paclitaxel/Carboplatin with Pembrolizumab
Started	30	61
Completed	30	61

Baseline characteristics

Reporting groups

Reporting group title	Arm A - Paclitaxel/Carboplatin
Reporting group description: -	
Reporting group title	Arm B - Paclitaxel/Carboplatin with Pembrolizumab
Reporting group description: -	

Reporting group values	Arm A - Paclitaxel/Carboplatin	Arm B - Paclitaxel/Carboplatin with Pembrolizumab	Total
Number of subjects	30	61	91
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	33	51
From 65-84 years	12	28	40
85 years and over	0	0	0
Age continuous Units: years			
median	61.5	63	
full range (min-max)	40 to 79	42 to 76	-
Gender categorical Units: Subjects			
Female	30	61	91
ECOG Units: Subjects			
00	14	29	43
01	15	32	47
02	1	0	1
ECG Units: Subjects			
Normal	26	49	75
Abnormal NCS	3	10	13
NA	1	2	3
Germline BRCA mutation Units: Subjects			
No	16	31	47
Yes	14	30	44
Somatic BRCA mutation Units: Subjects			
No	12	17	29

Yes	18	44	62
BRCA			
Units: Subjects			
No	24	41	65
Yes	3	13	16
NA	3	7	10
Medical Review - Primary site			
Units: Subjects			
Ovary	30	54	84
Peritoneal	0	7	7
Medical Review - Adenocarcinoma type			
Units: Subjects			
Serous High Grade (a)	28	60	88
Serous Low Grade (b)	1	0	1
Clear cell	1	0	1
Undifferentiated	0	1	1
Medical Review - FIGO			
Units: Subjects			
II	1	0	1
IIIC	22	47	69
IV	7	14	21
If stage IV, localization of the visceral disease			
Units: Subjects			
Pleura	1	4	5
Liver	1	4	5
Lungs	1	1	2
Lymph node outside of the abdominal cavity	5	4	9
Mediastin	0	1	1
Pleural Effusion	0	1	1
Unknown	0	1	1
NA	22	45	67
Immune or allergic disease			
Units: Subjects			
Allergic rhinitis	1	1	2
Asthma	1	1	2
Basedow disease	0	1	1
Diabetes 2	2	1	3
Hypothyroidism 2	2	5	7
Other	4	11	15
NA	20	41	61
At least one sign and symptom of adverse events at baseline			
Units: Subjects			
No	19	40	59
Yes	11	21	32
List of adverse events at baseline			
Units: Subjects			
Anaemia	0	2	2
Hypothyroidism	0	1	1
Gastrointestinal disorders	8	12	20

General disorders and administration site conditio	0	2	2
Hepatobiliary disorders	1	1	2
Urinary tract infection	1	0	1
Investigations	2	1	3
Metabolism and nutrition disorders	1	3	4
Anxiety	0	1	1
Respiratory, thoracic and mediastinal	1	2	3
Vascular disorders	2	1	3
Gamma-glutamyl transferase Increased	1	1	2
Hypertension	0	1	1
Abdominal pain	1	0	1
Hydronephrosis	1	0	1
NA	11	33	44
Abnormal and Clinically Significant laboratory examination at inclusion: Hematology Units: Subjects			
Hemoglobin	1	1	2
Lymphocytes	0	0	0
Monocytes	0	0	0
Neutrophils	0	0	0
Platelets	0	0	0
White blood cells	0	0	0
NA	29	60	89
Abnormal and Clinically Significant laboratory examination at inclusion: Biochemistery Units: Subjects			
Albumin	0	2	2
Alkaline phosphatase	1	1	2
ALT/SGPT	1	0	1
AST/SGOT	1	0	1
Creatinine	0	0	0
Creatinine clearance	1	0	1
LDH	0	2	2
Total bilirubin	0	0	0
NA	26	56	82
Abnormal and Clinically Significant laboratory examination at inclusion: Hormonology Units: Subjects			
FREE T3	0	0	0
FREE T4	0	0	0
TSH	0	1	1
NA	30	60	90
Abnormal and Clinically Significant laboratory examination at inclusion: Urine Protein analysis Units: Subjects			
Negative	18	35	53
Trace	3	7	10
T+1	4	6	10

T+2	1	0	1
NA	4	13	17
Initial surgery : Type of approach Units: Subjects			
Laparotomy	1	7	8
Laparoscopy-Laparoscopic assisted	29	53	82
Biopsy	0	1	1
Initial surgery : Type of procedure Units: Subjects			
Primary Surgical Staging	1	0	1
Diagnostic procedure-biopsies	29	61	90
Initial surgery : Residual disease Units: Subjects			
Not applicable	27	59	86
CC3: residue > 2.5 cm	3	1	4
CC0 : No macroscopic	0	1	1
Reason for initial non resectability : Patient's status Units: Subjects			
Poor performance status	2	1	3
Denutrition	0	1	1
Venous thrombosis	0	1	1
NA	28	58	86
Fagotti Score Units: Subjects			
08	2	1	3
04	0	1	1
NA	28	59	87
Reason for initial non resectability : Other reason Units: Subjects			
Non resectable disease	14	29	43
PCI + Non resectable disease	9	24	33
No expert center	1	2	3
Patient's status + Non resectable disease	1	2	3
Fagotti score + Non resectable disease	0	2	2
Fagotti score + PCI + Non resectable disease	2	0	2
PCI	1	1	2
No identified reason	1	0	1
Progressive disease	0	1	1
Patient's status + PCI + Non resectable disease	1	0	1
Primary reason for end of treatment: Platinum Units: Subjects			
Completed as per protocol	27	53	80
Disease progression as per RECIST V1.1 criteria	1	4	5
Adverse event	1	1	2
Symptomatic deterioration	1	0	1
Death	0	1	1

Chip during IDS	0	1	1
Investigator decision	0	1	1
Primary reason for end of treatment: Bevacizumab Units: Subjects			
Completed as per protocol	9	20	29
Disease progression as per RECIST V1.1 criteria	14	22	36
Adverse event	4	10	14
Symptomatic deterioration	1	0	1
Breast cancer	1	0	1
Disease progression	0	1	1
Not applicable	0	4	4
Treatment not given	0	1	1
Patient died before adjuvant phase	0	1	1
Patient decision	0	1	1
NA	1	1	2
Primary reason for end of treatment: Pembrolizumab Units: Subjects			
Completed as per protocol	0	21	21
Disease progression as per RECIST V1.1 criteria	0	23	23
Adverse event	0	14	14
Death	0	1	1
Disease progression	0	1	1
Chip during IDS	0	1	1
NA	30	0	30
Interval debulking surgery Units: Subjects			
No	1	3	4
Yes	29	58	87
Interval debulking surgery : Type of approach Units: Subjects			
Laparotomy	24	49	73
Laparoscopy-Laparoscopic assisted	2	1	3
Coeloscopy	3	7	10
NA	1	4	5
Interval debulking surgery : Type of procedure Units: Subjects			
Interval debulking surgery after NACT	24	56	80
Restaging after previous surgery	2	0	2
2ry Debulking	3	2	5
NA	1	3	4
Reason for non-complete resectability during interval debulking surgery Units: Subjects			
Patient's status	1	1	2
Fagotti score of 7	0	1	1
Alteration of general state	1	0	1
Insufficiant response	1	0	1

No response	0	1	1
Stable disease	0	1	1
Stable disease or Insufficient response	0	1	1
Non resectable disease	7	13	20
NA	20	43	63
Localization of non resectable disease during interval debulking surgery Units: Subjects			
Mesenteric involvement	1	6	7
Massive omentum involvemen	1	4	5
Massive diaphragmatic dome	4	4	8
Hepatic hilum involvement	1	1	2
Diffuse digestive involvement	2	7	9
Massive ascites	0	1	1
Diffuse peritoneal carcinomatosis	7	8	15
Stage IV	2	3	5
Pleural involvement	1	1	2
Infracentimetric residuals	0	1	1
Stomach	0	1	1
NA	11	24	35
Weight Units: kilogram(s) median full range (min-max)	62.5 42.5 to 98	63 44 to 125	-
Height Units: centimetre median full range (min-max)	162 146 to 169	162 150 to 171	-
Systolic Blood Pressure Units: Millimetre of mercury median full range (min-max)	120.5 108 to 165	129 92 to 183	-
Diastolic Blood Pressure Units: Millimetre of mercury median full range (min-max)	76.50 52 to 88	78 55 to 103	-
CA125 Units: U/ml median full range (min-max)	542.00 18 to 3493	632.00 21 to 8911	-
PCI score Units: number median full range (min-max)	25 18 to 36	24 7 to 39	-
Number of chemotherapy cycles in Neoadjuvant phase: Carboplatin Units: Number median full range (min-max)	4 2 to 6	4 1 to 8	-
Number of chemotherapy cycles in Neoadjuvant phase: Paclitaxel Units: Number			

median full range (min-max)	4 1 to 6	4 1 to 8	-
Number of chemotherapy cycles in Neoadjuvant phase: Pembrolizumab Units: Number median full range (min-max)	0 0 to 0	4 1 to 8	-
Number of chemotherapy cycles in adjuvant phase: Carboplatin Units: number median full range (min-max)	3 0 to 6	3 0 to 5	-
Number of chemotherapy cycles in adjuvant phase: Paclitaxel Units: number median full range (min-max)	3 0 to 6	3 0 to 5	-
Number of chemotherapy cycles in adjuvant phase: Pembrolizumab Units: number median full range (min-max)	0 0 to 0	15 0 to 24	-
Interval debulking surgery : Time from randomization to surgery Units: month median full range (min-max)	3.25 2.60 to 7.42	3.19 2.37 to 7.33	-

Subject analysis sets

Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The analysis was performed on the ITT population (N=91).

Intention-to-treat (ITT) population is defined as all patients randomized in the trial, regardless of whether they actually received treatment. The population will be described according to randomization.

Reporting group values	ITT population		
Number of subjects	91		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	51		
From 65-84 years	40		
85 years and over	0		

Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female			
ECOG Units: Subjects			
00			
01			
02			
ECG Units: Subjects			
Normal	75		
Abnormal NCS	13		
NA	3		
Germline BRCA mutation Units: Subjects			
No			
Yes			
Somatic BRCA mutation Units: Subjects			
No			
Yes			
BRCA Units: Subjects			
No			
Yes			
NA			
Medical Review - Primary site Units: Subjects			
Ovary			
Peritoneal			
Medical Review - Adenocarcinoma type Units: Subjects			
Serous High Grade (a)			
Serous Low Grade (b)			
Clear cell			
Undifferentiated			
Medical Review - FIGO Units: Subjects			
II			
IIIC			
IV			
If stage IV, localization of the visceral disease Units: Subjects			
Pleura	5		
Liver	5		
Lungs	2		

Lymph node outside of the abdominal cavity	9		
Mediastin	1		
Pleural Effusion	1		
Unknown	1		
NA	67		
Immune or allergic disease			
Units: Subjects			
Allergic rhinitis			
Asthma			
Basedow disease			
Diabetes 2			
Hypothyroidism 2			
Other			
NA			
At least one sign and symptom of adverse events at baseline			
Units: Subjects			
No			
Yes			
List of adverse events at baseline			
Units: Subjects			
Anaemia			
Hypothyroidism			
Gastrointestinal disorders			
General disorders and administration site conditio			
Hepatobiliary disorders			
Urinary tract infection			
Investigations			
Metabolism and nutrition disorders			
Anxiety			
Respiratory, thoracic and mediastinal			
Vascular disorders			
Gamma-glutamyl transferase Increased			
Hypertension			
Abdominal pain			
Hydronephrosis			
NA			
Abnormal and Clinically Significant laboratory examination at inclusion: Hematology			
Units: Subjects			
Hemoglobin			
Lymphocytes			
Monocytes			
Neutrophils			
Platelets			
White blood cells			
NA			
Abnormal and Clinically Significant laboratory examination at inclusion:			

Biochemistery			
Units: Subjects			
Albumin			
Alkaline phosphatase			
ALT/SGPT			
AST/SGOT			
Creatinine			
Creatinine clearance			
LDH			
Total bilirubin			
NA			
Abnormal and Clinically Significant laboratory examination at inclusion: Hormonology			
Units: Subjects			
FREE T3	0		
FREE T4	0		
TSH	1		
NA	90		
Abnormal and Clinically Significant laboratory examination at inclusion: Urine Protein analysis			
Units: Subjects			
Negative			
Trace			
T+1			
T+2			
NA			
Initial surgery : Type of approach			
Units: Subjects			
Laparotomy	8		
Laparoscopy-Laparoscopic assisted	82		
Biopsy	1		
Initial surgery : Type of procedure			
Units: Subjects			
Primary Surgical Staging			
Diagnostic procedure-biopsies			
Initial surgery : Residual disease			
Units: Subjects			
Not applicable			
CC3: residue > 2.5 cm			
CC0 : No macroscopic			
Reason for initial non resectability : Patient's status			
Units: Subjects			
Poor performance status			
Denutrition			
Venous thrombosis			
NA			
Fagotti Score			
Units: Subjects			
08			
04			

NA			
Reason for initial non resecability : Other reason Units: Subjects			
Non resecable disease PCI + Non resecable disease No expert center Patient's status + Non resecable disease Fagotti score + Non resecable disease Fagotti score + PCI + Non resecable disease PCI No identified reason Progressive disease Patient's status + PCI + Non resecable disease			
Primary reason for end of treatment: Platinum Units: Subjects			
Completed as per protocol Disease progression as per RECIST V1.1 criteria Adverse event Symptomatic deterioration Death Chip during IDS Investigator decision			
Primary reason for end of treatment: Bevacizumab Units: Subjects			
Completed as per protocol Disease progression as per RECIST V1.1 criteria Adverse event Symptomatic deterioration Breast cancer Disease progression Not applicable Treatment not given Patient died before adjuvant phase Patient decision NA	29 36 14 1 1 1 4 1 1 1 1 2		
Primary reason for end of treatment: Pembrolizumab Units: Subjects			
Completed as per protocol Disease progression as per RECIST V1.1 criteria Adverse event Death Disease progression Chip during IDS NA	21 23 14 1 1 1 30		

Interval debulking surgery Units: Subjects			
No Yes			
Interval debulking surgery : Type of approach Units: Subjects			
Laparotomy Laparoscopy-Laparoscopic assisted Coeloscopy NA			
Interval debulking surgery : Type of procedure Units: Subjects			
Interval debulking surgery after NACT Restaging after previous surgery 2ry Debulking NA			
Reason for non-complete resectability during interval debulking surgery Units: Subjects			
Patient's status Fagotti score of 7 Alteration of general state Insufficient response No response Stable disease Stable disease or Insufficient response Non resectable disease NA			
Localization of non resectable disease during interval debulking surgery Units: Subjects			
Mesenteric involvement Massive omentum involvemen Massive diaphragmatic dome Hepatic hilum involvement Diffuse digestive involvement Massive ascites Diffuse peritoneal carcinomatosis Stage IV Pleural involvement Infracentimetric residuals Stomach NA			
Weight Units: kilogram(s) median full range (min-max)			
Height Units: centimetre			

<p>median</p> <p>full range (min-max)</p>			
<p>Systolic Blood Pressure</p> <p>Units: Millimetre of mercury</p> <p>median</p> <p>full range (min-max)</p>			
<p>Diastolic Blood Pressure</p> <p>Units: Millimetre of mercury</p> <p>median</p> <p>full range (min-max)</p>	<p>77</p> <p>52 to 103</p>		
<p>CA125</p> <p>Units: U/ml</p> <p>median</p> <p>full range (min-max)</p>	<p>562.60</p> <p>18 to 8911</p>		
<p>PCI score</p> <p>Units: number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Number of chemotherapy cycles in Neoadjuvant phase: Carboplatin</p> <p>Units: Number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Number of chemotherapy cycles in Neoadjuvant phase: Paclitaxel</p> <p>Units: Number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Number of chemotherapy cycles in Neoadjuvant phase: Pembrolizumab</p> <p>Units: Number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Number of chemotherapy cycles in adjuvant phase: Carboplatin</p> <p>Units: number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Number of chemotherapy cycles in adjuvant phase: Paclitaxel</p> <p>Units: number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Number of chemotherapy cycles in adjuvant phase: Pembrolizumab</p> <p>Units: number</p> <p>median</p> <p>full range (min-max)</p>			
<p>Interval debulking surgery : Time from randomization to surgery</p> <p>Units: month</p> <p>median</p> <p>full range (min-max)</p>	<p>3.22</p> <p>2.37 to 7.42</p>		

End points

End points reporting groups

Reporting group title	Arm A - Paclitaxel/Carboplatin
Reporting group description: -	
Reporting group title	Arm B - Paclitaxel/Carboplatin with Pembrolizumab
Reporting group description: -	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The analysis was performed on the ITT population (N=91).

Intention-to-treat (ITT) population is defined as all patients randomized in the trial, regardless of whether they actually received treatment. The population will be described according to randomization.

Primary: Rate of complete debulking

End point title	Rate of complete debulking
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End point description:

According to the hypothesis, 33 successes over 54 evaluable patients were expected in arm B treated with pembrolizumab (P0=50%, P1=70%). According to our results, the resection was complete (CC0) for 45 patients (73.8%) in arm B treated with pembrolizumab and thus were considered in success. In conclusion, treatment with neoadjuvant pembrolizumab and chemotherapy showed efficacy in this study.

End point type	Primary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carboplatin	Arm B - Paclitaxel/Carboplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Complete debulking (1)	21	45	66	
NA	9	16	25	

Statistical analyses

Statistical analysis title	Descriptive statistics
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Statistical analysis description:

No statistical test will be performed in this study.

Comparison groups	Arm A - Paclitaxel/Carboplatin v Arm B - Paclitaxel/Carboplatin with Pembrolizumab
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Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.05
Method	Descriptive analysis

Notes:

[1] - Descriptive statistics

Primary: CCI according to central review

End point title	CCI according to central review
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End point description:

End point type	Primary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
CC0 : No macroscopic	21	45	66	
CC1: <= 0.25 cm	0	2	2	
CC3: residue > 2.5 cm	8	11	19	
NA	1	3	4	

Statistical analyses

Statistical analysis title	Descriptive statistics
Comparison groups	Arm B - Paclitaxel/Carboplatin with Pembrolizumab v Arm A - Paclitaxel/Carboplatin
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	< 0.05
Method	Descriptive analysis

Notes:

[2] - Descriptive statistics

Primary: Rate of complete debulking – Sensitivity analysis

End point title	Rate of complete debulking – Sensitivity analysis
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End point description:

End point type	Primary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Complete debulking (2)	17	41	58	
NA	13	20	33	

Statistical analyses

Statistical analysis title	Descriptive statistics
Comparison groups	Arm B - Paclitaxel/Carboplatin with Pembrolizumab v Arm A - Paclitaxel/Carboplatin
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	< 0.05
Method	Descriptive analysis

Notes:

[3] - Descriptive statistics

Secondary: PCI score : Response at IDS compared to baseline PCI

End point title	PCI score : Response at IDS compared to baseline PCI
End point description:	
End point type	Secondary
End point timeframe:	
Overall period	

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
No	4	11	15	
Yes	23	44	67	
NA	3	6	9	

Statistical analyses

No statistical analyses for this end point

Secondary: PCI score (sugarbaker index)

End point title	PCI score (sugarbaker index)
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End point description:

Overall, 81.7% of patients had a response at Interval Debulking Surgery (IDS) compared to baseline as Peritoneal Cancer Index (PCI), in which the mean change in PCI score was -9.99 (9.00) for 80 patients. This decrease in PCI score estimated better prognosis after IDS.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: number				
arithmetic mean (standard deviation)				
PCI score at baseline	21.48 (± 7.87)	20.41 (± 9.45)	20.74 (± 8.95)	
PCI score before IDS	11.64 (± 8.25)	9.71 (± 9.17)	10.36 (± 8.87)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall rate response (ORR)

End point title	Overall rate response (ORR)
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End point description:

At the end of neoadjuvant period, 4 patients (5%) had a complete response, 58 patients (65%) had partial response, 25 patients (28%) were in stable disease, and 2 patients (2%) were in progression. In addition, two patients didn't have tumor assessment. They have started 2 and 1 cycles of treatment respectively and stopped it due to an adverse event.

Regarding overall response rate at the end of neo-adjuvant phase, 18 patients (62.1%) in arm A showed CR or PR response compared to 44 patients (73.3%) in arm B.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
ORR at the end of neo-adjuvant phase	18	44	62	
NA	12	17	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall rate response (ORR) : Tumor response observed

End point title	Overall rate response (ORR) : Tumor response observed
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End point description:

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Complete response	2	2	4	
Partial response	16	42	58	
Stable disease	11	14	25	
Progressive disease	0	2	2	
NA	1	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Best response to the global strategy assessed by RECIST

End point title	Best response to the global strategy assessed by RECIST
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End point description:

According to RECIST 1.1 criteria, 37 complete responses (61.7%) and 17 partial responses (28.3%) were observed in arm B compared to 14 CR (48.3%) and 10 PR (34.5%) responses in arm A.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Complete response	14	37	51	
Partial response	10	17	27	
Stable disease	5	6	11	
Progressive disease	1	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Best response before IDS assessed by CA125

End point title	Best response before IDS assessed by CA125
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End point description:

According to CA-125 evaluation, 31 normalized responses (50.8%) and 22 non-normalized responses (36.1%) were observed in arm B before IDS compared to 15 normalized responses (50.0%) and 10 non-normalized responses (33.3%) responses in arm A.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Response and normalized	15	31	46	
Response without normalized	10	22	32	
Normalized	1	1	2	
No response or PD	2	2	4	
Normal baseline CA-125	1	4	5	

NE (no baseline and/or post-baseline sample)	1	1	2	
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Statistical analyses

No statistical analyses for this end point

Secondary: Best response to the global strategy assessed by CA125

End point title	Best response to the global strategy assessed by CA125
End point description: Regarding best response to global strategy, 46 normalized responses (75.4%) and 7 non-normalized responses (11.5%) were observed in arm B compared to 22 normalized responses (73.3%) and 3 non-normalized responses (10.0%) responses in arm A.	
End point type	Secondary
End point timeframe: Overall period	

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Response and normalized	22	46	68	
Response without normalized	3	7	10	
Normalized	1	1	2	
No response or PD	2	2	4	
Normal baseline CA-125	1	4	5	
NE (no baseline and/or post-baseline sample)	1	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) according to RECIST or symptomatic deterioration

End point title	Progression-free survival (PFS) according to RECIST or symptomatic deterioration
End point description: Disease progression according to RECIST or death occurred in 20 patients (66.7%) in arm A compared to 34 patients (55.7%) in arm B treated with pembrolizumab.	
End point type	Secondary

End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
No	11	29	40	
Yes	19	32	51	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) according to RECIST or symptomatic deterioration or death

End point title	Progression-free survival (PFS) according to RECIST or symptomatic deterioration or death
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End point description:

As shown in Figure 6, median PFS was 20.8 months (95%CI [15.0-24.5]) in arm A compared to 19.3 months [17.0; 23.4] in arm B treated with pembrolizumab.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
No	10	27	37	
Yes	20	34	54	

Attachments (see zip file)	Figure 6. Progression free survival (PFS)/Figure 6. Progression
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Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS): Death

End point title	Overall survival (OS): Death
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End point description:

The follow-up of alive patients is at median of 22 months (min: 6.8, max: 32.5).

At the time of the analysis, 19 deaths were notified, 6 (20%) in arm A and 13 (21.3%) in arm B treated with pembrolizumab.

Median were not estimable both arms: arm A (95% CI 22.9) and arm B (95% CI 25.2) as illustrated in Figure 7.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
No	24	48	72	
Yes	6	13	19	

Attachments (see zip file)	Figure 7. Overall survival (OS)/Figure 7. Overall survival (OS).
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Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS): Cause of death

End point title	Overall survival (OS): Cause of death
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End point description:

Moreover, 14 patients died of progression, 1 of acute leukemia, 1 of neurological complications, 1 of peritonitis after debulking surgery and 1 without reason mentioned.

End point type	Secondary
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End point timeframe:

Overall period

End point values	Arm A - Paclitaxel/Carb oplatin	Arm B - Paclitaxel/Carb oplatin with Pembrolizumab	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	61	91	
Units: Patients				
Disease progression	4	10	14	
Discovery of acute leukemia	1	0	1	
Neurological complications	0	1	1	
Peritonitis after debulking	0	1	1	
Unknown	1	1	2	
NA	24	48	72	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall period

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.03
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Reporting groups

Reporting group title	Arm A - Paclitaxel/Carboplatin
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Reporting group description: -

Reporting group title	Arm B - Paclitaxel/Carboplatin + Pembrolizumab
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Reporting group description: -

Serious adverse events	Arm A - Paclitaxel/Carboplatin	Arm B - Paclitaxel/Carboplatin + Pembrolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 30 (36.67%)	27 / 61 (44.26%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE LEUKAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
PANCREATIC CARCINOMA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENOUS THROMBOSIS			

subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
EVENTRATION REPAIR			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA CLOSURE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMPAIRED HEALING			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
DYSпноEA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			

subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORGANISING PNEUMONIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONGESTIVE CARDIOMYOPATHY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
HEADACHE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 30 (6.67%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHOCELE			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE BONE MARROW APLASIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOCYTOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
COLITIS			
subjects affected / exposed	0 / 30 (0.00%)	3 / 61 (4.92%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	3 / 61 (4.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL FISTULA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			

subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATOCELLULAR INJURY			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLANGITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
DERMATITIS BULLOUS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYTHEMA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROTEINURIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
HYPOTHYROIDISM			

subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THYROIDITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
INFECTED LYMPHOCELE			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONITIS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
SEPSIS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERINEPHRIC ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

PYELONEPHRITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A - Paclitaxel/Carboplatin	Arm B - Paclitaxel/Carboplatin + Pembrolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)	61 / 61 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE LEUKAEMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
PANCREATIC CARCINOMA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	

SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	6 / 30 (20.00%)	16 / 61 (26.23%)	
occurrences (all)	6	16	
HOT FLUSH			
subjects affected / exposed	5 / 30 (16.67%)	3 / 61 (4.92%)	
occurrences (all)	5	3	
VENOUS THROMBOSIS			
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)	
occurrences (all)	1	2	
LYMPHOEDEMA			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
PHLEBITIS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
ANGIOPATHY			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
HYPOTENSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PELVIC VENOUS THROMBOSIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
VENOUS THROMBOSIS LIMB			

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 61 (0.00%) 0	
Surgical and medical procedures TOOTH EXTRACTION subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 61 (0.00%) 0	
EVENTRATION REPAIR subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 61 (1.64%) 1	
STOMA CLOSURE subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 61 (0.00%) 0	
TRANSFUSION subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 61 (1.64%) 1	
General disorders and administration site conditions ASTHENIA subjects affected / exposed occurrences (all)	19 / 30 (63.33%) 19	42 / 61 (68.85%) 42	
MUCOSAL INFLAMMATION subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	9 / 61 (14.75%) 9	
FATIGUE subjects affected / exposed occurrences (all)	5 / 30 (16.67%) 5	4 / 61 (6.56%) 4	
OEDEMA PERIPHERAL subjects affected / exposed occurrences (all)	4 / 30 (13.33%) 4	3 / 61 (4.92%) 3	
IMPAIRED HEALING subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	3 / 61 (4.92%) 3	
PYREXIA subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	2 / 61 (3.28%) 2	
GENERAL PHYSICAL HEALTH DETERIORATION			

subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
ILL-DEFINED DISORDER		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
PAIN		
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)
occurrences (all)	2	0
XEROSIS		
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)
occurrences (all)	2	0
ADVERSE DRUG REACTION		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
CATHETER SITE INFLAMMATION		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
CATHETER SITE OEDEMA		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
CATHETER SITE PAIN		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
CATHETER SITE RASH		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
CHEST PAIN		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
DYSPLASIA		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
FEELING COLD		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
INFLAMMATION		

subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
MEDICAL DEVICE PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
NODULE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
SENSE OF OPPRESSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 30 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	4	
HYPERSENSITIVITY			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
ANAPHYLACTIC REACTION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
SARCOIDOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
VULVOVAGINAL DRYNESS			
subjects affected / exposed	4 / 30 (13.33%)	1 / 61 (1.64%)	
occurrences (all)	4	1	
METRORRHAGIA			
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)	
occurrences (all)	1	2	
VAGINAL DISCHARGE			

subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
CYSTOCELE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
OEDEMA GENITAL			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PELVIC DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PELVIC PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PRURITUS GENITAL			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
VAGINAL HAEMORRHAGE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
EPISTAXIS			
subjects affected / exposed	6 / 30 (20.00%)	15 / 61 (24.59%)	
occurrences (all)	6	15	
COUGH			
subjects affected / exposed	1 / 30 (3.33%)	8 / 61 (13.11%)	
occurrences (all)	1	8	
DYSPNOEA			
subjects affected / exposed	3 / 30 (10.00%)	14 / 61 (22.95%)	
occurrences (all)	3	14	
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 30 (6.67%)	5 / 61 (8.20%)	
occurrences (all)	2	5	
RHINORRHOEA			

subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)	
occurrences (all)	1	2	
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
DYSпноEA EXERTIONAL			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
HAEMOPTYSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
NASAL DRYNESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
ORGANISING PNEUMONIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PLEURAL DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PNEUMONITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
RESPIRATORY DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	2 / 30 (6.67%)	7 / 61 (11.48%)	
occurrences (all)	2	7	

INSOMNIA			
subjects affected / exposed	4 / 30 (13.33%)	4 / 61 (6.56%)	
occurrences (all)	4	4	
DEPRESSION			
subjects affected / exposed	0 / 30 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	4	
MAJOR DEPRESSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
SLEEP DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	5 / 30 (16.67%)	0 / 61 (0.00%)	
occurrences (all)	5	0	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
BLOOD THYROID STIMULATING HORMONE INCREASED			

subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
THYROID FUNCTION TEST ABNORMAL			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
WEIGHT INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
PROCEDURAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
BURN OESOPHAGEAL			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
FALL			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
TOOTH FRACTURE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
CONGESTIVE CARDIOMYOPATHY			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
TACHYCARDIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
NEUROPATHY PERIPHERAL			
subjects affected / exposed	12 / 30 (40.00%)	27 / 61 (44.26%)	
occurrences (all)	12	27	
HEADACHE			
subjects affected / exposed	7 / 30 (23.33%)	13 / 61 (21.31%)	
occurrences (all)	7	13	
PARAESTHESIA			
subjects affected / exposed	3 / 30 (10.00%)	11 / 61 (18.03%)	
occurrences (all)	3	11	
DYSGEUSIA			
subjects affected / exposed	4 / 30 (13.33%)	7 / 61 (11.48%)	
occurrences (all)	4	7	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 30 (3.33%)	5 / 61 (8.20%)	
occurrences (all)	1	5	
NEUROTOXICITY			
subjects affected / exposed	1 / 30 (3.33%)	3 / 61 (4.92%)	
occurrences (all)	1	3	
SCIATICA			

subjects affected / exposed	0 / 30 (0.00%)	3 / 61 (4.92%)	
occurrences (all)	0	3	
DIZZINESS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
NEURALGIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
ANOSMIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
DYSAESTHESIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
EPILEPSY			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
HYPOAESTHESIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
MONOPLEGIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	17 / 30 (56.67%)	33 / 61 (54.10%)	
occurrences (all)	17	33	
NEUTROPENIA			
subjects affected / exposed	12 / 30 (40.00%)	24 / 61 (39.34%)	
occurrences (all)	12	24	
THROMBOCYTOPENIA			
subjects affected / exposed	8 / 30 (26.67%)	18 / 61 (29.51%)	
occurrences (all)	8	18	
LEUKOPENIA			
subjects affected / exposed	6 / 30 (20.00%)	6 / 61 (9.84%)	
occurrences (all)	6	6	
LYMPHOPENIA			
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)	
occurrences (all)	1	2	
EOSINOPHILIA			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
LYMPHOCELE			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
FEBRILE BONE MARROW APLASIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
LEUKOCYTOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
DEAFNESS BILATERAL			

subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
VERTIGO			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Eye disorders			
DRY EYE			
subjects affected / exposed	2 / 30 (6.67%)	2 / 61 (3.28%)	
occurrences (all)	2	2	
EYELID OEDEMA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
LACRIMATION INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
VISUAL ACUITY REDUCED			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
XEROPHTHALMIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	12 / 30 (40.00%)	33 / 61 (54.10%)	
occurrences (all)	12	33	
ABDOMINAL PAIN			
subjects affected / exposed	12 / 30 (40.00%)	25 / 61 (40.98%)	
occurrences (all)	12	25	
CONSTIPATION			
subjects affected / exposed	11 / 30 (36.67%)	25 / 61 (40.98%)	
occurrences (all)	11	25	
DIARRHOEA			
subjects affected / exposed	11 / 30 (36.67%)	23 / 61 (37.70%)	
occurrences (all)	11	23	
VOMITING			

subjects affected / exposed	6 / 30 (20.00%)	12 / 61 (19.67%)
occurrences (all)	6	12
ABDOMINAL PAIN UPPER		
subjects affected / exposed	6 / 30 (20.00%)	10 / 61 (16.39%)
occurrences (all)	6	10
GINGIVAL BLEEDING		
subjects affected / exposed	3 / 30 (10.00%)	6 / 61 (9.84%)
occurrences (all)	3	6
TOOTHACHE		
subjects affected / exposed	2 / 30 (6.67%)	5 / 61 (8.20%)
occurrences (all)	2	5
DYSPEPSIA		
subjects affected / exposed	1 / 30 (3.33%)	5 / 61 (8.20%)
occurrences (all)	1	5
GASTROOESOPHAGEAL REFLUX DISEASE		
subjects affected / exposed	2 / 30 (6.67%)	3 / 61 (4.92%)
occurrences (all)	2	3
INTESTINAL OBSTRUCTION		
subjects affected / exposed	1 / 30 (3.33%)	4 / 61 (6.56%)
occurrences (all)	1	4
COLITIS		
subjects affected / exposed	0 / 30 (0.00%)	4 / 61 (6.56%)
occurrences (all)	0	4
HAEMORRHOIDS		
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)
occurrences (all)	1	2
ABDOMINAL DISTENSION		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
ASCITES		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
GASTRITIS		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2

GASTROINTESTINAL DISORDER			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
STOMATITIS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
ABDOMINAL HERNIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
ABDOMINAL RIGIDITY			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
ANAL FISTULA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
APHTHOUS ULCER			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
APTALISM			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
DENTAL CYST			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
DYSPHAGIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	

EPIGASTRIC DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
FAECALOMA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
GASTROINTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
IMPAIRED GASTRIC EMPTYING			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
INTRA-ABDOMINAL FLUID COLLECTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
MESENTERIC ARTERY THROMBOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
NONINFECTIVE GINGIVITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
OESOPHAGEAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
OESOPHAGITIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
PERIODONTAL DISEASE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
RECTAL DISCHARGE			

subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
RECTAL OBSTRUCTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
SENSITIVITY OF TEETH			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
SUBILEUS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
HEPATOCELLULAR INJURY			
subjects affected / exposed	1 / 30 (3.33%)	5 / 61 (8.20%)	
occurrences (all)	1	5	
CHOLESTASIS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
AUTOIMMUNE HEPATITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
CHOLANGITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	10 / 30 (33.33%)	18 / 61 (29.51%)	
occurrences (all)	10	18	
RASH			
subjects affected / exposed	3 / 30 (10.00%)	13 / 61 (21.31%)	
occurrences (all)	3	13	
PRURITUS			

subjects affected / exposed	3 / 30 (10.00%)	9 / 61 (14.75%)
occurrences (all)	3	9
ERYTHEMA		
subjects affected / exposed	0 / 30 (0.00%)	6 / 61 (9.84%)
occurrences (all)	0	6
DRY SKIN		
subjects affected / exposed	0 / 30 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	3
URTICARIA		
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)
occurrences (all)	1	2
HYPERHIDROSIS		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
NAIL DISORDER		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
RASH PAPULAR		
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)
occurrences (all)	2	0
RASH PRURITIC		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
SKIN TOXICITY		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
XERODERMA		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
DERMATITIS ACNEIFORM		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
DERMATITIS BULLOUS		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
ECZEMA		

subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
HYPERKERATOSIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
NIGHT SWEATS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PRURIGO			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
PRURITUS GENERALISED			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
PURPURA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
RASH MACULAR			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
SCAR PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
SKIN REACTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Renal and urinary disorders			
PROTEINURIA			
subjects affected / exposed	3 / 30 (10.00%)	3 / 61 (4.92%)	
occurrences (all)	3	3	
RENAL FAILURE			
subjects affected / exposed	1 / 30 (3.33%)	3 / 61 (4.92%)	
occurrences (all)	1	3	
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)	
occurrences (all)	1	2	

DYSURIA			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
URINARY INCONTINENCE			
subjects affected / exposed	2 / 30 (6.67%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
HAEMATURIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
RENAL COLIC			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	2 / 30 (6.67%)	17 / 61 (27.87%)	
occurrences (all)	2	17	
HYPERTHYROIDISM			
subjects affected / exposed	0 / 30 (0.00%)	9 / 61 (14.75%)	
occurrences (all)	0	9	
THYROID DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
BASEDOW'S DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
THYROIDITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	14 / 30 (46.67%)	31 / 61 (50.82%)	
occurrences (all)	14	31	
MYALGIA			

subjects affected / exposed	2 / 30 (6.67%)	11 / 61 (18.03%)
occurrences (all)	2	11
PAIN IN EXTREMITY		
subjects affected / exposed	5 / 30 (16.67%)	8 / 61 (13.11%)
occurrences (all)	5	8
BACK PAIN		
subjects affected / exposed	4 / 30 (13.33%)	7 / 61 (11.48%)
occurrences (all)	4	7
MUSCULOSKELETAL PAIN		
subjects affected / exposed	3 / 30 (10.00%)	6 / 61 (9.84%)
occurrences (all)	3	6
MUSCLE SPASMS		
subjects affected / exposed	2 / 30 (6.67%)	3 / 61 (4.92%)
occurrences (all)	2	3
NECK PAIN		
subjects affected / exposed	0 / 30 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	3
PAIN IN JAW		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
TENDONITIS		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
ARTHRITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
BONE PAIN		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
FLANK PAIN		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
GROIN PAIN		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
INTERVERTEBRAL DISC		

PROTRUSION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
JOINT STIFFNESS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
OSTEOARTHRITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
OSTEONECROSIS OF JAW			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
RHEUMATIC DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
SJOJREN'S SYNDROME			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
TENDON PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 30 (13.33%)	13 / 61 (21.31%)	
occurrences (all)	4	13	
NASOPHARYNGITIS			
subjects affected / exposed	3 / 30 (10.00%)	4 / 61 (6.56%)	
occurrences (all)	3	4	
CYSTITIS			

subjects affected / exposed	2 / 30 (6.67%)	3 / 61 (4.92%)
occurrences (all)	2	3
GASTROENTERITIS		
subjects affected / exposed	1 / 30 (3.33%)	3 / 61 (4.92%)
occurrences (all)	1	3
VULVOVAGINAL MYCOTIC INFECTION		
subjects affected / exposed	0 / 30 (0.00%)	4 / 61 (6.56%)
occurrences (all)	0	4
BRONCHITIS		
subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)
occurrences (all)	1	2
BARTHOLINITIS		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
FUNGAL INFECTION		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
GINGIVITIS		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
INFECTED LYMPHOCELE		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
ORAL FUNGAL INFECTION		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
PERITONITIS		
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	2
PHARYNGITIS		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
PYELONEPHRITIS		
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1

SEPSIS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
TOOTH ABSCESS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)	
occurrences (all)	1	1	
VIRAL INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	2 / 61 (3.28%)	
occurrences (all)	0	2	
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
BRAIN EMPYEMA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
occurrences (all)	0	1	
ENTEROBIASIS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
EPSTEIN-BARR VIRUS INFECTION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
ERYSIPELAS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	
HEPATITIS B REACTIVATION			
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
occurrences (all)	1	0	

HERPES VIRUS INFECTION		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
INFECTED DERMAL CYST		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
INFECTION		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
INFLUENZA		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
LARYNGITIS		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
LYMPHANGITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
PARONYCHIA		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
PERINEPHRIC ABSCESS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
PERIODONTITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
PNEUMONIA		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
RHINITIS		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
SEPTIC SHOCK		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1

SINUSITIS	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
SKIN INFECTION	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
SUBDIAPHRAGMATIC ABSCESS	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
TOOTH INFECTION	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
VIRAL RHINITIS	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
VIRAL UPPER RESPIRATORY TRACT INFECTION	subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)	
	occurrences (all)	1	0	
VULVITIS	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
WOUND INFECTION	subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)	
	occurrences (all)	0	1	
Metabolism and nutrition disorders	DECREASED APPETITE			
	subjects affected / exposed	4 / 30 (13.33%)	9 / 61 (14.75%)	
	occurrences (all)	4	9	
HYPOKALAEMIA	subjects affected / exposed	0 / 30 (0.00%)	5 / 61 (8.20%)	
	occurrences (all)	0	5	
CELL DEATH	subjects affected / exposed	1 / 30 (3.33%)	2 / 61 (3.28%)	
	occurrences (all)	1	2	
HYPERKALAEMIA				

subjects affected / exposed	1 / 30 (3.33%)	1 / 61 (1.64%)
occurrences (all)	1	1
DEHYDRATION		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
ELECTROLYTE IMBALANCE		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
HYPERCREATININAEMIA		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
HYPERTRIGLYCERIDAEMIA		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
HYPOALBUMINAEMIA		
subjects affected / exposed	1 / 30 (3.33%)	0 / 61 (0.00%)
occurrences (all)	1	0
IRON DEFICIENCY		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
MALNUTRITION		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1
VITAMIN D DEFICIENCY		
subjects affected / exposed	0 / 30 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2019	Amendment 1- Version 2.0 Clarification of inclusion criteria, amended management of pembrolizumab adverse event
03 June 2020	Amendment 2 – Version 3.0 Modification of the primary endpoint, addition of two secondary endpoints and one exploratory criterion

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The main limitation of the trial is the small sample size and the non-comparative statistical design, which does not allow the estimation of pembrolizumab contribution (including its impact on survival) to the treatment regime.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39013870>