Clinical trial results:
A Randomized, Multicenter, Double-blind, Placebo-controlled Phase 3 Study of Nivolumab
Versus Placebo in Combination With Neoadjuvant Chemotherapy and Adjuvant Endocrine
Therapy in Patients With High-risk, Estrogen Receptor-Positive (ER+), Human Epidermal
Growth Factor Receptor 2-Negative (HER2-) Primary Breast Cancer (CheckMate 7FL: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 7FL)

Summary

EudraCT number	2019-002469-37
Trial protocol	AT DE CZ FR PL NL BE DK FI IE ES PT GB IT RO
Global end of trial date	27 December 2023

Results information

Result version number	v1 (current)
This version publication date	01 January 2025
First version publication date	01 January 2025

Trial information

Trial identification

Sponsor protocol code	CA209-7FL

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	20 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the efficacy and safety of nivolumab or nivolumab placebo combined with standard neoadjuvant anthracycline-taxane-based chemotherapy, followed by nivolumab combined with endocrine therapy (ET) or ET alone as adjuvant treatment, in participants with high-risk, estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) primary breast cancer (BC).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2019
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	United States: 36
Country: Number of subjects enrolled	Argentina: 46
Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Brazil: 42
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Chile: 29
Country: Number of subjects enrolled	China: 28
Country: Number of subjects enrolled	Colombia: 35
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Ireland: 3

Country: Number of subjects enrolled	Italy: 28
Country: Number of subjects enrolled	Mexico: 65
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Romania: 25
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	Singapore: 6
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Türkiye: 12
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	521
EEA total number of subjects	166

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)	450
From 65 to 84 years	71
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

2 Participants planned for Arm B treatment received Arm A treatment.

Period 1

Period 1 title	Pre-treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab 360 mg Q3W + AC Q3W or Nivolumab 240 mg Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Nivolumab 480 mg Q4W + Endocrine Therapy (ET)

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

Dosage and administration details:

80 mg/m^2 weekly

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

360 mg Q3W

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg Q2W

Investigational medicinal product name	Endocrine Therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:	
May include tamoxifen, letrozole, anastrozole, or exemestane, to be administered per the respective package inserts	
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
60 mg/m^2 Q2W or Q3W determined by the Investigator	
Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
90 mg/m^2 Q2W or Q3W determined by the Investigator	
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
600 mg/m^2 Q2W or Q3W determined by the Investigator	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
480 mg Q4W	
Arm title	Arm B
Arm description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab Placebo Q3W + AC Q3W or Nivolumab Placebo Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Endocrine Therapy (ET)	
Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	PTX
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
80 mg/m^2 weekly	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Q3W	

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Q2W

Investigational medicinal product name	Endocrine Therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

May include tamoxifen, letrozole, anastrozole, or exemestane, to be administered per the respective package inserts

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

90 mg/m^2 Q2W or Q3W determined by the Investigator

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg/m^2 Q2W or Q3W determined by the Investigator

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

60 mg/m^2 Q2W or Q3W determined by the Investigator

Number of subjects in period 1	Arm A	Arm B
Started	263	258
Completed	260	257
Not completed	3	1
Participant withdrew consent	2	-
Participant no longer meets study criteria	1	1

Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab 360 mg Q3W + AC Q3W or Nivolumab 240 mg Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Nivolumab 480 mg Q4W + Endocrine Therapy (ET)

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

Dosage and administration details:

80 mg/m^2 weekly

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

60 mg/m^2 Q2W or Q3W determined by the Investigator

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

90 mg/m^2 Q2W or Q3W determined by the Investigator

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg/m^2 Q2W or Q3W determined by the Investigator

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use
Dosage and administration details: 480 mg Q4W	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 360 mg Q3W	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 240 mg Q2W	
Investigational medicinal product name	Endocrine Therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: May include tamoxifen, letrozole, anastrozole, or exemestane, to be administered per the respective package inserts	
Arm title	Arm B
Arm description: Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab Placebo Q3W + AC Q3W or Nivolumab Placebo Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Endocrine Therapy (ET)	
Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	PTX
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 80 mg/m^2 weekly	
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 60 mg/m^2 Q2W or Q3W determined by the Investigator	
Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details: 90 mg/m^2 Q2W or Q3W determined by the Investigator	
Investigational medicinal product name	Endocrine Therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: May include tamoxifen, letrozole, anastrozole, or exemestane, to be administered per the respective package inserts	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: Q3W	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: Q2W	
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 600 mg/m^2 Q2W or Q3W determined by the Investigator	

Number of subjects in period 2	Arm A	Arm B
Started	260	257
Received Arm A Treatment	0 [1]	2 [2]
Completed	167	174
Not completed	93	83
Adverse event, serious fatal	3	-
Adverse Event unrelated to Study drug	1	-
Participant no longer meets study criteria	2	2
Other reasons	17	23
Administrative reasons by sponsor	2	3
Disease Progression	4	7
Consent withdrawn by subject	8	8
Adverse event, non-fatal	23	7

Participant request to discontinue Study treatment	15	14
Study drug toxicity	12	5
Not reported	4	8
Disease Recurrence	-	2
Lack of efficacy	2	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Represents the subjects that received arm A treatment

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Represents the subjects that received arm A treatment

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab 360 mg Q3W + AC Q3W or Nivolumab 240 mg Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Nivolumab 480 mg Q4W + Endocrine Therapy (ET)	
Reporting group title	Arm B
Reporting group description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab Placebo Q3W + AC Q3W or Nivolumab Placebo Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Endocrine Therapy (ET)	

Reporting group values	Arm A	Arm B	Total
Number of subjects	263	258	521
Age categorical Units:			
Age Continuous Units: years			
arithmetic mean	49.9	50.9	
standard deviation	± 12.0	± 11.8	-
Sex: Female, Male Units: Participants			
Female	262	257	519
Male	1	1	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	18	17	35
Asian	24	18	42
Native Hawaiian or Other Pacific Islander	2	3	5
Black or African American	6	8	14
White	202	193	395
More than one race	0	0	0
Unknown or Not Reported	11	19	30
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	74	80	154
Not Hispanic or Latino	102	121	223
Unknown or Not Reported	87	57	144

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab 360 mg Q3W + AC Q3W or Nivolumab 240 mg Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Nivolumab 480 mg Q4W + Endocrine Therapy (ET)	

Reporting group title	Arm B
Reporting group description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab Placebo Q3W + AC Q3W or Nivolumab Placebo Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Endocrine Therapy (ET)	

Reporting group title	Arm A
Reporting group description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab 360 mg Q3W + AC Q3W or Nivolumab 240 mg Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Nivolumab 480 mg Q4W + Endocrine Therapy (ET)	

Reporting group title	Arm B
Reporting group description:	
Neoadjuvant (Pre-surgery) Phase 8 cycles maximum: Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW Followed by: Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W or Q3W): Nivolumab Placebo Q3W + AC Q3W or Nivolumab Placebo Q2W + AC Q2W Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum: Adjuvant Cycles 1-7 (1 cycle = Q4W): Endocrine Therapy (ET)	

Primary: Pathological Complete Response (pCR) Rate

End point title	Pathological Complete Response (pCR) Rate
End point description:	
pCR rate is defined as the percentage of participants who achieved pCR. pCR is defined as no invasive residual disease in breast and lymph nodes performed by a local pathologist. Criteria for evaluation of pCR includes the following: pCR in breast, axillary lymph nodes and non-axillary sentinel node; no histologic evidence of invasive tumor cells; and pCR in the breast.	
End point type	Primary
End point timeframe:	
Up to approximately 37 months	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	253		
Units: Percentage of participants				
number (confidence interval 95%)	24.5 (19.4 to 30.2)	13.8 (9.8 to 18.7)		

Statistical analyses

Statistical analysis title	Adjusted Difference of pCR Rates
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted Difference of pCR Rates
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	16.9

Statistical analysis title	Odds Ratio (OR)
Statistical analysis description:	
Arm A over Arm B	
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0021
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	3.27

Secondary: Pathological Complete Response (pCR) Rate (PD-L1 >=1%)

End point title	Pathological Complete Response (pCR) Rate (PD-L1 >=1%)

End point description:

pCR rate is defined as the percentage of participants who achieved pCR. pCR is defined as no invasive residual disease in breast and lymph nodes performed by a local pathologist. Criteria for evaluation of pCR includes the following: pCR in breast, axillary lymph nodes and non-axillary sentinel node; no histologic evidence of invasive tumor cells; and pCR in the breast.

End point type	Secondary

End point timeframe:
Up to approximately 37 months

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	84		
Units: Percentage of participants				
number (confidence interval 95%)	44.3 (33.7 to 55.3)	20.2 (12.3 to 30.4)		

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Statistical analysis description: Arm A over Arm B	
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Odds ratio (OR)
Point estimate	3.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.58
upper limit	6.11

Statistical analysis title	Adjusted Difference of pCR Rates
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted Difference of pCR Rates
Point estimate	24.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.7
upper limit	37.5

Secondary: Number of Participants with Residual Cancer Burden (RCB)

End point title	Number of Participants with Residual Cancer Burden (RCB)

End point description:

RCB is estimated from routine pathologic sections of the primary breast tumor site and the regional lymph nodes after the completion of neoadjuvant therapy. RCB is categorized into the following 4 classes: RCB-0: no residual disease; RCB-1: minimal residual disease; RCB-II: moderate residual disease; RCB-III: and extensive residual disease.

End point type	Secondary

End point timeframe:

Up to approximately 37 months

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	253		
Units: Participants				
RCB-0	62	34		
RCB-I	17	20		
RCB-II	90	106		
RCB-III	57	73		
Not Reported	31	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Residual Cancer Burden (RCB) PD-L1 >=1%

End point title	Number of Participants with Residual Cancer Burden (RCB) PD-L1 >=1%

End point description:

RCB is estimated from routine pathologic sections of the primary breast tumor site and the regional lymph nodes after the completion of neoadjuvant therapy. RCB is categorized into the following 4 classes: RCB-0: no residual disease; RCB-1: minimal residual disease; RCB-II: moderate residual disease; RCB-III: and extensive residual disease.

End point type	Secondary

End point timeframe:

Up to approximately 37 months

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	84		
Units: Participants				
RCB-0	38	16		
RCB-I	10	6		
RCB-II	25	36		
RCB-III	9	20		
Not Reported	6	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

Number of participants with any grade adverse events (AEs). An AE is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation participant administered study treatment that does not necessarily have a causal relation with this treatment. Toxicities will be graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose of neoadjuvant or adjuvant study therapy (Up to approximately 19 months)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	255		
Units: participants				
Adverse Events (AEs)	259	252		
Drug-Related AEs	254	236		
AEs leading to discontinuation	41	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serious Adverse Events (SAEs)

End point title	Number of Participants with Serious Adverse Events (SAEs)

End point description:

Number of participants with any grade serious adverse events (SAE). SAE is defined as any untoward medical occurrence that, at any dose: Results in death; is life threatening; requires inpatient hospitalization; results in persistent or significant disability; is a congenital anomaly/birth defect. Toxicities will be graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose of neoadjuvant or adjuvant study therapy (Up to approximately 19 months)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	255		
Units: participants	80	45		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Died

End point title	Number of Participants Who Died

End point description:

Number of participants who died due to any cause.

End point type	Secondary

End point timeframe:

Up to approximately 41 months

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	262	255		
Units: participants	15	8		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for all-cause mortality from their first dose to their study completion (up to approximately 41 months). SAEs and Other AEs were assessed from first dose up to 100 days post last dose (Up to approximately 21 months).

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants based on the treatment received. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Arm A: Nivo + Chemo (PTX QW + AC Q3W) / Nivo + ET

Reporting group description:

Neoadjuvant (Pre-surgery) Phase 8 cycles maximum:

Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW

Followed by:

Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q3W):

Nivolumab 360 mg Q3W + AC Q3W

Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum:

Adjuvant Cycles 1-7 (1 cycle = Q4W):

Nivolumab 480 mg Q4W + Endocrine Therapy (ET)

Reporting group title	Arm B: Nivo Placebo + Chemo (PTX QW + AC Q2W) / ET

Reporting group description:

Neoadjuvant (Pre-surgery) Phase 8 cycles maximum:

Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW

Followed by:

Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W):

Nivolumab Placebo Q2W + AC Q2W

Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum:

Adjuvant Cycles 1-7 (1 cycle = Q4W):

Endocrine Therapy (ET)

Reporting group title	Arm B: Nivo Placebo + Chemo (PTX QW + AC Q3W) / ET

Reporting group description:

Neoadjuvant (Pre-surgery) Phase 8 cycles maximum:

Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab Placebo Q3W + PTX QW

Followed by:

Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q3W):

Nivolumab Placebo Q3W + AC Q3W

Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum:

Adjuvant Cycles 1-7 (1 cycle = Q4W):

Endocrine Therapy (ET)

Reporting group title	Arm A: Nivo + Chemo (PTX QW + AC Q2W) / Nivo + ET

Reporting group description:

Neoadjuvant (Pre-surgery) Phase 8 cycles maximum:

Paclitaxel (PTX) Cycles 1-4 (1 cycle = Q3W): Nivolumab 360 mg Q3W + PTX QW

Followed by:

Anthracycline-Cyclophosphamide (AC) Cycles 1-4 (1 cycle = Q2W):

Nivolumab 240 mg Q2W + AC Q2W

Surgery and Adjuvant (Post-surgery) Phase 7 cycles maximum:

Adjuvant Cycles 1-7 (1 cycle = Q4W):

Nivolumab 480 mg Q4W + Endocrine Therapy (ET)

Serious adverse events	Arm A: Nivo + Chemo (PTX QW + AC Q3W) / Nivo + ET	Arm B: Nivo Placebo + Chemo (PTX QW + AC Q2W) / ET	Arm B: Nivo Placebo + Chemo (PTX QW + AC Q3W) / ET
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 127 (29.92%)	26 / 132 (19.70%)	20 / 123 (16.26%)
number of deaths (all causes)	8	4	4
number of deaths resulting from adverse events	6	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	2 / 127 (1.57%)	1 / 132 (0.76%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cervix carcinoma			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Vascular disorders			

Arterial thrombosis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
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 / 127 (0.79%)	1 / 132 (0.76%)	0 / 123 (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
Embolism			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Pyrexia			

subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Malaise			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Immune-mediated lung disease			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 127 (1.57%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Interstitial lung disease			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Product issues			
Device occlusion			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
White blood cell count decreased			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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

Inflammatory marker increased			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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 creatinine increased			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniofacial fracture			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical procedure repeated			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Wound dehiscence			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Left ventricular failure			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Myocarditis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 127 (0.79%)	1 / 132 (0.76%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac perfusion defect			

subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
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			
Syncope			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Headache			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar syndrome			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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 and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelosuppression			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Anaemia			
subjects affected / exposed	2 / 127 (1.57%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	3 / 127 (2.36%)	4 / 132 (3.03%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	3 / 3	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 127 (1.57%)	0 / 132 (0.00%)	2 / 123 (1.63%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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			
Gastritis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	2 / 123 (1.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Nausea			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Vomiting			
subjects affected / exposed	1 / 127 (0.79%)	1 / 132 (0.76%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	2 / 2	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Hepatobiliary disorders			
Hepatitis cholestatic			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Hepatitis			

subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pemphigoid			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Rash			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Pruritus			

subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Acute kidney injury			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Thyroiditis subacute			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Immune-mediated adrenal insufficiency			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Myositis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Breast abscess			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 127 (0.79%)	1 / 132 (0.76%)	0 / 123 (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
Mastitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Device related infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cellulitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	3 / 127 (2.36%)	0 / 132 (0.00%)	0 / 123 (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
COVID-19			
subjects affected / exposed	2 / 127 (1.57%)	1 / 132 (0.76%)	2 / 123 (1.63%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cellulitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 sepsis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Septic shock			

subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 127 (0.79%)	3 / 132 (2.27%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 1	4 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Postoperative wound infection			
subjects affected / exposed	2 / 127 (1.57%)	0 / 132 (0.00%)	0 / 123 (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
Pulmonary tuberculosis			

subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Wound infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Vascular access site infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic infection			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			

subjects affected / exposed	1 / 127 (0.79%)	0 / 132 (0.00%)	0 / 123 (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
Dehydration			
subjects affected / exposed	0 / 127 (0.00%)	1 / 132 (0.76%)	0 / 123 (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
Hyponatraemia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 132 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm A: Nivo + Chemo (PTX QW + AC Q2W) / Nivo + ET		
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 135 (37.78%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			

subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervix carcinoma			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			

subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Disease progression				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	4 / 135 (2.96%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic shock				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anaphylactic reaction				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Breast inflammation				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Immune-mediated lung disease			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Pulmonary embolism			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device occlusion			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
White blood cell count decreased			

subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	2 / 135 (1.48%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Inflammatory marker increased				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Radiation skin injury				
subjects affected / exposed	2 / 135 (1.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Craniofacial fracture				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haematoma				

subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical procedure repeated				
subjects affected / exposed	2 / 135 (1.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardio-respiratory arrest				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular failure				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Supraventricular tachycardia				

subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac perfusion defect				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial pressure increased				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				

subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebellar syndrome			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myelosuppression			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences causally related to treatment / all	10 / 10		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			

Vertigo				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Gastritis				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				

subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis cholestatic			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cholelithiasis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Autoimmune hepatitis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pemphigoid			

subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pruritus				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Urinary retention				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Glomerulonephritis				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Thyroiditis subacute				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated adrenal insufficiency				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Hypopituitarism			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Adrenal insufficiency			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Breast abscess			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mastitis			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis infectious			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Device related infection			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic infection			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Catheter site infection			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	5 / 135 (3.70%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Breast cellulitis			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SARS-CoV-2 sepsis			

subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii infection				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 135 (2.22%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				

subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 135 (0.74%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular access site infection				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 135 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Systemic infection			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	2 / 135 (1.48%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Hypoalbuminaemia			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	1 / 135 (0.74%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A: Nivo + Chemo (PTX QW + AC Q3W) / Nivo + ET	Arm B: Nivo Placebo + Chemo (PTX QW + AC Q2W) / ET	Arm B: Nivo Placebo + Chemo (PTX QW + AC Q3W) / ET
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 127 (99.21%)	130 / 132 (98.48%)	120 / 123 (97.56%)
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 127 (8.66%)	7 / 132 (5.30%)	5 / 123 (4.07%)
occurrences (all)	12	10	5
Hot flush			
subjects affected / exposed	9 / 127 (7.09%)	30 / 132 (22.73%)	12 / 123 (9.76%)
occurrences (all)	12	34	12
Lymphoedema			
subjects affected / exposed	2 / 127 (1.57%)	7 / 132 (5.30%)	2 / 123 (1.63%)
occurrences (all)	2	8	2
Flushing			
subjects affected / exposed	0 / 127 (0.00%)	7 / 132 (5.30%)	3 / 123 (2.44%)
occurrences (all)	0	10	4
General disorders and administration site conditions			
Illness			
subjects affected / exposed	7 / 127 (5.51%)	1 / 132 (0.76%)	2 / 123 (1.63%)
occurrences (all)	13	1	5
Fatigue			
subjects affected / exposed	34 / 127 (26.77%)	52 / 132 (39.39%)	24 / 123 (19.51%)
occurrences (all)	47	86	32
Chills			
subjects affected / exposed	1 / 127 (0.79%)	2 / 132 (1.52%)	1 / 123 (0.81%)
occurrences (all)	1	2	1
Asthenia			
subjects affected / exposed	27 / 127 (21.26%)	27 / 132 (20.45%)	30 / 123 (24.39%)
occurrences (all)	72	37	143
Mucosal inflammation			
subjects affected / exposed	7 / 127 (5.51%)	19 / 132 (14.39%)	6 / 123 (4.88%)
occurrences (all)	7	20	8
Pain			
subjects affected / exposed	5 / 127 (3.94%)	3 / 132 (2.27%)	2 / 123 (1.63%)
occurrences (all)	8	3	2

Pyrexia			
subjects affected / exposed	11 / 127 (8.66%)	10 / 132 (7.58%)	7 / 123 (5.69%)
occurrences (all)	16	12	7
Oedema peripheral			
subjects affected / exposed	5 / 127 (3.94%)	13 / 132 (9.85%)	6 / 123 (4.88%)
occurrences (all)	5	16	9
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	8 / 127 (6.30%)	8 / 132 (6.06%)	5 / 123 (4.07%)
occurrences (all)	10	9	9
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	4 / 127 (3.15%)	14 / 132 (10.61%)	6 / 123 (4.88%)
occurrences (all)	4	16	6
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	3 / 127 (2.36%)	0 / 132 (0.00%)	4 / 123 (3.25%)
occurrences (all)	4	0	5
Oropharyngeal pain			
subjects affected / exposed	3 / 127 (2.36%)	6 / 132 (4.55%)	4 / 123 (3.25%)
occurrences (all)	3	8	7
Epistaxis			
subjects affected / exposed	11 / 127 (8.66%)	12 / 132 (9.09%)	8 / 123 (6.50%)
occurrences (all)	14	12	8
Dyspnoea			
subjects affected / exposed	4 / 127 (3.15%)	10 / 132 (7.58%)	9 / 123 (7.32%)
occurrences (all)	5	10	10
Cough			
subjects affected / exposed	13 / 127 (10.24%)	16 / 132 (12.12%)	9 / 123 (7.32%)
occurrences (all)	14	17	11
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 127 (6.30%)	20 / 132 (15.15%)	8 / 123 (6.50%)
occurrences (all)	9	22	8
Depression			

subjects affected / exposed	3 / 127 (2.36%)	8 / 132 (6.06%)	0 / 123 (0.00%)
occurrences (all)	3	8	0
Anxiety			
subjects affected / exposed	6 / 127 (4.72%)	6 / 132 (4.55%)	2 / 123 (1.63%)
occurrences (all)	6	6	3
Investigations			
Blood calcium increased			
subjects affected / exposed	0 / 127 (0.00%)	3 / 132 (2.27%)	0 / 123 (0.00%)
occurrences (all)	0	4	0
Blood alkaline phosphatase increased			
subjects affected / exposed	10 / 127 (7.87%)	5 / 132 (3.79%)	4 / 123 (3.25%)
occurrences (all)	13	5	9
Aspartate aminotransferase increased			
subjects affected / exposed	32 / 127 (25.20%)	19 / 132 (14.39%)	23 / 123 (18.70%)
occurrences (all)	55	33	28
Alanine aminotransferase increased			
subjects affected / exposed	27 / 127 (21.26%)	20 / 132 (15.15%)	23 / 123 (18.70%)
occurrences (all)	46	29	33
Blood glucose increased			
subjects affected / exposed	0 / 127 (0.00%)	2 / 132 (1.52%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	6 / 127 (4.72%)	9 / 132 (6.82%)	5 / 123 (4.07%)
occurrences (all)	7	10	9
Blood sodium decreased			
subjects affected / exposed	0 / 127 (0.00%)	5 / 132 (3.79%)	0 / 123 (0.00%)
occurrences (all)	0	9	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	4 / 127 (3.15%)	3 / 132 (2.27%)	0 / 123 (0.00%)
occurrences (all)	4	3	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	5 / 127 (3.94%)	4 / 132 (3.03%)	3 / 123 (2.44%)
occurrences (all)	6	9	4
Lymphocyte count decreased			

subjects affected / exposed	4 / 127 (3.15%)	3 / 132 (2.27%)	2 / 123 (1.63%)
occurrences (all)	6	8	4
Neutrophil count decreased			
subjects affected / exposed	20 / 127 (15.75%)	11 / 132 (8.33%)	11 / 123 (8.94%)
occurrences (all)	52	13	30
Weight decreased			
subjects affected / exposed	7 / 127 (5.51%)	3 / 132 (2.27%)	3 / 123 (2.44%)
occurrences (all)	7	3	4
White blood cell count decreased			
subjects affected / exposed	15 / 127 (11.81%)	5 / 132 (3.79%)	8 / 123 (6.50%)
occurrences (all)	49	8	26
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	12 / 127 (9.45%)	12 / 132 (9.09%)	10 / 123 (8.13%)
occurrences (all)	14	13	14
Procedural pain			
subjects affected / exposed	3 / 127 (2.36%)	5 / 132 (3.79%)	5 / 123 (4.07%)
occurrences (all)	3	6	5
Radiation skin injury			
subjects affected / exposed	15 / 127 (11.81%)	20 / 132 (15.15%)	13 / 123 (10.57%)
occurrences (all)	15	20	13
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 127 (2.36%)	4 / 132 (3.03%)	0 / 123 (0.00%)
occurrences (all)	4	4	0
Palpitations			
subjects affected / exposed	2 / 127 (1.57%)	7 / 132 (5.30%)	1 / 123 (0.81%)
occurrences (all)	2	7	1
Nervous system disorders			
Taste disorder			
subjects affected / exposed	0 / 127 (0.00%)	9 / 132 (6.82%)	1 / 123 (0.81%)
occurrences (all)	0	10	1
Dizziness			
subjects affected / exposed	9 / 127 (7.09%)	8 / 132 (6.06%)	7 / 123 (5.69%)
occurrences (all)	11	8	10
Dysgeusia			

subjects affected / exposed	9 / 127 (7.09%)	14 / 132 (10.61%)	8 / 123 (6.50%)
occurrences (all)	10	14	8
Headache			
subjects affected / exposed	24 / 127 (18.90%)	33 / 132 (25.00%)	24 / 123 (19.51%)
occurrences (all)	39	53	38
Neuropathy peripheral			
subjects affected / exposed	26 / 127 (20.47%)	32 / 132 (24.24%)	19 / 123 (15.45%)
occurrences (all)	27	37	19
Paraesthesia			
subjects affected / exposed	8 / 127 (6.30%)	13 / 132 (9.85%)	8 / 123 (6.50%)
occurrences (all)	10	17	8
Peripheral sensory neuropathy			
subjects affected / exposed	8 / 127 (6.30%)	16 / 132 (12.12%)	10 / 123 (8.13%)
occurrences (all)	8	16	12
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	24 / 127 (18.90%)	24 / 132 (18.18%)	27 / 123 (21.95%)
occurrences (all)	39	36	57
Lymphopenia			
subjects affected / exposed	15 / 127 (11.81%)	12 / 132 (9.09%)	8 / 123 (6.50%)
occurrences (all)	18	19	13
Leukopenia			
subjects affected / exposed	8 / 127 (6.30%)	11 / 132 (8.33%)	12 / 123 (9.76%)
occurrences (all)	10	22	18
Anaemia			
subjects affected / exposed	47 / 127 (37.01%)	62 / 132 (46.97%)	32 / 123 (26.02%)
occurrences (all)	76	86	58
Thrombocytopenia			
subjects affected / exposed	2 / 127 (1.57%)	3 / 132 (2.27%)	1 / 123 (0.81%)
occurrences (all)	2	3	1
Eye disorders			
Lacrimation increased			
subjects affected / exposed	4 / 127 (3.15%)	5 / 132 (3.79%)	5 / 123 (4.07%)
occurrences (all)	4	5	6
Dry eye			

subjects affected / exposed	4 / 127 (3.15%)	11 / 132 (8.33%)	4 / 123 (3.25%)
occurrences (all)	5	11	4
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	4 / 127 (3.15%)	12 / 132 (9.09%)	4 / 123 (3.25%)
occurrences (all)	4	14	5
Abdominal pain			
subjects affected / exposed	6 / 127 (4.72%)	12 / 132 (9.09%)	9 / 123 (7.32%)
occurrences (all)	7	15	11
Abdominal pain upper			
subjects affected / exposed	7 / 127 (5.51%)	9 / 132 (6.82%)	4 / 123 (3.25%)
occurrences (all)	8	16	4
Constipation			
subjects affected / exposed	23 / 127 (18.11%)	30 / 132 (22.73%)	19 / 123 (15.45%)
occurrences (all)	30	35	25
Diarrhoea			
subjects affected / exposed	30 / 127 (23.62%)	40 / 132 (30.30%)	26 / 123 (21.14%)
occurrences (all)	47	63	37
Dry mouth			
subjects affected / exposed	5 / 127 (3.94%)	7 / 132 (5.30%)	4 / 123 (3.25%)
occurrences (all)	5	7	5
Dyspepsia			
subjects affected / exposed	9 / 127 (7.09%)	5 / 132 (3.79%)	5 / 123 (4.07%)
occurrences (all)	13	6	6
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 127 (3.15%)	14 / 132 (10.61%)	2 / 123 (1.63%)
occurrences (all)	4	15	2
Nausea			
subjects affected / exposed	61 / 127 (48.03%)	59 / 132 (44.70%)	55 / 123 (44.72%)
occurrences (all)	107	118	104
Vomiting			
subjects affected / exposed	26 / 127 (20.47%)	13 / 132 (9.85%)	25 / 123 (20.33%)
occurrences (all)	39	21	42
Skin and subcutaneous tissue disorders			
Nail disorder			

subjects affected / exposed	3 / 127 (2.36%)	9 / 132 (6.82%)	10 / 123 (8.13%)
occurrences (all)	3	9	10
Dry skin			
subjects affected / exposed	3 / 127 (2.36%)	8 / 132 (6.06%)	3 / 123 (2.44%)
occurrences (all)	4	8	3
Alopecia			
subjects affected / exposed	83 / 127 (65.35%)	69 / 132 (52.27%)	80 / 123 (65.04%)
occurrences (all)	83	70	80
Rash maculo-papular			
subjects affected / exposed	3 / 127 (2.36%)	8 / 132 (6.06%)	1 / 123 (0.81%)
occurrences (all)	5	8	1
Rash			
subjects affected / exposed	18 / 127 (14.17%)	28 / 132 (21.21%)	16 / 123 (13.01%)
occurrences (all)	21	33	17
Pruritus			
subjects affected / exposed	12 / 127 (9.45%)	18 / 132 (13.64%)	5 / 123 (4.07%)
occurrences (all)	16	23	5
Onycholysis			
subjects affected / exposed	3 / 127 (2.36%)	8 / 132 (6.06%)	1 / 123 (0.81%)
occurrences (all)	3	8	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	7 / 127 (5.51%)	5 / 132 (3.79%)	2 / 123 (1.63%)
occurrences (all)	7	5	2
Hypothyroidism			
subjects affected / exposed	19 / 127 (14.96%)	5 / 132 (3.79%)	8 / 123 (6.50%)
occurrences (all)	21	5	8
Adrenal insufficiency			
subjects affected / exposed	5 / 127 (3.94%)	1 / 132 (0.76%)	0 / 123 (0.00%)
occurrences (all)	5	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 127 (16.54%)	42 / 132 (31.82%)	20 / 123 (16.26%)
occurrences (all)	25	48	22
Back pain			

subjects affected / exposed	8 / 127 (6.30%)	17 / 132 (12.88%)	5 / 123 (4.07%)
occurrences (all)	8	27	6
Bone pain			
subjects affected / exposed	3 / 127 (2.36%)	10 / 132 (7.58%)	4 / 123 (3.25%)
occurrences (all)	5	14	5
Myalgia			
subjects affected / exposed	14 / 127 (11.02%)	22 / 132 (16.67%)	13 / 123 (10.57%)
occurrences (all)	19	29	19
Pain in extremity			
subjects affected / exposed	7 / 127 (5.51%)	12 / 132 (9.09%)	8 / 123 (6.50%)
occurrences (all)	7	13	8
Infections and infestations			
COVID-19			
subjects affected / exposed	21 / 127 (16.54%)	29 / 132 (21.97%)	18 / 123 (14.63%)
occurrences (all)	23	29	20
Folliculitis			
subjects affected / exposed	6 / 127 (4.72%)	5 / 132 (3.79%)	1 / 123 (0.81%)
occurrences (all)	6	5	1
Nasopharyngitis			
subjects affected / exposed	4 / 127 (3.15%)	7 / 132 (5.30%)	1 / 123 (0.81%)
occurrences (all)	4	9	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 127 (0.79%)	5 / 132 (3.79%)	8 / 123 (6.50%)
occurrences (all)	1	5	9
Urinary tract infection			
subjects affected / exposed	12 / 127 (9.45%)	11 / 132 (8.33%)	9 / 123 (7.32%)
occurrences (all)	13	14	10
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	16 / 127 (12.60%)	10 / 132 (7.58%)	13 / 123 (10.57%)
occurrences (all)	24	12	21
Hyperglycaemia			
subjects affected / exposed	15 / 127 (11.81%)	4 / 132 (3.03%)	8 / 123 (6.50%)
occurrences (all)	19	6	8
Hypokalaemia			

subjects affected / exposed	4 / 127 (3.15%)	6 / 132 (4.55%)	0 / 123 (0.00%)
occurrences (all)	4	9	0
Hyponatraemia			
subjects affected / exposed	4 / 127 (3.15%)	7 / 132 (5.30%)	2 / 123 (1.63%)
occurrences (all)	6	7	3

Non-serious adverse events	Arm A: Nivo + Chemo (PTX QW + AC Q2W) / Nivo + ET		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 135 (97.78%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	12		
Hot flush			
subjects affected / exposed	33 / 135 (24.44%)		
occurrences (all)	35		
Lymphoedema			
subjects affected / exposed	5 / 135 (3.70%)		
occurrences (all)	5		
Flushing			
subjects affected / exposed	7 / 135 (5.19%)		
occurrences (all)	7		
General disorders and administration site conditions			
Illness			
subjects affected / exposed	0 / 135 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	67 / 135 (49.63%)		
occurrences (all)	104		
Chills			
subjects affected / exposed	8 / 135 (5.93%)		
occurrences (all)	9		
Asthenia			
subjects affected / exposed	25 / 135 (18.52%)		
occurrences (all)	27		

Mucosal inflammation subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	16 / 135 (11.85%) 19 11 / 135 (8.15%) 13 21 / 135 (15.56%) 26 12 / 135 (8.89%) 12		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	3 / 135 (2.22%) 3		
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	13 / 135 (9.63%) 14		
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	7 / 135 (5.19%) 7 7 / 135 (5.19%) 7 9 / 135 (6.67%) 10 9 / 135 (6.67%) 9 29 / 135 (21.48%) 34		

Psychiatric disorders			
Insomnia			
subjects affected / exposed	25 / 135 (18.52%)		
occurrences (all)	30		
Depression			
subjects affected / exposed	7 / 135 (5.19%)		
occurrences (all)	7		
Anxiety			
subjects affected / exposed	10 / 135 (7.41%)		
occurrences (all)	12		
Investigations			
Blood calcium increased			
subjects affected / exposed	7 / 135 (5.19%)		
occurrences (all)	7		
Blood alkaline phosphatase increased			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	10		
Aspartate aminotransferase increased			
subjects affected / exposed	30 / 135 (22.22%)		
occurrences (all)	51		
Alanine aminotransferase increased			
subjects affected / exposed	31 / 135 (22.96%)		
occurrences (all)	54		
Blood glucose increased			
subjects affected / exposed	7 / 135 (5.19%)		
occurrences (all)	16		
Blood lactate dehydrogenase increased			
subjects affected / exposed	6 / 135 (4.44%)		
occurrences (all)	7		
Blood sodium decreased			
subjects affected / exposed	8 / 135 (5.93%)		
occurrences (all)	15		
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	11 / 135 (8.15%)		
occurrences (all)	11		

Blood thyroid stimulating hormone increased			
subjects affected / exposed	15 / 135 (11.11%)		
occurrences (all)	23		
Lymphocyte count decreased			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	10		
Neutrophil count decreased			
subjects affected / exposed	16 / 135 (11.85%)		
occurrences (all)	27		
Weight decreased			
subjects affected / exposed	10 / 135 (7.41%)		
occurrences (all)	11		
White blood cell count decreased			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	17		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	25 / 135 (18.52%)		
occurrences (all)	31		
Procedural pain			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	9		
Radiation skin injury			
subjects affected / exposed	22 / 135 (16.30%)		
occurrences (all)	23		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	8 / 135 (5.93%)		
occurrences (all)	8		
Palpitations			
subjects affected / exposed	6 / 135 (4.44%)		
occurrences (all)	7		
Nervous system disorders			
Taste disorder			
subjects affected / exposed	3 / 135 (2.22%)		
occurrences (all)	4		

Dizziness subjects affected / exposed occurrences (all)	10 / 135 (7.41%) 12		
Dysgeusia subjects affected / exposed occurrences (all)	26 / 135 (19.26%) 26		
Headache subjects affected / exposed occurrences (all)	43 / 135 (31.85%) 62		
Neuropathy peripheral subjects affected / exposed occurrences (all)	38 / 135 (28.15%) 42		
Paraesthesia subjects affected / exposed occurrences (all)	10 / 135 (7.41%) 11		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	21 / 135 (15.56%) 21		
Blood and lymphatic system disorders			
Neutropenia subjects affected / exposed occurrences (all)	26 / 135 (19.26%) 45		
Lymphopenia subjects affected / exposed occurrences (all)	9 / 135 (6.67%) 15		
Leukopenia subjects affected / exposed occurrences (all)	8 / 135 (5.93%) 17		
Anaemia subjects affected / exposed occurrences (all)	65 / 135 (48.15%) 99		
Thrombocytopenia subjects affected / exposed occurrences (all)	7 / 135 (5.19%) 10		
Eye disorders			

Lacrimation increased			
subjects affected / exposed	7 / 135 (5.19%)		
occurrences (all)	7		
Dry eye			
subjects affected / exposed	10 / 135 (7.41%)		
occurrences (all)	10		
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	14 / 135 (10.37%)		
occurrences (all)	18		
Abdominal pain			
subjects affected / exposed	15 / 135 (11.11%)		
occurrences (all)	16		
Abdominal pain upper			
subjects affected / exposed	12 / 135 (8.89%)		
occurrences (all)	15		
Constipation			
subjects affected / exposed	36 / 135 (26.67%)		
occurrences (all)	48		
Diarrhoea			
subjects affected / exposed	48 / 135 (35.56%)		
occurrences (all)	85		
Dry mouth			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	10		
Dyspepsia			
subjects affected / exposed	10 / 135 (7.41%)		
occurrences (all)	13		
Gastrooesophageal reflux disease			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	77 / 135 (57.04%)		
occurrences (all)	133		
Vomiting			

subjects affected / exposed occurrences (all)	27 / 135 (20.00%) 35		
Skin and subcutaneous tissue disorders Nail disorder subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Onycholysis subjects affected / exposed occurrences (all)	 10 / 135 (7.41%) 11 7 / 135 (5.19%) 7 64 / 135 (47.41%) 65 5 / 135 (3.70%) 7 30 / 135 (22.22%) 42 22 / 135 (16.30%) 24 5 / 135 (3.70%) 5		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all) Adrenal insufficiency subjects affected / exposed occurrences (all)	 13 / 135 (9.63%) 13 30 / 135 (22.22%) 32 10 / 135 (7.41%) 11		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	41 / 135 (30.37%)		
occurrences (all)	52		
Back pain			
subjects affected / exposed	16 / 135 (11.85%)		
occurrences (all)	20		
Bone pain			
subjects affected / exposed	12 / 135 (8.89%)		
occurrences (all)	15		
Myalgia			
subjects affected / exposed	26 / 135 (19.26%)		
occurrences (all)	29		
Pain in extremity			
subjects affected / exposed	14 / 135 (10.37%)		
occurrences (all)	17		
Infections and infestations			
COVID-19			
subjects affected / exposed	29 / 135 (21.48%)		
occurrences (all)	31		
Folliculitis			
subjects affected / exposed	9 / 135 (6.67%)		
occurrences (all)	10		
Nasopharyngitis			
subjects affected / exposed	6 / 135 (4.44%)		
occurrences (all)	6		
Upper respiratory tract infection			
subjects affected / exposed	7 / 135 (5.19%)		
occurrences (all)	7		
Urinary tract infection			
subjects affected / exposed	8 / 135 (5.93%)		
occurrences (all)	9		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	19 / 135 (14.07%)		
occurrences (all)	21		
Hyperglycaemia			

subjects affected / exposed	13 / 135 (9.63%)		
occurrences (all)	20		
Hypokalaemia			
subjects affected / exposed	12 / 135 (8.89%)		
occurrences (all)	14		
Hyponatraemia			
subjects affected / exposed	3 / 135 (2.22%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2020	Study procedures update per local practice
21 May 2021	clarify expectations for eligibility, assessments, sample collection, and treatment administration.
27 June 2022	Details of study enrollment closure with provision for enrolled participants on treatment to continue in the study. The study objectives, endpoints, and statistical analysis have been updated and clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported