Clinical trial results:
A PHASE II ONE-ARM OPEN-LABEL NEOADJUVANT STUDY OF PEMBROLIZUMAB IN COMBINATION WITH NAB-PACLITAXEL FOLLOWED BY PEMBROLIZUMAB IN COMBINATION WITH EPIRUBICIN AND CYCLOPHOSPHAMIDE IN PATIENTS WITH TRIPLE NEGATIVE BREAST CANCER

Summary

EudraCT number	2016-003102-14
Trial protocol	DE
Global end of trial date	27 August 2020

Results information

Result version number	v1 (current)
This version publication date	24 December 2021
First version publication date	24 December 2021

Trial information

Trial identification

Sponsor protocol code	IFG-NIB-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03289819
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS-ID:: DRKS00011738

Notes:

Sponsors

Sponsor organisation name	Institut für Frauengesundheit GmbH
Sponsor organisation address	Universitätsstraße 21-23, Erlangen, Germany, 91054
Public contact	Clinical Trials Information, Institut für Frauengesundheit GmbH, +49 091318536167, nib@ifg-erlangen.de
Scientific contact	Clinical Trials Information, Institut für Frauengesundheit GmbH, +49 091318536167, nib@ifg-erlangen.de

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	05 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2020
Global end of trial reached?	Yes
Global end of trial date	27 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy as measured by pCR after completion of neoadjuvant chemotherapy in combination with pembrolizumab.

Protection of trial subjects:

The clinical trial was conducted in accordance with current ethical standards, the Declaration of Helsinki from 1996 and the Guidelines of the International Conference on Harmonization Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 2018
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	Germany: 56
Worldwide total number of subjects	56
EEA total number of subjects	56

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)	46
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The clinical trial was conducted in 4 main trial sites in Germany. Patients were recruited between 23.03.2018 and 08.10.2019. The date of last patient last visit was 27.08.2020. The date of database lock was on 22.01.2021.

Pre-assignment

Screening details:

A total of 56 patients signed the informed consent form and were enrolled into the NeoImmunoboost trial.
Of these patients 3 patients were screening failures and excluded from the study. A total of 53 patients started trial treatment and were included in the safety analysis set. One patient withdrew consent and two patients stopped the treatment a

Period 1

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

Arms

Arm title	nab-paclitaxel/pembrolizumab followed by EC/pembrolizumab

Arm description:

Patients received 12 doses of weekly nab-paclitaxel intravenous (i.v.) 125 mg/m² body surface area (BSA) in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w; followed by 4 cycles of epirubicin i.v. 90 mg/m² BSA and cyclophosphamide i.v. 600 mg/m² BSA, q3w in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w. After the 25th patient had started trial treatment, all further included patients received 1 cycle of pembrolizumab i.v. 200 mg q3w monotherapy followed by 12 doses of weekly nab-paclitaxel i.v. 125 mg/m² BSA in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w; followed by 4 cycles of epirubicin i.v. 90 mg/m² BSA and cyclophosphamide i.v. 600 mg/m² BSA, q3w in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w.

Arm type	Experimental
Investigational medicinal product name	nab-paclitaxel
Investigational medicinal product code	
Other name	abraxane
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received 125 mg/m² BSA q1w for 12 doses as i.v. infusion

Investigational medicinal product name	pembrolizumab
Investigational medicinal product code	
Other name	keytruda
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 200 mg fixed dose as i.v. infusion q3w for 8 cycles/ q3w for 9 cycles

Number of subjects in period 1[1]	nab-paclitaxel/pembrolizumab followed by EC/pembrolizumab
Started	53
Completed	39
Not completed	14
Physician decision	1
Consent withdrawn by subject	1
Adverse event, non-fatal	4
Tumor progression	3
Protocol deviation	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 3 patients were entered into the trial and identified as screening failures. They have never started trial treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	53	53	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	51.5		
standard deviation	± 11.7	-	
Gender categorical Units: Subjects			
Female	53	53	
Male	0	0	
Ethnicity Units: Subjects			
Caucasian	53	53	
Other	0	0	
Menopausal state Units: Subjects			
Pre-/ perimenopausal	30	30	
Postmenopausal	23	23	
Tumor stage Units: Subjects			
cT1	24	24	
cT2	25	25	
cT3	2	2	
cT4	2	2	
Clinical lymph node status Units: Subjects			
cN0	34	34	
cN1-3	16	16	
cNX	3	3	
Previous Lymph node Procedure			

Units: Subjects			
Yes	20	20	
No	33	33	
Pathological lymph node status Units: Subjects			
pN0	6	6	
pN1-3	14	14	
not applicable	33	33	
cM Units: Subjects			
cM0	51	51	
cMX	1	1	
not available	1	1	
Grading Units: Subjects			
G1	0	0	
G2	11	11	
G3	41	41	
not available	1	1	
Histological subtype Units: Subjects			
Ductal	39	39	
Lobular	1	1	
Mixed ductal/lobular	2	2	
Other	9	9	
not available	2	2	
BRCA Units: Subjects			
BRCA1 mutation yes	2	2	
BRCA 1 mutation no	16	16	
not available	35	35	
ECOG Units: Subjects			
ECOG 0	51	51	
ECOG 1	2	2	
Comorbidities			
Number of Comorbidities			
Units: Subjects			
None	17	17	
One	13	13	
More than 2	23	23	
Initiation boost Units: Subjects			
yes	28	28	
no	25	25	
Time from primary diagnosis to therapy begin Units: days			
arithmetic mean	30.4		
standard deviation	± 10.3	-	
Time from primary diagnosis to study entry			

Units: days			
arithmetic mean	21.6		
standard deviation	± 9.9	-	

Subject analysis sets

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis included all subjects who were randomized and had at least received one dose of IP nab-paclitaxel and/ or pembrolizumab and/ or E/C. Data collected on subjects in this subset during the period of randomization to the primary analysis data cut-off date were included, regardless of compliance with the protocol.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set included all patients who received at least who received at least one full treatment cycle q21d nab-paclitaxel (d1, d8, d15) and pembrolizumab (d1).

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per protocol set was defined as all patients with a protocol-defined diagnosis who had at least received 2 cycles of nab-paclitaxel (reflecting 6 doses) with concomitant pembrolizumab treatment, and who had completed at least 2 cycles of epirubicin/ cyclophosphamide with concomitant pembrolizumab treatment.
Subjects with deviations from the protocol-specified in- and exclusion criteria were also excluded from the per protocol set.

Reporting group values	Safety analysis set	Full Analysis Set	Per Protocol Set
Number of subjects	53	50	39
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	51.5	52.2	52.3
standard deviation	± 11.7	± 11.5	± 11.5
Gender categorical Units: Subjects			
Female	53	50	39
Male	0	0	0

Ethnicity Units: Subjects			
Caucasian	53	50	39
Other	0	0	0
Menopausal state Units: Subjects			
Pre-/ perimenopausal	30	27	20
Postmenopausal	23	23	19
Tumor stage Units: Subjects			
cT1	24	24	20
cT2	25	23	17
cT3	2	2	1
cT4	2	1	1
Clinical lymph node status Units: Subjects			
cN0	34	32	24
cN1-3	16	15	13
cNX	3	3	2
Previous Lymph node Procedure Units: Subjects			
Yes	20	19	17
No	33	31	22
Pathological lymph node status Units: Subjects			
pN0	6	6	5
pN1-3	14	13	12
not applicable	33	31	22
cM Units: Subjects			
cM0	51	49	38
cMX	1	1	1
not available	1	0	0
Grading Units: Subjects			
G1	0	0	0
G2	11	10	8
G3	41	39	31
not available			
Histological subtype Units: Subjects			
Ductal	39	36	26
Lobular	1	1	0
Mixed ductal/lobular	2	2	2
Other	9	9	9
not available	2	2	2
BRCA Units: Subjects			
BRCA1 mutation yes	2	2	2
BRCA 1 mutation no	16	16	12
not available	35	33	25

ECOG Units: Subjects			
ECOG 0	51	48	37
ECOG 1	2	2	2
Comorbidities			
Number of Comorbidities			
Units: Subjects			
None	17	16	12
One	13	11	8
More than 2	23	23	19
Initiation boost Units: Subjects			
yes	28	27	23
no	25	23	16
Time from primary diagnosis to therapy begin Units: days			
arithmetic mean	30.4	30.6	29.1
standard deviation	± 10.3	± 10.6	± 8.9
Time from primary diagnosis to study entry Units: days			
arithmetic mean	21.6	21.7	20.4
standard deviation	± 9.9	± 10.1	± 9.1

End points

End points reporting groups

Reporting group title	nab-paclitaxel/pembrolizumab followed by EC/pembrolizumab

Reporting group description:

Patients received 12 doses of weekly nab-paclitaxel intravenous (i.v.) 125 mg/m² body surface area (BSA) in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w; followed by 4 cycles of epirubicin i.v. 90 mg/m² BSA and cyclophosphamide i.v. 600 mg/m² BSA, q3w in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w. After the 25th patient had started trial treatment, all further included patients received 1 cycle of pembrolizumab i.v. 200 mg q3w monotherapy followed by 12 doses of weekly nab-paclitaxel i.v. 125 mg/m² BSA in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w; followed by 4 cycles of epirubicin i.v. 90 mg/m² BSA and cyclophosphamide i.v. 600 mg/m² BSA, q3w in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w.

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis included all subjects who were randomized and had at least received one dose of IP nab-paclitaxel and/ or pembrolizumab and/ or E/C. Data collected on subjects in this subset during the period of randomization to the primary analysis data cut-off date were included, regardless of compliance with the protocol.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set included all patients who received at least who received at least one full treatment cycle q21d nab-paclitaxel (d1, d8, d15) and pembrolizumab (d1).

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per protocol set was defined as all patients with a protocol-defined diagnosis who had at least received 2 cycles of nab-paclitaxel (reflecting 6 doses) with concomitant pembrolizumab treatment, and who had completed at least 2 cycles of epirubicin/ cyclophosphamide with concomitant pembrolizumab treatment.
Subjects with deviations from the protocol-specified in- and exclusion criteria were also excluded from the per protocol set.

Primary: pCR rate

End point title	pCR rate[1]

End point description:

ypT0/is ypN0

End point type	Primary

End point timeframe:

Final surgery

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The null hypothesis stating that the pCR rate is at most 50% was tested with a one-sided binomial test with significance level α = 0.05

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	39		
Units: percent				
number (confidence interval 95%)	66.0 (51.2 to 78.8)	71.8 (55.1 to 85.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response rate evaluated 6 weeks after initiation of nab-paclitaxel/ pembrolizumab

End point title	Clinical response rate evaluated 6 weeks after initiation of nab-paclitaxel/ pembrolizumab

End point description:

End point type	Secondary

End point timeframe:

6 weeks after initiation of nab-paclitaxel/ pembrolizumab

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	35		
Units: percent				
number (confidence interval 95%)				
complete response	4.3 (0.5 to 14.8)	5.7 (0.7 to 19.2)		
partial response	65.2 (49.8 to 78.6)	71.4 (53.7 to 85.4)		
stable disease	26.1 (14.3 to 41.1)	20.0 (8.4 to 36.9)		
progressive disease	2.2 (0.1 to 11.5)	0 (0 to 0)		
not evaluable	2.2 (0.1 to 11.5)	2.9 (0.1 to 14.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response rate evaluated before first E/C/ pembrolizumab

End point title	Clinical response rate evaluated before first E/C/ pembrolizumab

End point description:

End point type	Secondary

End point timeframe:
before first E/C/ pembrolizumab

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45	36		
Units: percent				
number (confidence interval 95%)				
complete response	26.7 (14.6 to 41.9)	30.6 (16.3 to 48.1)		
partial response	42.2 (27.7 to 57.8)	44.4 (27.9 to 61.9)		
stable disease	26.7 (14.6 to 41.9)	25 (12.1 to 42.1)		
progressive disease	4.4 (0.5 to 15.1)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response rate evaluated 6 weeks after initiation of E/C/ pembrolizumab

End point title	Clinical response rate evaluated 6 weeks after initiation of E/C/ pembrolizumab

End point description:

End point type	Secondary

End point timeframe:
6 weeks after initiation of E/C/ pembrolizumab

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	35	31		
Units: percent				
number (confidence interval 95%)				
complete response	37.1 (21.5 to 55.1)	41.9 (24.5 to 60.9)		
partial response	31.4 (16.9 to 49.3)	25.8 (11.9 to 44.6)		
stable disease	28.6 (14.4 to 46.3)	29.0 (14.2 to 48.0)		
not evaluable	2.9 (0.1 to 14.9)	3.2 (0.1 to 16.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response rate evaluated at time of surgery/ end of treatment

End point title	Clinical response rate evaluated at time of surgery/ end of treatment

End point description:

End point type	Secondary

End point timeframe:

time of surgery/ end of treatment whichever is earlier

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	33		
Units: percent				
number (confidence interval 95%)				
complete response	53.7 (37.4 to 69.3)	60.6 (42.1 to 77.1)		
partial response	22.0 (10.6 to 37.6)	18.2 (7.0 to 35.5)		
stable disease	19.5 (8.8 to 34.9)	18.2 (7.0 to 35.5)		
progressive disease	2.4 (0.1 to 12.9)	0 (0 to 0)		
not evaluable	2.4 (0.1 to 12.9)	3.0 (0.1 to 15.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summarized clinical response rate in the full analysis set

End point title	Summarized clinical response rate in the full analysis set

End point description:

End point type	Secondary

End point timeframe:

End of treatment

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	39		
Units: percent				
number (confidence interval 95%)				
complete response	50 (35.5 to 64.5)	59.0 (42.1 to 74.4)		
partial response	70 (55.4 to 82.1)	74.4 (57.9 to 87)		
stable disease	48 (33.7 to 62.6)	46.2 (30.1 to 62.8)		
progressive disease	6 (1.3 to 16.5)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Global Health

End point title	Global Health
End point description:	
Global health subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe:	
Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[2]	39[3]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	72.0 (± 15.4)	73.8 (± 14.3)		
1.nbP/Pbr	75.4 (± 17.2)	76.2 (± 16.9)		
3.nbP/Pbr	59.8 (± 20.0)	60.0 (± 19.5)		
1.EC/Pbr	52.5 (± 18.9)	53.7 (± 17.0)		
3.EC/Pbr	54.7 (± 19.0)	55.3 (± 19.6)		
Surgery	53.7 (± 20.9)	59.9 (± 19.5)		
Safety-FU	72.0 (± 15.4)	72.2 (± 15.5)		

Notes:

[2] - Only questionnaires with item information were considered for analysis.

[3] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Physical Functioning

End point title	Physical Functioning

End point description:

Physical Functioning subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks.

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[4]	39[5]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	93.1 (± 9.3)	92.7 (± 9.9)		
1.nbP/Pbr	91.2 (± 14.5)	90.9 (± 15.1)		
3.nbP/Pbr	76.2 (± 22.5)	76.1 (± 23.1)		
1.EC/Pbr	60.8 (± 25.0)	61.7 (± 23.1)		
3.EC/Pbr	61.6 (± 22.0)	61.2 (± 22.5)		
Surgery	67.2 (± 24.9)	67.4 (± 26.4)		
Safety-FU	82.0 (± 16.5)	81.7 (± 18.4)		

Notes:

[4] - Only questionnaires with item information were considered for analysis.

[5] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Role Functioning

End point title	Role Functioning

End point description:

Role funtioning subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[6]	39[7]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	84.0 (± 20.7)	88.1 (± 15.0)		

1.nbP/Pbr	84.8 (± 20.9)	84.8 (± 20.0)		
3.nbP/Pbr	60.2 (± 27.7)	60.3 (± 28.4)		
1.EC/Pbr	45.3 (± 29.4)	46.3 (± 29.6)		
3.EC/Pbr	43.2 (± 29.0)	43.4 (± 29.1)		
Surgery	48.8 (± 32.1)	51.6 (± 33.4)		
Safety-FU	68.5 (± 27.2)	67.9 (± 28.1)		

Notes:

[6] - Only questionnaires with item information were considered for analysis.

[7] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Emotional Functioning

End point title	Emotional Functioning

End point description:

Emotional functioning subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[8]	39[9]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	62.4 (± 18.3)	63.6 (± 19.7)		
1.nbP/Pbr	65.8 (± 23.2)	64.4 (± 23.6)		
3.nbP/Pbr	69.5 (± 19.6)	67.9 (± 19.0)		
1.EC/Pbr	65.7 (± 18.0)	64.8 (± 18.4)		
3.EC/Pbr	65.1 (± 20.0)	65.7 (± 20.3)		
Surgery	64.8 (± 23.2)	66.4 (± 23.5)		
Safety-FU	75.7 (± 19.6)	74.4 (± 19.9)		

Notes:

[8] - Only questionnaires with item information were considered for analysis.

[9] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Cognitive Functioning

End point title	Cognitive Functioning

End point description:

Cognitive functioning according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:
Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[10]	39[11]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	88.0 (± 16.3)	90.5 (± 14.5)		
1.nbP/Pbr	86.0 (± 19.3)	86.2 (± 20.4)		
3.nbP/Pbr	79.2 (± 25.2)	80.4 (± 26.1)		
1.EC/Pbr	71.7 (± 19.1)	72.2 (± 19.5)		
3.EC/Pbr	71.2 (± 26.2)	71.2 (± 26.4)		
Surgery	68.7 (± 25.9)	72.0 (± 23.3)		
Safety-FU	77.9 (± 24.5)	76.5 (± 25.4)		

Notes:
[10] - Only questionnaires with item information were considered for analysis.
[11] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Social Functioning

End point title	Social Functioning

End point description:
Social functioning subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:
Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[12]	39[13]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	71.3 (± 26.6)	71.4 (± 28.0)		
1.nbP/Pbr	78.8 (± 23.4)	76.2 (± 24.7)		
3.nbP/Pbr	61.4 (± 25.4)	59.8 (± 26.0)		
1.EC/Pbr	51.9 (± 28.7)	52.8 (± 27.5)		
3.EC/Pbr	53.2 (± 29.6)	53.0 (± 28.7)		
Surgery	54.2 (± 32.8)	52.2 (± 33.0)		
Safety-FU	69.8 (± 23.5)	66.7 (± 23.6)		

Notes:
[12] - Only questionnaires with item information were considered for analysis.
[13] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Fatigue

End point title	Fatigue

End point description:
Fatigue subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:
Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[14]	39[15]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	20.4 (± 14.6)	19.0 (± 15.0)		
1.nbP/Pbr	24.7 (± 20.0)	26.7 (± 19.7)		
3.nbP/Pbr	50.3 (± 25.0)	49.7 (± 25.3)		
1.EC/Pbr	59.2 (± 25.0)	59.0 (± 23.9)		
3.EC/Pbr	55.6 (± 25.9)	56.6 (± 27.0)		
Surgery	48.1 (± 30.2)	44.8 (± 29.5)		
Safety-FU	30.9 (± 23.7)	32.9 (± 25.1)		

Notes:
[14] - Only questionnaires with item information were considered for analysis.
[15] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Nausea and vomiting

End point title	Nausea and vomiting

End point description:
Nausea and vomiting subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:
Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[16]	39[17]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	1.9 (± 4.6)	0.8 (± 3.6)		
1.nbP/Pbr	1.5 (± 6.0)	1.0 (± 3.9)		
3.nbP/Pbr	12.1 (± 19.1)	11.8 (± 14.5)		
1.EC/Pbr	10.1 (± 19.6)	9.3 (± 17.1)		
3.EC/Pbr	18.5 (± 21.4)	19.7 (± 22.2)		
Surgery	11.7 (± 22.7)	11.8 (± 22.8)		
Safety-FU	5.4 (± 13.6)	6.8 (± 15.5)		

Notes:

[16] - Only questionnaires with item information were considered for analysis.

[17] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Pain

End point title	Pain
End point description: Pain subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[18]	39[19]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	18.0 (± 20.9)	15.1 (± 18.2)		
1.nbP/Pbr	17.0 (± 21.7)	18.6 (± 23.1)		
3.nbP/Pbr	22.3 (± 26.4)	22.5 (± 24.9)		
1.EC/Pbr	39.5 (± 28.2)	38.4 (± 25.5)		
3.EC/Pbr	36.9 (± 24.6)	36.4 (± 25.8)		
Surgery	32.1 (± 28.8)	29.6 (± 26.4)		
safety-FU	20.7 (± 23.4)	20.4 (± 25.5)		

Notes:

[18] - Only questionnaires with item information were considered for analysis.

[19] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Dyspnea

End point title	Dyspnea

End point description:

Dyspnea subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks.

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[20]	39[21]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	6.7 (± 16.7)	3.2 (± 10.0)		
1.nbP/Pbr	12.9 (± 21.8)	12.4 (± 23.0)		
3.nbP/Pbr	33.3 (± 29.1)	31.4 (± 28.4)		
1.EC/Pbr	38.8 (± 28.1)	35.2 (± 26.4)		
3.EC/Pbr	37.8 (± 29.6)	37.4 (± 28.6)		
Surgery	32.5 (± 28.7)	29.0 (± 28.2)		
Safety-FU	21.6 (± 30.6)	17.3 (± 31.2)		

Notes:

[20] - Only questionnaires with item information were considered for analysis.

[21] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Insomnia

End point title	Insomnia

End point description:

Insomnia subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[22]	39[23]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	33.3 (± 28.9)	30.2 (± 29.6)		
1.nbP/Pbr	32.6 (± 29.2)	33.3 (± 29.1)		
3.nbP/Pbr	39.4 (± 32.4)	42.2 (± 32.1)		
1.EC/Pbr	50.4 (± 34.4)	53.7 (± 33.1)		
3.EC/Pbr	38.7 (± 28.9)	38.4 (± 30.2)		
Surgery	40.0 (± 32.2)	40.9 (± 30.7)		
Safety-FU	36.9 (± 34.1)	39.5 (± 37.0)		

Notes:

[22] - Only questionnaires with item information were considered for analysis.

[23] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Appetite loss

End point title	Appetite loss

End point description:

Appetite loss subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[24]	39[25]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	6.7 (± 13.6)	4.8 (± 12.0)		
1.nbP/Pbr	7.6 (± 17.4)	8.6 (± 18.7)		
3.nbP/Pbr	22.0 (± 29.6)	18.6 (± 24.9)		
1.EC/Pbr	32.6 (± 31.3)	31.5 (± 30.8)		
3.EC/Pbr	36.0 (± 32.8)	37.4 (± 34.1)		
Surgery	34.2 (± 38.1)	32.3 (± 39.0)		
Safety-FU	11.7 (± 23.9)	11.1 (± 24.5)		

Notes:

[24] - Only questionnaires with item information were considered for analysis.

[25] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Constipation

End point title	Constipation
End point description: Constipation subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[26]	39[27]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	0.0 (± 0.0)	0.0 (± 0.0)		
1.nbP/Pbr	5.3 (± 16.0)	5.7 (± 17.1)		
3.nbP/Pbr	12.1 (± 22.8)	15.7 (± 24.9)		
1.EC/Pbr	14.7 (± 25.5)	15.7 (± 25.8)		
3.EC/Pbr	12.6 (± 19.8)	11.1 (± 17.8)		
Surgery	12.5 (± 26.9)	14.0 (± 28.3)		
Safety-FU	9.0 (± 18.7)	11.1 (± 20.7)		

Notes:

[26] - Only questionnaires with item information were considered for analysis.

[27] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Diarrhea

End point title	Diarrhea
End point description: Diarrhea subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[28]	39[29]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	12.0 (± 16.3)	11.1 (± 16.1)		
1.nbP/Pbr	7.6 (± 14.1)	8.6 (± 14.8)		
3.nbP/Pbr	18.6 (± 31.1)	15.7 (± 26.3)		

1.EC/Pbr	11.6 (± 17.6)	11.1 (± 17.8)		
3.EC/Pbr	17.1 (± 24.4)	15.2 (± 23.7)		
Surgery	15.0 (± 30.1)	15.1 (± 29.6)		
Safety-FU	7.2 (± 19.5)	4.9 (± 20.1)		

Notes:

[28] - Only questionnaires with item information were considered for analysis.

[29] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Financial difficulties

End point title	Financial difficulties

End point description:

Financial difficulties subscale according to EORTC-QLQ-C30

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[30]	39[31]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	10.7 (± 18.6)	11.1 (± 19.2)		
1.nbP/Pbr	15.2 (± 25.4)	16.2 (± 27.3)		
3.nbP/Pbr	21.2 (± 27.0)	19.6 (± 27.4)		
1. EC/Pbr	22.5 (± 28.8)	20.4 (± 27.9)		
3. EC/Pbr	18.0 (± 24.3)	16.2 (± 25.2)		
Surgery	18.3 (± 22.6)	16.1 (± 20.9)		
Safety-FU	18.9 (± 27.8)	14.8 (± 23.3)		

Notes:

[30] - Only questionnaires with item information were considered for analysis.

[31] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Body Image

End point title	Body Image

End point description:

Body image subscale according to EORTC-QLQ-BR23

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[32]	39[33]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	91.0 (± 17.0)	92.9 (± 10.6)		
1.nbP/Pbr	85.9 (± 15.8)	86.5 (± 13.6)		
3.nbP/Pbr	70.5 (± 26.2)	68.1 (± 26.6)		
1.EC/Pbr	67.5 (± 25.3)	66.7 (± 25.1)		
3.EC/Pbr	69.4 (± 22.6)	69.4 (± 22.4)		
Surgery	69.9 (± 25.8)	69.9 (± 24.3)		
Safety-FU	82.2 (± 18.8)	84.6 (± 16.8)		

Notes:

[32] - Only questionnaires with item information were considered for analysis.

[33] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Sexual functioning

End point title	Sexual functioning
End point description:	
Sexual functioning subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe:	
Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[34]	39[35]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	29.2 (± 29.2)	26.7 (± 28.8)		
1.nbP/Pbr	30.2 (± 27.1)	26.8 (± 25.7)		
3.nbP/Pbr	20.2 (± 22.3)	13.5 (± 17.7)		
1.EC/Pbr	11.5 (± 18.2)	11.0 (± 18.1)		
3.EC/Pbr	12.5 (± 17.5)	11.5 (± 17.7)		
Surgery	11.1 (± 16.8)	6.7 (± 12.1)		
Safety-FU	27.0 (± 22.7)	26.5 (± 24.1)		

Notes:

[34] - Only questionnaires with item information were considered for analysis.

[35] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Sexual enjoyment

End point title	Sexual enjoyment

End point description:

Sexual enjoyment subscale according to EORTC-QLQ-BR23

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[36]	39[37]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	78.8 (± 27.0)	79.2 (± 24.8)		
1.nbP/Pbr	77.8 (± 24.3)	73.3 (± 25.8)		
3.nbP/Pbr	75.0 (± 22.8)	74.1 (± 22.2)		
1.EC/Pbr	50.0 (± 23.6)	58.3 (± 15.4)		
3.EC/Pbr	51.5 (± 34.5)	58.3 (± 38.8)		
Surgery	56.7 (± 27.4)	46.7 (± 29.8)		
Safety-FU	70.2 (± 27.0)	74.4 (± 27.7)		

Notes:

[36] - Only questionnaires with item information were considered for analysis.

[37] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Future Perspective

End point title	Future Perspective

End point description:

Future perspective subscale according to EORTC-QLQ-BR23

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[38]	39[39]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	36.0 (± 30.3)	38.1 (± 30.3)		
1.nbP/Pbr	41.7 (± 30.6)	43.8 (± 30.0)		
3.nbP/Pbr	41.7 (± 25.0)	40.2 (± 24.3)		
1.EC/Pbr	42.1 (± 28.6)	40.7 (± 28.9)		
3.EC/Pbr	40.5 (± 25.0)	40.4 (± 26.0)		
Surgery	45.8 (± 23.5)	47.3 (± 20.7)		
Safety-FU	55.0 (± 28.6)	56.8 (± 24.1)		

Notes:

[38] - Only questionnaires with item information were considered for analysis.

[39] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Therapy Side Effects

End point title	Systemic Therapy Side Effects

End point description:

Systemic therapy side effects subscale according to EORTC-QLQ-BR23

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[40]	39[41]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	7.2 (± 6.8)	7.5 (± 7.2)		
1.nbP/Pbr	9.2 (± 9.9)	10.1 (± 10.0)		
3.nbP/Pbr	41.7 (± 15.9)	41.1 (± 16.8)		
1.EC/Pbr	43.9 (± 14.2)	44.0 (± 15.1)		
3.EC/Pbr	43.5 (± 14.0)	44.3 (± 14.4)		
Surgery	33.7 (± 18.2)	30.4 (± 17.6)		
Safety-FU	25.2 (± 16.7)	25.0 (± 16.8)		

Notes:

[40] - Only questionnaires with item information were considered for analysis.

[41] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Breast Symptoms

End point title	Breast Symptoms
End point description:	
Breast symptoms subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe:	
Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[42]	39[43]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	12.7 (± 14.5)	13.1 (± 14.6)		
1.nbP/Pbr	16.1 (± 18.4)	16.2 (± 17.1)		
3.nbP/Pbr	7.8 (± 10.4)	7.6 (± 10.1)		
1.EC/Pbr	11.7 (± 12.1)	12.3 (± 10.7)		
3.EC/Pbr	11.3 (± 12.6)	10.4 (± 12.3)		
Surgery	12.6 (± 15.9)	11.7 (± 15.1)		
Safety-FU	24.8 (± 21.4)	27.0 (± 23.2)		

Notes:

[42] - Only questionnaires with item information were considered for analysis.

[43] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Arm Symptoms

End point title	Arm Symptoms
End point description:	
Arm symptoms subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe:	
Every 6 weeks	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[44]	39[45]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	20.4 (± 15.9)	21.7 (± 15.1)		
1.nbP/Pbr	18.4 (± 18.4)	19.4 (± 18.5)		
3.nbP/Pbr	14.9 (± 19.2)	12.4 (± 14.9)		

1.EC/Pbr	16.8 (± 23.0)	16.7 (± 20.1)		
3.EC/Pbr	19.6 (± 15.6)	19.6 (± 16.3)		
Surgery	18.7 (± 20.7)	18.7 (± 18.4)		
Safety-FU	18.0 (± 18.2)	18.1 (± 19.3)		

Notes:

[44] - Only questionnaires with item information were considered for analysis.

[45] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Upset by Hair Loss

End point title	Upset by Hair Loss

End point description:

Upset by hair loss subscale according to EORTC-QLQ-BR23

End point type	Secondary

End point timeframe:

Every 6 weeks

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50[46]	39[47]		
Units: score on scale				
arithmetic mean (standard deviation)				
Pbr	0.0 (± 0.0)	0.0 (± 0.0)		
1.nbP/Pbr	0.8 (± 5.0)	1.0 (± 5.6)		
3.nbP/Pbr	54.8 (± 31.1)	57.3 (± 28.4)		
1.EC/Pbr	41.0 (± 35.4)	40.6 (± 34.6)		
3.EC/Pbr	30.4 (± 32.2)	32.2 (± 32.1)		
Surgery	20.4 (± 35.0)	16.0 (± 31.2)		
Safety-FU	11.7 (± 26.3)	6.2 (± 22.7)		

Notes:

[46] - Only questionnaires with item information were considered for analysis.

[47] - Only questionnaires with item information were considered for analysis.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: pCR rate

End point title	pCR rate

End point description:

ypT0 ypN0

End point type	Other pre-specified

End point timeframe:

Final surgery

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	39		
Units: percent				
number (confidence interval 95%)	62.0 (47.2 to 75.3)	66.7 (49.8 to 80.9)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Influence of Initiation boost with pembrolizumab on pCR

End point title	Influence of Initiation boost with pembrolizumab on pCR
End point description: Influence of Initiation boost with pembrolizumab on pCR (ypT0/is ypN0)	
End point type	Other pre-specified
End point timeframe: Final surgery	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	39		
Units: percent				
number (confidence interval 95%)				
Initiation boost	59.3 (38.8 to 77.6)	65.2 (42.7 to 83.6)		
No initiation boost	73.9 (51.6 to 89.8)	81.2 (54.4 to 96.0)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Influence of Initiation boost with pembrolizumab on pCR

End point title	Influence of Initiation boost with pembrolizumab on pCR
End point description: Influence of Initiation boost with pembrolizumab on pCR (ypT0 ypN0)	
End point type	Other pre-specified
End point timeframe: Final surgery	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	39		
Units: percent				
number (confidence interval 95%)				
Initiation boost	55.6 (35.3 to 74.5)	60.9 (38.5 to 80.3)		
No initiation boost	69.6 (47.1 to 86.8)	75.0 (47.6 to 92.7)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: pCR rates (ypT0/is ypN0) according to CPS score

End point title	pCR rates (ypT0/is ypN0) according to CPS score

End point description:

End point type	Post-hoc

End point timeframe:

Final surgery

End point values	nab-paclitaxel/pembrolizumab followed by EC/pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: percent				
number (confidence interval 95%)				
<1	42.9 (9.9 to 81.6)			
>=1	69.2 (52.4 to 83.0)			
>=10	68.2 (45.1 to 86.1)			
>=20	80.0 (44.4 to 97.5)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: pCR rates (ypT0 ypN0) according to CPS score

End point title	pCR rates (ypT0 ypN0) according to CPS score

End point description:

End point type	Post-hoc

End point timeframe:

Final surgery

End point values	nab-paclitaxel/pembrolizumab followed by EC/pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: percent				
number (confidence interval 95%)				
<1	42.9 (9.9 to 81.6)			
>=1	66.7 (49.8 to 80.9)			
>=10	68.2 (45.1 to 86.1)			
>=20	80.0 (44.4 to 97.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Time of signing ICF until 30 days after cessation of treatment or until last study visit,whichever period is longer.	
Adverse event reporting additional description:	
Adverse events are reported separately for nab-paclitaxel and pembrolizumab	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	nab-Paclitaxel
Reporting group description:	
Patients were considered for safety analysis if they had received at least one dose of IP nab-paclitaxel.	
Reporting group title	Pembrolizumab
Reporting group description:	
Patients were considered for safety analysis if they had received at least one dose of IP pembrolizumab.	

Serious adverse events	nab-Paclitaxel	Pembrolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 53 (62.26%)	33 / 53 (62.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences causally related to treatment / all	3 / 4	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			

alternative assessment type: Systematic			
subjects affected / exposed	8 / 53 (15.09%)	8 / 53 (15.09%)	
occurrences causally related to treatment / all	1 / 9	3 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	1 / 4	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Autoimmune disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			

alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	1 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphonia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
alternative assessment type:			

Systematic			
subjects affected / exposed	6 / 53 (11.32%)	6 / 53 (11.32%)	
occurrences causally related to treatment / all	1 / 8	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences causally related to treatment / all	1 / 4	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
alternative assessment type:			

Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malabsorption			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomach pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash acneiform			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders - Other, specify			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	0 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter related infection			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	2 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	2 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	nab-Paclitaxel	Pembrolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 53 (100.00%)	53 / 53 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Vascular disorders			
Hot flashes			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 53 (20.75%)	11 / 53 (20.75%)	
occurrences (all)	11	11	
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Lymphedema			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Phlebitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Thromboembolic event			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Surgical and medical procedures			
Surgical and medical procedures - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
General disorders and administration site conditions			

Chills			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	6	6	
Edema limbs			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	4	4	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 53 (54.72%)	29 / 53 (54.72%)	
occurrences (all)	31	31	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Flu like symptoms			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 53 (13.21%)	7 / 53 (13.21%)	
occurrences (all)	8	8	
General disorders and administration site conditions - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Infusion related reaction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Localized edema			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Pain			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Reproductive system and breast disorders			
Breast pain			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 53 (9.43%)	5 / 53 (9.43%)	
occurrences (all)	6	6	
Respiratory, thoracic and mediastinal disorders			
Allergic rhinitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	5	5	
Dyspnea			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Epistaxis			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 53 (11.32%)	6 / 53 (11.32%)	
occurrences (all)	6	6	
Nasal congestion			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Productive cough			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders - Other, specify			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Psychiatric disorders			
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	2	2	
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 53 (20.75%)	11 / 53 (20.75%)	
occurrences (all)	11	11	
Psychiatric disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 53 (9.43%)	5 / 53 (9.43%)	
occurrences (all)	5	5	
Alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 53 (9.43%)	5 / 53 (9.43%)	
occurrences (all)	5	5	
Electrocardiogram QT corrected interval prolonged			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
International normalised ratio increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Investigations - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Lymphocyte count increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 53 (50.94%)	27 / 53 (50.94%)	
occurrences (all)	35	35	
Platelet count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Weight loss			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
White blood cell decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Left ventricular systolic dysfunction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Palpitations			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Sinus tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Nervous system disorders			
Concentration impairment			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 53 (9.43%)	5 / 53 (9.43%)	
occurrences (all)	8	8	
Dysgeusia			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 53 (22.64%)	12 / 53 (22.64%)	
occurrences (all)	12	12	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 53 (16.98%)	9 / 53 (16.98%)	
occurrences (all)	11	11	
Hypersomnia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Nervous system disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 53 (11.32%)	6 / 53 (11.32%)	
occurrences (all)	7	7	
Peripheral sensory neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	28 / 53 (52.83%)	28 / 53 (52.83%)	
occurrences (all)	28	28	
Presyncope			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Anemia			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 53 (18.87%)	10 / 53 (18.87%)	
occurrences (all)	12	12	
Blood and lymphatic system disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	4	4	
Febrile neutropenia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Leukocytosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Thrombotic thrombocytopenic purpura			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Ear and labyrinth disorders			
Hearing impaired			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Tinnitus			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Vertigo			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Eye disorders			
Blurred vision			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Dry eye			
alternative assessment type: Systematic			

subjects affected / exposed	5 / 53 (9.43%)	5 / 53 (9.43%)	
occurrences (all)	5	5	
Eye disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Floaters			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Retinal vascular disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Watering eyes			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	4	4	
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 53 (15.09%)	8 / 53 (15.09%)	
occurrences (all)	9	9	
Diarrhea			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 53 (20.75%)	11 / 53 (20.75%)	
occurrences (all)	13	13	
Esophageal pain			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Gastroesophageal reflux disease			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	4	4	
Hemorrhoids			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Mucositis oral			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 53 (26.42%)	14 / 53 (26.42%)	
occurrences (all)	18	18	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 53 (39.62%)	21 / 53 (39.62%)	
occurrences (all)	22	22	
Periodontal disease			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Small intestinal mucositis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Stomach pain			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	5	5	

Hepatobiliary disorders			
Hepatobiliary disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 53 (28.30%)	15 / 53 (28.30%)	
occurrences (all)	15	15	
Bullous dermatitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Dry skin			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	4	4	
Erythema multiforme			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Nail discoloration			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Nail loss			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Nail ridging			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Pain of skin			

alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Rash acneiform			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 53 (11.32%)	6 / 53 (11.32%)	
occurrences (all)	6	6	
Skin and subcutaneous tissue disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 53 (35.85%)	19 / 53 (35.85%)	
occurrences (all)	20	20	
Skin hyperpigmentation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Skin ulceration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Renal and urinary disorders - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Endocrine disorders			

Hyperparathyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Hyperthyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	4	4	
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 53 (7.55%)	4 / 53 (7.55%)	
occurrences (all)	4	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	5	5	
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 53 (15.09%)	8 / 53 (15.09%)	
occurrences (all)	8	8	
Bone pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Generalized muscle weakness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Joint effusion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Muscle weakness lower limb			
alternative assessment type:			

Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorder - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 53 (9.43%)	5 / 53 (9.43%)	
occurrences (all)	5	5	
Neck pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	4	4	
Infections and infestations			
Breast infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Catheter related infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Infections and infestations - Other, specify			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Paronychia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Rhinitis infective			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Sinusitis			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Skin infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Tooth infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
Upper respiratory infection			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 53 (5.66%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 53 (3.77%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
Metabolism and nutrition disorders			
Anorexia			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 53 (13.21%)	7 / 53 (13.21%)	
occurrences (all)	7	7	
Hypocalcaemia			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	1 / 53 (1.89%) 1	1 / 53 (1.89%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2018	Changes to the protocol included the addition of ECG and electrocardiography to be performed during the safety-follow-up visit. Also the collection of fecal samples was added to the exploratory trial objectives. With the publication of IB version 15 of pembrolizumab the recommendations for treating immune-related adverse events were updated. This was reflected in the trial protocol.
10 October 2018	The treatment plan was amended that all patients enrolled into the trial after the 25th patient had started trial treatment would receive one additional dose of pembrolizumab 200 mg q21d as initiation boost before receiving 12 doses of weekly nab-paclitaxel intravenous (i.v.) 125 mg/m² BSA in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w; followed by 4 cycles of epirubicin i.v. 90 mg/m² BSA and cyclophosphamide i.v. 600 mg/m² BSA, q3w in combination with 4 cycles of pembrolizumab i.v. 200 mg q3w. Additional biomaterial (blood, fresh tissue tumor sample, stool sample) was collected after this initiation boost. The comparison of patients receiving the initiation boost vs. patients without initiation boost was added to the exploratory study objectives.
07 November 2018	The changes regarded a prolongation of the safety follow-up period from 30 days to 120 days as recommended by the IEC. Also response evaluation was updated to reflect inflammatory carcinomas.
11 March 2019	Brexit-related changes to IMPD.
12 August 2019	Administrative changes due to Brexit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 August 2018	Recruitment interruption due to preparation of Amendment A03	10 December 2018

Notes:

Limitations and caveats

None reported