Clinical trial results:
Phase 1/2 Study to Evaluate the Safety and Preliminary Efficacy of Nivolumab Combined with Daratumumab in Participants with Advanced or Metastatic Solid Tumors

Summary

EudraCT number	2017-000367-33
Trial protocol	DE ES FR IT
Global end of trial date	02 July 2020

Results information

Result version number	v1 (current)
This version publication date	18 July 2021
First version publication date	18 July 2021

Trial information

Trial identification

Sponsor protocol code	CA209-9GW

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	15 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2020
Global end of trial reached?	Yes
Global end of trial date	02 July 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish the tolerability of the combination of Nivolumab and Daratumumab in participants with advanced or metastatic solid tumors.

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 subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 28
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Switzerland: 12
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	Italy: 10
Worldwide total number of subjects	105
EEA total number of subjects	64

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)	74
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

105 participants treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nivolumab + Daratumumab (TNBC)

Arm description:

Triple-negative breast cancer (TNBC) treated with Triple-negative breast cancer (TNBC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)

Arm type	Experimental
Investigational medicinal product name	Nivolumab+Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)

Arm title	Nivolumab + Daratumumab (NSCLC)

Arm description:

Non-small cell lung cancer (NSCLC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)

Arm type	Experimental
Investigational medicinal product name	Nivolumab+Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)

Arm title	Nivolumab + Daratumumab (PAC)

Arm description:

Pancreatic adenocarcinoma cancer (PAC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)

Arm type	Experimental

Investigational medicinal product name	Nivolumab+Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)

Number of subjects in period 1	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)
Started	41	21	43
Completed	0	1	0
Not completed	41	20	43
Adverse event, serious fatal	1	-	-
Adverse Event unrelated to Study Drug	6	-	1
Other reasons	2	-	-
Study Drug Toxicity	2	1	-
Disease Progression	30	19	41
Administrative reason by sponsor	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Nivolumab + Daratumumab (TNBC)
Reporting group description:	
Triple-negative breast cancer (TNBC) treated with Triple-negative breast cancer (TNBC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	
Reporting group title	Nivolumab + Daratumumab (NSCLC)
Reporting group description:	
Non-small cell lung cancer (NSCLC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	
Reporting group title	Nivolumab + Daratumumab (PAC)
Reporting group description:	
Pancreatic adenocarcinoma cancer (PAC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	

Reporting group values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)
Number of subjects	41	21	43
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	17	26
From 65-84 years	10	4	17
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	55.1	59.5	61.9
standard deviation	± 13.1	± 8.5	± 9.4
Sex: Female, Male Units: Participants			
Female	41	7	20
Male	0	14	23
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	33	21	35
More than one race	0	0	0
Other	5	0	8

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	20	3	21
Unknown or Not Reported	20	18	22

Reporting group values	Total		
Number of subjects	105		
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)	74		
From 65-84 years	31		
85 years and over	0		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Participants			
Female	68		
Male	37		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	89		
More than one race	0		
Other	13		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	44		
Unknown or Not Reported	60		

End points

End points reporting groups

Reporting group title	Nivolumab + Daratumumab (TNBC)
Reporting group description:	
Triple-negative breast cancer (TNBC) treated with Triple-negative breast cancer (TNBC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	
Reporting group title	Nivolumab + Daratumumab (NSCLC)
Reporting group description:	
Non-small cell lung cancer (NSCLC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	
Reporting group title	Nivolumab + Daratumumab (PAC)
Reporting group description:	
Pancreatic adenocarcinoma cancer (PAC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[1]
End point description:	
Number of participants with any grade of adverse events (AEs) graded by Common Terminology Criteria for Adverse Events (CTCAE v4.0) to determine the safety and tolerability of Nivolumab and Daratumumab	
End point type	Primary
End point timeframe:	
From first dose to 30 days post last dose (up to 34 months)	

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: Only summary statistics planned for this endpoint

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	21	43	
Units: Participants	41	21	42	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants with Serious Adverse Events (SAEs)[2]
End point description:	
Number of participants with any grade of serious adverse events (SAEs) graded by Common Terminology Criteria for Adverse Events (CTCAE v4.0) to determine the safety and tolerability of Nivolumab and Daratumumab	
End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to 34 months)

Notes:

[2] - 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: Only summary statistics planned for this endpoint

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	21	43	
Units: Participants	29	14	29	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Laboratory Abnormalities in Specific Liver Tests

End point title	Number of Participants with Laboratory Abnormalities in Specific Liver Tests[3]

End point description:

Number of participants with laboratory abnormalities in specific liver tests based on US conventional units to determine the safety and tolerability of Nivolumab and Daratumumab. The number of participants with the following laboratory abnormalities from on-treatment evaluations will be summarized: - ALT or AST > 3 x ULN, > 5 x ULN, > 10 x ULN and > 20 x ULN - Total bilirubin > 2 x ULN - ALP > 1.5 x ULN - Concurrent (within 1 day) ALT or AST > 3 x ULN and total bilirubin > 1.5 x ULN - Concurrent (within 30 days) ALT or AST > 3 x ULN and total bilirubin > 1.5 x ULN - Concurrent (within 1 day) ALT or AST > 3 x ULN and total bilirubin > 2 x ULN - Concurrent (within 30 days) ALT or AST > 3 x ULN and total bilirubin > 2 x ULN

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to 34 months)

Notes:

[3] - 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: Only summary statistics planned for this endpoint

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	21	43	
Units: Participants				
ALT OR AST > 3XULN	6	2	10	
ALT OR AST > 5XULN	5	2	6	
ALT OR AST > 10XULN	2	1	3	
ALT OR AST > 20XULN	0	0	0	
TOTAL BILIRUBIN > 2XULN	1	1	8	
ALP > 1.5XULN	10	5	34	
ALT/AST ELEV>3XULN WITH TTL BILI>1.5XULN w/ 1 DAY	1	1	5	

ALT/AST ELEV>3XULN w/ TTL BILI>1.5XULN w/ 30 DAYS	1	1	5	
ALT/AST ELEV>3XULN WITH TOTAL BILI>2XULN w/ 1 DAY	1	1	5	
ALT/AST ELEV>3XULN w/ TOTAL BILI>2XULN w/ 30 DAYS	1	1	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Laboratory Abnormalities in Specific Thyroid Tests

End point title	Number of Participants with Laboratory Abnormalities in Specific Thyroid Tests[4]

End point description:

Number of participants with laboratory abnormalities in specific thyroid tests based on US conventional units to determine the safety and tolerability of Nivolumab and Daratumumab. The number of subjects with the following laboratory abnormalities from on-treatment evaluations will be summarized: - TSH value > ULN and - with baseline TSH value <= ULN - with at least one FT3/FT4 test value < LLN within 2-week window after the abnormal TSH test - with all FT3/FT4 test values >= LLN within 2-week window after the abnormal TSH test - with FT3/FT4 missing within 2-week window after the abnormal TSH test. - TSH < LLN and - with baseline TSH value >= LLN - with at least one FT3/FT4 test value > ULN within 2-week window after the abnormal TSH test - with all FT3/FT4 test values <= ULN within 2-week window after the abnormal TSH test - with FT3/FT4 missing within 2-week window after the abnormal TSH test

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to 34 months)

Notes:

[4] - 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: Only summary statistics planned for this endpoint

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	15	21	
Units: Participants				
TSH > ULN	4	3	4	
TSH>ULN w/ TSH<=ULN AT BASELINE	4	3	2	
TSH>ULN w/ AT LEAST ONE FT3/FT4 TEST VALUE<LLN	1	1	3	
TSH>ULN w/ ALL OTHER FT3/FT4 TEST VALUES>=LLN	2	2	0	
TSH>ULN w/ FT3/FT4 TEST MISSING	1	0	1	
TSH < LLN	1	2	2	
TSH<LLN w/ TSH>=LLN AT BASELINE	1	2	1	
TSH<LLN w/ AT LEAST ONE FT3/FT4 TEST VALUE>ULN	1	0	0	
TSH<LLN w/ ALL OTHER FT3/FT4 TEST VALUES<=ULN	0	2	1	
TSH<LLN w/ FT3/FT4 TEST MISSING	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Laboratory Results of Worst CTC Grade

End point title	Number of Participants with Laboratory Results of Worst CTC Grade[5]

End point description:

Number of participants with laboratory test results of worst (CTC v4.0) grades 0-4 to determine the safety and tolerability of Nivolumab and Daratumumab

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to 34 months)

Notes:

[5] - 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: Only summary statistics planned for this endpoint

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	21	43	
Units: Participants				
Hemoglobin Grade 0	13	5	5	
Hemoglobin Grade 1	14	9	23	
Hemoglobin Grade 2	7	7	12	
Hemoglobin Grade 3	5	0	3	
Hemoglobin Not Reported	2	0	0	
Platelet Count Grade 0	29	16	24	
Platelet Count Grade 1	4	4	18	
Platelet Count Grade 2	0	0	0	
Platelet Count Grade 3	1	1	1	
Platelet Count Grade 4	5	0	0	
Platelet Count Not Reported	2	0	0	
Leukocytes Grade 0	27	18	35	
Leukocytes Grade 1	7	1	3	
Leukocytes Grade 2	4	1	5	
Leukocytes Grade 3	1	1	0	
Leukocytes Grade 4	0	0	0	
Leukocytes Not Reported	2	0	0	
Alkaline Phosphatase Grade 0	23	13	6	
Alkaline Phosphatase Grade 1	7	4	11	
Alkaline Phosphatase Grade 2	4	1	13	
Alkaline Phosphatase Grade 3	2	3	13	
Alkaline Phosphatase Grade 4	0	0	0	
Alkaline Phosphatase Not Reported	5	0	0	

Aspartate Aminotransferase Grade 0	16	16	20	
Aspartate Aminotransferase Grade 1	15	3	13	
Aspartate Aminotransferase Grade 2	2	1	5	
Aspartate Aminotransferase Grade 3	4	1	5	
Aspartate Aminotransferase Grade 4	0	0	0	
Aspartate Aminotransferase Not Reported	4	0	0	
Alanine Aminotransferase Grade 0	19	12	19	
Alanine Aminotransferase Grade 1	15	6	19	
Alanine Aminotransferase Grade 2	1	0	1	
Alanine Aminotransferase Grade 3	2	2	4	
Alanine Aminotransferase Grade 4	0	0	0	
Alanine Aminotransferase Not Reported	4	1	0	
Bilirubin Grade 0	30	18	30	
Bilirubin Grade 1	5	1	4	
Bilirubin Grade 2	0	1	3	
Bilirubin Grade 3	1	1	6	
Bilirubin Grade 4	0	0	0	
Bilirubin Not Reported	5	0	0	
Creatinine Grade 0	30	15	38	
Creatinine Grade 1	5	5	4	
Creatinine Grade 2	1	1	0	
Creatinine Grade 3	0	0	0	
Creatinine Grade 4	0	0	0	
Creatinine Not Reported	5	0	1	
Phosphorous Grade 0	29	15	33	
Phosphorous Grade 1	0	0	2	
Phosphorous Grade 2	4	5	4	
Phosphorous Grade 3	2	1	3	
Phosphorous Grade 4	0	0	0	
Phosphorous Not Reported	6	0	1	
Albumin Grade 0	15	15	15	
Albumin Grade 1	13	4	14	
Albumin Grade 2	6	2	12	
Albumin Grade 3	0	0	1	
Albumin Grade 4	0	0	0	
Albumin Not Reported	7	0	1	
Amylase Grade 0	9	5	36	
Amylase Grade 1	1	2	1	
Amylase Grade 2	0	1	0	
Amylase Grade 3	0	0	1	
Amylase Grade 4	0	0	0	
Amylase Not Reported	31	13	5	
Lipase Grade 0	15	6	31	
Lipase Grade 1	1	1	5	
Lipase Grade 2	0	1	1	
Lipase Grade 3	0	0	3	
Lipase Grade 4	0	0	1	
Lipase Not Reported	25	13	2	
Hypernatremia Grade 0	35	20	42	
Hypernatremia Grade 1	1	0	0	
Hypernatremia Grade 2	0	0	0	

Hypernatremia Grade 3	0	0	0	
Hypernatremia Grade 4	0	0	0	
Hypernatremia Not Reported	5	1	1	
Hyponatremia Grade 0	23	12	20	
Hyponatremia Grade 1	12	7	15	
Hyponatremia Grade 2	0	0	0	
Hyponatremia Grade 3	1	1	7	
Hyponatremia Grade 4	0	0	0	
Hyponatremia Not Reported	5	1	1	
Hyperkalemia Grade 0	30	17	35	
Hyperkalemia Grade 1	4	3	5	
Hyperkalemia Grade 2	3	0	1	
Hyperkalemia Grade 3	0	0	1	
Hyperkalemia Grade 4	0	0	0	
Hyperkalemia Not Reported	4	1	1	
Hypokalemia Grade 0	33	19	33	
Hypokalemia Grade 1	4	1	6	
Hypokalemia Grade 2	0	0	0	
Hypokalemia Grade 3	0	0	3	
Hypokalemia Grade 4	0	0	0	
Hypokalemia Not Reported	4	1	1	
Hypercalcemia Grade 0	33	16	42	
Hypercalcemia Grade 1	2	4	0	
Hypercalcemia Grade 2	0	1	0	
Hypercalcemia Grade 3	0	0	0	
Hypercalcemia Grade 4	0	0	0	
Hypercalcemia Not Reported	6	0	1	
Hypocalcemia Grade 0	25	14	15	
Hypocalcemia Grade 1	8	7	21	
Hypocalcemia Grade 2	2	0	6	
Hypocalcemia Grade 3	0	0	0	
Hypocalcemia Grade 4	0	0	0	
Hypocalcemia Not Reported	6	0	1	
Hypermagnesemia Grade 0	34	21	40	
Hypermagnesemia Grade 1	1	0	2	
Hypermagnesemia Grade 2	0	0	0	
Hypermagnesemia Grade 3	0	0	0	
Hypermagnesemia Grade 4	0	0	0	
Hypermagnesemia Not Reported	6	0	1	
Hypomagnesemia Grade 0	33	17	38	
Hypomagnesemia Grade 1	2	4	4	
Hypomagnesemia Grade 2	0	0	0	
Hypomagnesemia Grade 3	0	0	0	
Hypomagnesemia Grade 4	0	0	0	
Hypomagnesemia Not Reported	6	0	1	
Hyperglycemia Grade 0	10	1	7	
Hyperglycemia Grade 1	9	4	6	
Hyperglycemia Grade 2	0	1	1	
Hyperglycemia Grade 3	0	0	1	
Hyperglycemia Grade 4	0	0	0	
Hyperglycemia Not Reported	22	15	28	
Hypoglycemia Grade 0	19	6	14	

Hypoglycemia Grade 1	0	0	1	
Hypoglycemia Grade 2	0	0	1	
Hypoglycemia Grade 3	0	0	0	
Hypoglycemia Grade 4	0	0	0	
Hypoglycemia Not Reported	22	15	27	

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

Objective response rate (ORR) is defined as the percentage of treated participants who achieve a best response of complete response (CR) or partial response (PR) based on investigator assessments (using RECIST v1.1 criteria)

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	21	43	
Units: Percentage of Participants				
number (confidence interval 95%)	4.9 (0.6 to 16.5)	9.5 (1.2 to 30.4)	0 (0.0 to 8.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Duration of response (DOR) is defined as the time between the date of first documented response (Complete response or partial response) to the date of the first documented tumor progression as determined by Investigator (per RECIST v1.1 criteria), or death due to any cause, whichever occurs first

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	2	0[6]	
Units: Months				
median (confidence interval 95%)	4.17 (00000 to 99999)	9.40 (7.72 to 11.07)	(to)	

Notes:

[6] - There were no patients with BOR in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR)

End point title	Best Overall Response (BOR)

End point description:

Best overall response (BOR) is defined as the best response, as determined by Investigator, recorded between the date of first dose and the date of objectively documented progression per RECIST v1.1 criteria or the date of subsequent therapy, whichever occurs first.

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	21	43	
Units: Participants				
Complete Response (CR)	0	0	0	
Partial Response (PR)	2	2	0	
Stable Disease (SD)	8	10	9	
Progressive Disease (PD)	22	9	31	
Unable to Determine (UTD)	9	0	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Progression Free Survival (PFS) is defined as the time between the date of treatment start day and the date of first documented tumor progression, based on Investigator assessments (per RECIST v1.1 criteria), or death due to any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	21	43	
Units: Months				
median (confidence interval 95%)	1.22 (1.15 to 1.41)	4.85 (1.12 to 7.69)	1.22 (1.15 to 1.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Nivolumab Serum Concentrations

End point title	Nivolumab Serum Concentrations

End point description:

Pharmacokinetics (PK) assessed using serum concentration data for Nivolumab

End point type	Secondary

End point timeframe:

From day 1 to follow-up 2 (up to 36 months)

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12[7]	11[8]	16[9]	
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 3 Day 1	52.9 (± 34.8)	43.5 (± 26.6)	42.5 (± 29.7)	
Cycle 4 Day 1	87.0 (± 34.0)	77.9 (± 37.6)	64.3 (± 31.4)	
Cycle 7 Day 1	44.8 (± 32.8)	116.2 (± 23.8)	83.3 (± 99999)	
Cycle 11 Day 1	99999 (± 99999)	124.3 (± 46.5)	99999 (± 99999)	
Follow-up 1	48.9 (± 44.0)	71.6 (± 58.9)	32.8 (± 48.6)	
Follow-up 2	23.5 (± 60.6)	17.4 (± 96.1)	6.3 (± 89.7)	

Notes:

[7] - cycle 3=12 subjects cycle 4=6 subjects cycle 7=2 subjects FU1=7 subjects FU2=5 subjects

[8] - cycle3=11subjects cycle4=11subjects cycle7=8subjects cycle11=4subjects FU1=7subjects FU2=3subjects

[9] - cycle 3=16 subjects cycle 4=5 subjects cycle 7=1 subjects FU1=9 subjects FU2=4 subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Daratumumab Serum Concentrations

End point title	Daratumumab Serum Concentrations

End point description:

Pharmacokinetics (PK) assessed using serum concentration data for Daratumumab

End point type	Secondary

End point timeframe:

From day 1 to follow-up 2 (up to 36 months)

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[10]	21[11]	38[12]	
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (hour 8)	334.1819 (± 28.1)	310.7272 (± 15.6)	277.6708 (± 28.4)	
Cycle 2 Day 1 (hour 0)	332.9353 (± 29.6)	321.6084 (± 25.7)	275.1521 (± 35.9)	
Cycle 2 Day 1 (hour 4)	735.2131 (± 36.9)	641.8146 (± 26.3)	569.8158 (± 27.4)	
Cycle 3 day 1	629.9607 (± 19.8)	477.6488 (± 25.0)	473.0335 (± 23.8)	
Cycle 4 day 1	559.8988 (± 31.0)	393.5442 (± 48.9)	406.9487 (± 28.2)	
Cycle 7 day 1	294.8322 (± 99999)	515.2495 (± 21.9)	229.0854 (± 99999)	
Follow-up 1	177.5615 (± 65.0)	157.5960 (± 62.2)	184.1510 (± 51.7)	
Follow-up 2	134.0478 (± 99999)	57.3349 (± 99999)	8.4517 (± 158.4)	

Notes:

[10] - Subjects analyzed:
C1=31
C2(0)=25
C2(4)=24
C3=10
C4=5
C7=1
FU1=6
FU2=1

[11] - Subjects analyzed:
C1=21
C2(0)=12
C2(4)=11
C3=10
C4=7
C7=4
FU1=5
FU2=1

[12] - Subjects analyzed:
C1=38
C2(0)=28

C2(4)=28
C3=13
C4=5
C7=1
FU1=9
FU2=4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Anti Drug Antibody (ADA) by Positivity

End point title	Percentage of Participants Anti Drug Antibody (ADA) by Positivity

End point description:

Percentage of participants Anti Drug Antibody (ADA) to assess immunogenicity by ADA positive status and ADA negative status, relative to baseline. ADA positive is a participant with at least one ADA-positive sample relative to baseline (ADA negative at baseline or ADA titer to be at least 4-fold or greater (>=) than baseline positive titer) at any time after initiation of treatment. ADA Negative is a participant with no ADA-positive sample after initiation of treatment

End point type	Secondary

End point timeframe:

Up to 36 months

End point values	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (NSCLC)	Nivolumab + Daratumumab (PAC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41[13]	21[14]	43[15]	
Units: Percentage of Participants				
number (not applicable)				
Nivolumab Baseline ADA positive	0.00	6.3	0.00	
Daratumumab Baseline ADA positive	0.00	5.6	0.00	
Nivolumab ADA Positive	0.00	0.00	0.00	
Nivolumab ADA Negative	100.0	100.0	100.0	
Daratumumab ADA Positive	0.00	0.00	0.00	
Daratumumab ADA Negative	100.0	100.0	100.0	

Notes:

[13] - Nivolumab =17 subjects analyzed Daratumumab = 29 subjects analyzed

[14] - Nivolumab = 16 subjects analyzed Daratumumab = 18 subjects analyzed

[15] - Nivolumab = 18 subjects analyzed Daratumumab = 33 subjects analyzed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All adverse events were collected from the first dose up to 100 days after the last treatment dose	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Nivolumab + Daratumumab (TNBC)
Reporting group description:	
Triple-negative breast cancer (TNBC) treated with Triple-negative breast cancer (TNBC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	
Reporting group title	Nivolumab + Daratumumab (PAC)
Reporting group description:	
Pancreatic adenocarcinoma cancer (PAC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	
Reporting group title	Nivolumab + Daratumumab (NSCLC)
Reporting group description:	
Non-small cell lung cancer (NSCLC) treated with Nivolumab IV 240 mg Q2W (weeks 3 to 24) + Daratumumab IV 16 mg/kg Q1W (weeks 1 to 8), Daratumumab IV 16 mg/kg Q2W (weeks 9-24)	

Serious adverse events	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (PAC)	Nivolumab + Daratumumab (NSCLC)
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 41 (87.80%)	36 / 43 (83.72%)	17 / 21 (80.95%)
number of deaths (all causes)	29	36	11
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	22 / 41 (53.66%)	26 / 43 (60.47%)	8 / 21 (38.10%)
occurrences causally related to treatment / all	0 / 23	0 / 30	0 / 12
deaths causally related to treatment / all	0 / 18	0 / 29	0 / 6
Metastases to central nervous system			

subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spinal cord			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Tumour pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tumour thrombosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 41 (4.88%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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

Fatigue			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Generalised oedema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Oedema peripheral			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Pyrexia			
subjects affected / exposed	2 / 41 (4.88%)	4 / 43 (9.30%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Respiratory, thoracic and mediastinal			

disorders			
Dyspnoea			
subjects affected / exposed	1 / 41 (2.44%)	2 / 43 (4.65%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Dyspnoea exertional			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Haemoptysis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	8 / 41 (19.51%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 11	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	0 / 21 (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
Pneumothorax			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 41 (4.88%)	2 / 43 (4.65%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Respiratory distress			

subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Respiratory failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Disorientation			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
General physical condition abnormal			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Procalcitonin increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Transaminases increased			

subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Fracture			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Lower limb fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Cardiac tamponade			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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

Cardio-respiratory arrest			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
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			
Headache			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Ischaemic stroke			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Seizure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Ileus paralytic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Intestinal ischaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 41 (0.00%)	2 / 43 (4.65%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Vomiting			

subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Hepatic failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (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
Hepatitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Haematuria			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Enterocolitis infectious			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lung abscess			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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

Nosocomial infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Skin infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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
Dehydration			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	0 / 21 (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
Diabetes mellitus			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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 / 41 (0.00%)	1 / 43 (2.33%)	0 / 21 (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

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

Non-serious adverse events	Nivolumab + Daratumumab (TNBC)	Nivolumab + Daratumumab (PAC)	Nivolumab + Daratumumab (NSCLC)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 41 (97.56%)	42 / 43 (97.67%)	21 / 21 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Vascular disorders			
Flushing			
subjects affected / exposed	3 / 41 (7.32%)	2 / 43 (4.65%)	2 / 21 (9.52%)
occurrences (all)	6	2	2
Hypotension			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Lymphoedema			

subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 41 (29.27%)	11 / 43 (25.58%)	12 / 21 (57.14%)
occurrences (all)	24	21	16
Chest pain			
subjects affected / exposed	9 / 41 (21.95%)	1 / 43 (2.33%)	1 / 21 (4.76%)
occurrences (all)	14	1	1
Chills			
subjects affected / exposed	3 / 41 (7.32%)	4 / 43 (9.30%)	2 / 21 (9.52%)
occurrences (all)	3	7	2
Fatigue			
subjects affected / exposed	8 / 41 (19.51%)	15 / 43 (34.88%)	3 / 21 (14.29%)
occurrences (all)	25	23	10
Mucosal inflammation			
subjects affected / exposed	2 / 41 (4.88%)	0 / 43 (0.00%)	3 / 21 (14.29%)
occurrences (all)	2	0	3
Non-cardiac chest pain			
subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences (all)	6	0	1
Oedema peripheral			
subjects affected / exposed	5 / 41 (12.20%)	10 / 43 (23.26%)	7 / 21 (33.33%)
occurrences (all)	5	13	11
Pain			
subjects affected / exposed	4 / 41 (9.76%)	1 / 43 (2.33%)	5 / 21 (23.81%)
occurrences (all)	4	1	6
Pyrexia			
subjects affected / exposed	10 / 41 (24.39%)	14 / 43 (32.56%)	7 / 21 (33.33%)
occurrences (all)	20	27	18
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	6 / 41 (14.63%)	7 / 43 (16.28%)	5 / 21 (23.81%)
occurrences (all)	9	7	5
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	15 / 41 (36.59%)	10 / 43 (23.26%)	6 / 21 (28.57%)
occurrences (all)	32	12	9
Cough			
subjects affected / exposed	18 / 41 (43.90%)	4 / 43 (9.30%)	6 / 21 (28.57%)
occurrences (all)	23	5	9
Pleural effusion			
subjects affected / exposed	4 / 41 (9.76%)	2 / 43 (4.65%)	0 / 21 (0.00%)
occurrences (all)	5	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Productive cough			
subjects affected / exposed	1 / 41 (2.44%)	2 / 43 (4.65%)	2 / 21 (9.52%)
occurrences (all)	1	2	2
Pulmonary embolism			
subjects affected / exposed	2 / 41 (4.88%)	5 / 43 (11.63%)	0 / 21 (0.00%)
occurrences (all)	2	5	0
Rhinorrhoea			
subjects affected / exposed	2 / 41 (4.88%)	0 / 43 (0.00%)	3 / 21 (14.29%)
occurrences (all)	2	0	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	8 / 41 (19.51%)	4 / 43 (9.30%)	2 / 21 (9.52%)
occurrences (all)	8	4	2
Insomnia			
subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	1 / 21 (4.76%)
occurrences (all)	1	4	1
Depression			
subjects affected / exposed	3 / 41 (7.32%)	2 / 43 (4.65%)	0 / 21 (0.00%)
occurrences (all)	4	2	0
Sleep disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	5 / 21 (23.81%)
occurrences (all)	1	0	7
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	5 / 41 (12.20%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences (all)	8	4	0
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 41 (14.63%)	4 / 43 (9.30%)	0 / 21 (0.00%)
occurrences (all)	9	5	0
Blood albumin decreased			
subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 41 (7.32%)	6 / 43 (13.95%)	2 / 21 (9.52%)
occurrences (all)	4	9	2
Blood bilirubin increased			
subjects affected / exposed	2 / 41 (4.88%)	4 / 43 (9.30%)	0 / 21 (0.00%)
occurrences (all)	3	4	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 41 (7.32%)	1 / 43 (2.33%)	0 / 21 (0.00%)
occurrences (all)	3	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 41 (7.32%)	4 / 43 (9.30%)	0 / 21 (0.00%)
occurrences (all)	4	6	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	2 / 21 (9.52%)
occurrences (all)	2	5	7
Platelet count decreased			
subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences (all)	5	0	0
Transaminases increased			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	1 / 41 (2.44%)	6 / 43 (13.95%)	3 / 21 (14.29%)
occurrences (all)	1	10	11
White blood cell count decreased			

subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences (all)	1	3	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	18 / 41 (43.90%)	18 / 43 (41.86%)	11 / 21 (52.38%)
occurrences (all)	28	28	14
Fall			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Vascular access site pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 41 (7.32%)	1 / 43 (2.33%)	3 / 21 (14.29%)
occurrences (all)	4	1	4
Dysgeusia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	3 / 21 (14.29%)
occurrences (all)	0	1	3
Headache			
subjects affected / exposed	10 / 41 (24.39%)	8 / 43 (18.60%)	4 / 21 (19.05%)
occurrences (all)	20	19	8
Paraesthesia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	2 / 21 (9.52%)
occurrences (all)	1	1	2
Somnolence			
subjects affected / exposed	5 / 41 (12.20%)	2 / 43 (4.65%)	3 / 21 (14.29%)
occurrences (all)	6	2	4
Tremor			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	2 / 21 (9.52%)
occurrences (all)	0	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 41 (19.51%)	7 / 43 (16.28%)	6 / 21 (28.57%)
occurrences (all)	17	10	10
Lymphopenia			

subjects affected / exposed	2 / 41 (4.88%)	1 / 43 (2.33%)	3 / 21 (14.29%)
occurrences (all)	2	1	5
Thrombocytopenia			
subjects affected / exposed	5 / 41 (12.20%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences (all)	17	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Eye pruritus			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Vision blurred			
subjects affected / exposed	3 / 41 (7.32%)	2 / 43 (4.65%)	1 / 21 (4.76%)
occurrences (all)	3	2	1
Ocular discomfort			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 41 (19.51%)	19 / 43 (44.19%)	4 / 21 (19.05%)
occurrences (all)	12	38	4
Abdominal pain upper			
subjects affected / exposed	5 / 41 (12.20%)	8 / 43 (18.60%)	4 / 21 (19.05%)
occurrences (all)	8	12	4
Ascites			
subjects affected / exposed	0 / 41 (0.00%)	7 / 43 (16.28%)	1 / 21 (4.76%)
occurrences (all)	0	9	1
Colitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	10
Diarrhoea			
subjects affected / exposed	9 / 41 (21.95%)	17 / 43 (39.53%)	9 / 21 (42.86%)
occurrences (all)	13	23	18
Constipation			

subjects affected / exposed	12 / 41 (29.27%)	13 / 43 (30.23%)	9 / 21 (42.86%)
occurrences (all)	14	24	12
Dry mouth			
subjects affected / exposed	3 / 41 (7.32%)	6 / 43 (13.95%)	5 / 21 (23.81%)
occurrences (all)	4	8	7
Dyspepsia			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	3 / 21 (14.29%)
occurrences (all)	0	3	5
Flatulence			
subjects affected / exposed	0 / 41 (0.00%)	2 / 43 (4.65%)	2 / 21 (9.52%)
occurrences (all)	0	2	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Nausea			
subjects affected / exposed	16 / 41 (39.02%)	18 / 43 (41.86%)	8 / 21 (38.10%)
occurrences (all)	23	30	14
Stomatitis			
subjects affected / exposed	2 / 41 (4.88%)	2 / 43 (4.65%)	2 / 21 (9.52%)
occurrences (all)	2	4	4
Vomiting			
subjects affected / exposed	12 / 41 (29.27%)	15 / 43 (34.88%)	6 / 21 (28.57%)
occurrences (all)	14	19	9
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	3 / 21 (14.29%)
occurrences (all)	0	0	3
Erythema			
subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	3	0	2
Hyperhidrosis			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	2 / 21 (9.52%)
occurrences (all)	0	4	2
Pruritus			
subjects affected / exposed	4 / 41 (9.76%)	2 / 43 (4.65%)	8 / 21 (38.10%)
occurrences (all)	4	2	8

Rash pruritic			
subjects affected / exposed	2 / 41 (4.88%)	0 / 43 (0.00%)	3 / 21 (14.29%)
occurrences (all)	2	0	4
Rash			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	3 / 21 (14.29%)
occurrences (all)	1	0	5
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	2 / 21 (9.52%)
occurrences (all)	1	3	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 41 (14.63%)	5 / 43 (11.63%)	4 / 21 (19.05%)
occurrences (all)	8	6	6
Back pain			
subjects affected / exposed	8 / 41 (19.51%)	3 / 43 (6.98%)	8 / 21 (38.10%)
occurrences (all)	13	3	15
Bone pain			
subjects affected / exposed	4 / 41 (9.76%)	2 / 43 (4.65%)	1 / 21 (4.76%)
occurrences (all)	4	2	1
Flank pain			
subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Muscle spasms			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	2 / 21 (9.52%)
occurrences (all)	1	1	2
Myalgia			
subjects affected / exposed	2 / 41 (4.88%)	3 / 43 (6.98%)	3 / 21 (14.29%)
occurrences (all)	2	3	3
Pain in extremity			
subjects affected / exposed	5 / 41 (12.20%)	1 / 43 (2.33%)	1 / 21 (4.76%)
occurrences (all)	9	1	1
Neck pain			
subjects affected / exposed	2 / 41 (4.88%)	1 / 43 (2.33%)	3 / 21 (14.29%)
occurrences (all)	2	1	3
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	4 / 41 (9.76%)	0 / 43 (0.00%)	6 / 21 (28.57%)
occurrences (all)	4	0	11
Oral fungal infection			
subjects affected / exposed	0 / 41 (0.00%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Respiratory tract infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	4 / 21 (19.05%)
occurrences (all)	1	0	5
Tooth infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	3
Upper respiratory tract infection			
subjects affected / exposed	1 / 41 (2.44%)	3 / 43 (6.98%)	0 / 21 (0.00%)
occurrences (all)	1	3	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	3 / 41 (7.32%)	0 / 43 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	2
Decreased appetite			
subjects affected / exposed	15 / 41 (36.59%)	14 / 43 (32.56%)	5 / 21 (23.81%)
occurrences (all)	24	22	6
Hypokalaemia			
subjects affected / exposed	2 / 41 (4.88%)	5 / 43 (11.63%)	1 / 21 (4.76%)
occurrences (all)	2	7	3
Hypoalbuminaemia			
subjects affected / exposed	2 / 41 (4.88%)	4 / 43 (9.30%)	0 / 21 (0.00%)
occurrences (all)	2	5	0
Hypomagnesaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	2 / 21 (9.52%)
occurrences (all)	0	1	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2017	Inclusion Criteria Update
14 June 2017	Inclusion Criteria Update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported