Clinical trial results:
A Safety study of Nivolumab in Patients with Recurrent and/or Metastatic Platinum-refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN).

Summary

EudraCT number	2017-000424-10
Trial protocol	FR
Global end of trial date	27 May 2022

Results information

Result version number	v1 (current)
This version publication date	28 June 2025
First version publication date	28 June 2025

Trial information

Trial identification

Sponsor protocol code	UC-0130/1703

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03226756
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
Public contact	Nourredine AIT RAHMOUNE,, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT RAHMOUNE, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr

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	10 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 February 2021
Global end of trial reached?	Yes
Global end of trial date	27 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To estimate the incidence of high-grade (i.e. Grade 3-5 of CTCAE v4.0) adverse events of interest (AEI) in patients with recurrent and/or metastatic platinum refractory SCCHN treated with nivolumab in monotherapy. AEI are defined as adverse reactions known to be related to nivolumab (i.e. skin, endocrinopathy, astrointestinal, hepatic, renal, pulmonary, and hypersensitivity adverse events) and other adverse events not related to carcinoma progression or to intercurrent disease clearly identified.

Protection of trial subjects:

This study was conducted in accordance with the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice (GCP) Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 July 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 343
Worldwide total number of subjects	343
EEA total number of subjects	343

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)	198

From 65 to 84 years	140
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

351 patients were included from 07-AUG-2017 to 05-NOV-2018 by 28 recruiting centers . Among them, eight patients were not treated: two did not receive any cure because of the appearance of brain metastasis before the first treatment, four of them died and the last one presented an adverse event clinically significant before their first treatment.

Pre-assignment

Screening details:

In this study, patients presented recurrent and/or metastatic platinum-refractory Squamous Cell Carcinoma of the Head and Neck
(SCCHN) were included. Following the signature of the informed consent form, all included patients received nivolumab treatment until immune Confirmed Progressive Disease (iCPD) the patients were followed-up for two years.

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	Nivolumab 3 mg/kg, every 2 weeks

Arm description:

All patients enrolled in the study will received Nivolumab injections, 3mg/kg IV, every 2 weeks, up to 12 cycles (1 cycle = 28 days) until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab isotonic aqueous solution (10 mg/mL) intravenously injected over 30 ± 5 min. to a final dose of 3 mg/kg, every two weeks for n cycles until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

Number of subjects in period 1	Nivolumab 3 mg/kg, every 2 weeks
Started	343
Completed	6
Not completed	337
Physician decision	11
Consent withdrawn by subject	6
Death	54
Other	17
Adverse event	25

Progressive disease	223
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	343	343	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	198	198	
From 65-84 years	140	140	
85 years and over	5	5	
Age continuous Units: years			
median	62		
inter-quartile range (Q1-Q3)	56 to 69	-	
Gender categorical Units: Subjects			
Female	64	64	
Male	279	279	
ECOG Units: Subjects			
ECOG 0	84	84	
ECOG 1	206	206	
ECOG 2	52	52	
Missing	1	1	
Primary site of cancer Units: Subjects			
Hypopharynx	68	68	
Larynx	52	52	
Oral cavity	83	83	
Oropharynx	138	138	
Unknown primary	2	2	
Metastatic disease Units: Subjects			
No	126	126	
Yes	217	217	
Loco regional Recurrent disease Units: Subjects			
No	102	102	

Yes	241	241	

End points

End points reporting groups

Reporting group title	Nivolumab 3 mg/kg, every 2 weeks

Reporting group description:

All patients enrolled in the study will received Nivolumab injections, 3mg/kg IV, every 2 weeks, up to 12 cycles (1 cycle = 28 days) until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

Primary: Time until Grade 5 SADR occurre

End point title	Time until Grade 5 SADR occurre[1]

End point description:

The primary endpoint of this study was to assess the incidence of nivolumab induced Grade 3, 4 and 5 ADRs and SADRs susceptible to promote skin, endocrinologic, gastrointestinal, hepatic, renal, pulmonary, or hypersensitivities as well as other AEs not related to either carcinoma progression or clearly identified intercurrent disease.

The 5 Grade 5 SADRs were recorded and consisted of 3 interstitial lung disease, 1 autoimmune hepatitis, and 1 cardi-respiratory arrest.

End point type	Primary

End point timeframe:

Last day dose + 100 d

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: No statistical analysis to report for this end point.

End point values	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Months				
number (not applicable)				
Interstitial lung disease 1	0.7228			
Autoimmune hepatitis	1.7413			
Interstitial lung disease 2	10.3491			
Interstitial lung disease 3	1.2813			
Cardio-respiratory arrest	0.2628			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival is defined as the time from date of inclusion to date of death due to any cause. Patients last known to be alive will be censored at date of last contact. Overall survival will be estimated by

Kaplan Meier method.

End point type	Secondary

End point timeframe:

Up to 36 months.

End point values	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Months				
median (confidence interval 95%)	7.4 (6.5 to 8.9)			

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 is defined as the time since the inclusion in the trial to the first event among progression and death, whatever the cause of death. Progression is defined according to RECIST 1.1. Patients last known to be alive without progression having occurred before will be censored at date of last contact. Progression free survival will be estimated by Kaplan Meier method.

End point type	Secondary

End point timeframe:

Up to 36 months.

End point values	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Months				
median (confidence interval 95%)	1.8 (1.8 to 1.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR) (complete response and partial response according to RECIST 1.1 and to iRECIST) during nivolumab treatment

End point title	Objective response rate (ORR) (complete response and partial

	response according to RECIST 1.1 and to iRECIST) during nivolumab treatment

End point description:

The rate of patients with objective response (complete response or partial response) will be provided. The response is the best response obtained at the evaluations performed during treatment and at the end of treatment. Two evaluations of the response will be done: one according to the RECIST 1.1 criteria and one according the Immune-related Response Criteria (iRECIST).

End point type	Secondary

End point timeframe:

The time between the fist dose of treatment until the best response, assessed up to 36 months.

End point values	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Patients				
Not evaluated N	67			
Progressive disease N	145			
Stable disease N	74			
Partial response N	45			
Complete response N	12			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period of observation of adverse events of interest was the period of nivolumab treatment and 180 days after.

Adverse event reporting additional description:

For non serious adverse events the number of occurrence are not available and will be always noted "1"

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Nivolumab 3 mg/kg, every 2 weeks

Reporting group description:

All patients enrolled in the study will received Nivolumab injections, 3mg/kg IV, every 2 weeks, up to 12 cycles (1 cycle = 28 days) until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

Serious adverse events	Nivolumab 3 mg/kg, every 2 weeks		
Total subjects affected by serious adverse events			
subjects affected / exposed	181 / 343 (52.77%)		
number of deaths (all causes)	291		
number of deaths resulting from adverse events	10		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastric carcinoma			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung metastases			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastatic bone pain			

subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal cancer				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Squamous cell carcinoma of skin				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumor bleeding				
subjects affected / exposed	15 / 343 (4.37%)			
occurrences causally related to treatment / all	0 / 17			
deaths causally related to treatment / all	0 / 5			
Tumor hemorrhage				
subjects affected / exposed	13 / 343 (3.79%)			
occurrences causally related to treatment / all	1 / 14			
deaths causally related to treatment / all	0 / 7			
Tumor pain				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tumor progression				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tumour bleeding				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Acute limb ischaemia				

subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Aortic stenosis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bleeding				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemoptysis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hemorrhage				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ischemic stroke				
subjects affected / exposed	3 / 343 (0.87%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Jugular vein thrombosis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary embolism				

subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tumor hemorrhage			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			
Scar revision			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TAVI			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgery			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Disease progression			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

Fever				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	20 / 343 (5.83%)			
occurrences causally related to treatment / all	1 / 20			
deaths causally related to treatment / all	1 / 9			
Hyperthermia				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	6 / 343 (1.75%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 3			
Sudden death				
subjects affected / exposed	3 / 343 (0.87%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	3 / 3			
Unknown cause of death				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Adult respiratory distress syndrome				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			

Aspiration pneumonia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial congestion			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial obstruction			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease exacerbation			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Dyspnea			
subjects affected / exposed	7 / 343 (2.04%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
Food aspiration			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hemoptysis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Inhalation pneumonia			

subjects affected / exposed	4 / 343 (1.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	4 / 343 (1.17%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	2 / 2			
Interstitial pneumonia				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial pneumonitis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Laryngeal dyspnea				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Laryngeal oedema				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Lung infection				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal hemorrhage				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Plaural effusion				

subjects affected / exposed	3 / 343 (0.87%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	3 / 343 (0.87%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Pneumopathy				
subjects affected / exposed	9 / 343 (2.62%)			
occurrences causally related to treatment / all	1 / 10			
deaths causally related to treatment / all	0 / 3			
Pneumothorax				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory tract hemorrhage				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxiety				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric decompensation				

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Catheter dislodgment			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prosthetic cardiac valve leakage			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Troponin increased			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight loss			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Arm fracture			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bleeding postoperative			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug overdose			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Fall				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrostomy tube site complication				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemopneumothorax				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leg fracture				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Subdural hematoma				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tracheal obstruction				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Vascular access complication				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac arrest				

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarct			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial infarction			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Takotsubo syndrome			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Consciousness loss			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			

subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial paralysis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Generalized tonic-clonic seizure				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Motor deficit				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Polyradiculoneuritis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischemic attack				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Eosinophilia				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombopenia				

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Bleeding mouth			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bowel obstruction			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhea			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	5 / 343 (1.46%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Femoral hernia strangulated			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hemorrhoids			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			

subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mouth pain				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal fistula				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral hemorrhage				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain esophageal				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tongue bleeding				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vomiting				

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute cholecystitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Autoimmune hepatitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Hepatitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis autoimmune			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Zona			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Acute renal insufficiency				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal insufficiency				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypophysitis				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hypothyroidism				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
SIADH				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Bone pain				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dorsal pain				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Osteoarthritis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in hip			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Bone infection			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchial infection			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary infection			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Catheter infection			
subjects affected / exposed	5 / 343 (1.46%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Catheter related infection			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis of face			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		
Device related infection			

subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infectious pneumonitis				
subjects affected / exposed	3 / 343 (0.87%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	7 / 343 (2.04%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 2			
Pneumonia				
subjects affected / exposed	4 / 343 (1.17%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	1 / 2			
Pulmonary sepsis				

subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Staphylococcus aureus septicemia				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcus epidermidis infection				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Superinfection				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory infection				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Anorexia				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Decreased appetite				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Hypercalcemia				

subjects affected / exposed	12 / 343 (3.50%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 3		
Hypokalemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatremia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Protein energy malnutrition			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nivolumab 3 mg/kg, every 2 weeks		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	343 / 343 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Tumour pain			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	55 / 343 (16.03%) 1		
Crepitations subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Fatigue subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Feeling cold subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
General physical health deterioration subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Hyperthermia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Mucosal inflammation subjects affected / exposed occurrences (all)	14 / 343 (4.08%) 1		
Oedema peripheral subjects affected / exposed occurrences (all)	5 / 343 (1.46%) 1		
Pain subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Pyrexia subjects affected / exposed occurrences (all)	10 / 343 (2.92%) 1		
Xerosis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Immune system disorders Hypersensitivity			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Angular cheilitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Folliculitis subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Herpes Zoster subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Encephalitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Reproductive system and breast disorders			
Gynaecomastia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Pruritus genital subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Cough subjects affected / exposed occurrences (all)	7 / 343 (2.04%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	9 / 343 (2.62%) 1		
Dyspnoea exertional			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Interstitial lung disease			
subjects affected / exposed	6 / 343 (1.75%)		
occurrences (all)	1		
Lung disorder			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Lung infiltration			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Pneumonitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	8 / 343 (2.33%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Tracheostomy malfunction			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			

Phimosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Deafness			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Ear pruritus			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Cyanosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Stress cardiomyopathy			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Dysaesthesia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Dysarthria			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Hyperaesthesia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Loss of consciousness			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Polyneuropathy			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	17 / 343 (4.96%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		

Leukocytosis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Lymphopenia subjects affected / exposed occurrences (all)	12 / 343 (3.50%) 1		
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Vision blurred subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Aptyalism subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Colitis subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Constipation subjects affected / exposed occurrences (all)	7 / 343 (2.04%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	18 / 343 (5.25%) 1		
Dry mouth			

subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	19 / 343 (5.54%)		
occurrences (all)	1		
Oral pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	9 / 343 (2.62%)		
occurrences (all)	1		
Tongue oedema			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	6 / 343 (1.75%)		
occurrences (all)	1		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Cholestasis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Hepatocellular injury			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Dermatitis			

subjects affected / exposed	2 / 343 (0.58%)			
occurrences (all)	1			
Dry skin				
subjects affected / exposed	11 / 343 (3.21%)			
occurrences (all)	1			
Eczema				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences (all)	1			
Erythema				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences (all)	1			
Hyoerhidrosis				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences (all)	1			
Night sweats				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences (all)	1			
Pemphigoid				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences (all)	1			
Pruritis				
subjects affected / exposed	19 / 343 (5.54%)			
occurrences (all)	1			
Pruritis generalised				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences (all)	1			
Psoriasis				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences (all)	1			
Rash				
subjects affected / exposed	11 / 343 (3.21%)			
occurrences (all)	1			
Seborrhoeic dermatitis				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences (all)	1			
Skin exfoliation				

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Skin fissures			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Skin toxicity			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Xeroderma			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Renal failure			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Hyperthyroidism			
subjects affected / exposed	10 / 343 (2.92%)		
occurrences (all)	1		
Hypophysitis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Hypothyroidism			
subjects affected / exposed	32 / 343 (9.33%)		
occurrences (all)	1		
Inappropriate antidiuretic hormone secretion			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Thyroid disorder			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 343 (2.04%)		
occurrences (all)	1		
Arthritis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Musculoskeletal discomfort			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Pain in extremity			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Phabdomyolysis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Encephalitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Oral fungal infection			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Rash pustular			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 343 (2.92%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hyperkalaemia			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypernatraemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypochloraemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2018	- Inclusion number increase to 250 - Nivolumab Investigator's Brochure update - Investigators' list modification - Addendum to the Information Note regarding the Informed Consent Form
10 April 2018	- Inclusion number increase to 350 - Supplemental ancillary biological study (galectine-9 measurement) for 100 subjects - Investigators' list modification - Update of both the Informed Consent Form and its Information Note
04 July 2018	- Protocol-related: Inlusion period extension from 12 to 18 months and Extended HPV status diagnosis to availability of archived or new tumor biopsies for oropharynx's SCC). Nivolumab therapeutic regimens and treatment duration/period: the maximum of 12 cycles was removed and replaced by "up to progression (immune Confirmed Progressive Disease (iCPD) using iRECIST) - Investigators' list modification - Update of both the Informed Consent Form and its Information Note - Supplemental information regarding General Data Protection Regulations for included patients being either currently treated or followed
28 May 2019	- Investigator's Brochure update - Investigators' list modification - Supplemental information "C" intended to the included patients being either currently treated or followed
10 September 2019	- Investigator's Brochure update - Addendum to both Informed Consent Form and its Information Note - Investigators' list modification
13 September 2021	- Treatement modalities update leading to SmPC update - Protocol and synopsis update: Follow-up period modification - Addendum to both Informed Consent Form and its Information Note to include new follow-up period - Investigator's Brochure update - Investigators' list modification

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported