Clinical trial results:
A Phase II, Multicenter, Non Randomized, Open Label Study of Nivolumab In Recurrent and/or Metastatic Salivary Gland Carcinoma of the Head and Neck.

Summary

EudraCT number	2016-001794-32
Trial protocol	FR
Global end of trial date	20 October 2021

Results information

Result version number	v1 (current)
This version publication date	13 August 2022
First version publication date	13 August 2022

Trial information

Trial identification

Sponsor protocol code	UC-0130/1619

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03132038
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Unicancer
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75013
Public contact	Nourredine AIT-RAHMOUNE, UNICANCER, 33 1 71 93 67 04, n.ait-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT-RAHMOUNE, UNICANCER, 33 1 71 93 67 04, 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	30 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the non progression rate at 6 months.

Protection of trial subjects:

In order to ensure the protection of the rights, safety and well-being of trial subjects, this study was conducted in accordance with the ethical principles that have their origins in the latest version of the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) on the conduct of clinical trials and subsequent texts (Eudralex Vol 10), and the applicable local regulatory requirements and laws (The Huriet Law N°88-1138 of the 20th December 1998 on the protection of persons taking part in biomedical research; The National Informatics and Freedoms Commission – Law N° 78-17 of the 6th January 1978 modified by the law N° 2004-801 of the 6th August 2004 concerning the protection of the person with regards to the use of personal data; Bioethical law N°2011-814 of the 8th July 2011).
Furthermore, independent Ethics Committees reviewed and gave favorable opinions to the study documents, including the initial protocol and all subsequent amendments, and all information and documents provided to subjects/patients.
Written informed consent was obtained from all patients prior to enrollment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
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: 98
Worldwide total number of subjects	98
EEA total number of subjects	98

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)	58
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The NISCAHN study was a multicenter, open-label, non-controlled, phase II study in patients who were suffering from recurrent and/or metastatic Salivary Glands Carcinoma (SGC) not eligible to local treatment, who have progressed during the 6 months period before entering the study and were eligible for nivolumab monotherapy.

Pre-assignment

Screening details:

The study consisted of a 28-day screening phase to establish patients' eligibility and document baseline measurements, a treatment phase (28-day cycle till disease progression - 12 cycles maximum), and a long-term follow-up to monitor the non-progression rate, progression-free survival, overall survival, and overall response rate.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Adenoid cystic carcinoma (ACC)

Arm description:

Salivary Glands Carcinoma were separated in two cohorts/sub-groups: Adenoid Cystic Carcinoma (ACC) and Non-Adenoid Cystic Carcinoma (Non ACC).
In this "Arm" we reported results from the ACC subgroup.

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 was given as a 60 minutes (± 5 minutes) intrvelous infusion at a fixed dose of 3 mg/kg every 2 weeks.

Arm title	Non-Adenoid Cystic Carcinoma (Non ACC)

Arm description:

Salivary Glands Carcinoma were separated in two cohorts/sub-groups: Adenoid Cystic Carcinoma (ACC) and Non-Adenoid Cystic Carcinoma (Non ACC).
In this "Arm" we reported results from the Non ACC subgroup.

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 was given as a 60 minutes (± 5 minutes) intrvelous infusion at a fixed dose of 3 mg/kg every 2 weeks.

Number of subjects in period 1	Adenoid cystic carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)
Started	46	52
Completed	10	4
Not completed	36	48
Physician decision	1	-
Patient decision	1	2
Disease progression	29	41
Adverse event, non-fatal	5	-
Death	-	5

Baseline characteristics

Reporting groups	
Reporting group title	Adenoid cystic carcinoma (ACC)
Reporting group description:	
Salivary Glands Carcinoma were separated in two cohorts/sub-groups: Adenoid Cystic Carcinoma (ACC) and Non-Adenoid Cystic Carcinoma (Non ACC). In this "Arm" we reported results from the ACC subgroup.	
Reporting group title	Non-Adenoid Cystic Carcinoma (Non ACC)
Reporting group description:	
Salivary Glands Carcinoma were separated in two cohorts/sub-groups: Adenoid Cystic Carcinoma (ACC) and Non-Adenoid Cystic Carcinoma (Non ACC). In this "Arm" we reported results from the Non ACC subgroup.	

Reporting group values	Adenoid cystic carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)	Total
Number of subjects	46	52	98
Age categorical Units: Subjects			
Adults (18-64 years)	27	30	57
From 65-84 years	19	22	41
Age continuous Units: years			
median	58.5	62.5	
full range (min-max)	36 to 80	29 to 81	-
Gender categorical Units: Subjects			
Female	20	23	43
Male	26	29	55
ECOG Units: Subjects			
PS 0	23	19	42
PS 1	23	32	55
PS 2	0	1	1
Metastatic disease Units: Subjects			
No	4	3	7
Yes	42	49	91
Loco-regional recurrent disease Units: Subjects			
No	35	34	69
Yes	11	18	29
Primary site of cancer : Major glands Units: Subjects			
No	14	8	22
Yes	32	44	76
Primary site of cancer : Minor glands Units: Subjects			
No	34	44	78
Yes	12	8	20

End points

End points reporting groups

Reporting group title	Adenoid cystic carcinoma (ACC)

Reporting group description:

Salivary Glands Carcinoma were separated in two cohorts/sub-groups: Adenoid Cystic Carcinoma (ACC) and Non-Adenoid Cystic Carcinoma (Non ACC).
In this "Arm" we reported results from the ACC subgroup.

Reporting group title	Non-Adenoid Cystic Carcinoma (Non ACC)

Reporting group description:

Salivary Glands Carcinoma were separated in two cohorts/sub-groups: Adenoid Cystic Carcinoma (ACC) and Non-Adenoid Cystic Carcinoma (Non ACC).
In this "Arm" we reported results from the Non ACC subgroup.

Primary: Response rate at 6 months

End point title	Response rate at 6 months[1]

End point description:

The primary objective was to evaluate the non progression rate at 6 months in patients with recurrent and/or metastatic salivary gland carcinoma of the head and neck who have progressed during the 6 months period before entering the study and who were eligible for nivolumab monotherapy.
Imaging were centrally reviewed.

End point type	Primary

End point timeframe:

The primary endpoint was the non-progression rate at 6 months. Radiological assessments performed at pre-baseline (in the 6-month period before baseline), at baseline and until 6 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: This study was not designed to compare ACC and Non-ACC population. Thus, statistical comparisons by hypothesis tests between groups were not planned.

End point values	Adenoid cystic carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	52		
Units: percent				
number (not applicable)				
Response rate	33.3	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival

End point description:

Progression Free Survival was evaluated using Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1).

End point type	Secondary

End point timeframe:

At baseline, every 8 weeks for the first year then every 12 weeks there after untill disease progression, up to 3 years.

End point values	Adenoid cystic carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	52		
Units: percent				
median (confidence interval 95%)	5.3 (3.2 to 5.6)	1.8 (1.7 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate

End point title	Objective response rate

End point description:

Objective response rate was defined as thepercentage of patients with a best overall response of confirmed complete response (CR) or partial response (PR). Best overall response was defined as the best response recorded between the date of first dose and the date of the initial objectively documented tumor progression per RECIST v1.1 or the date of subsequent therapy, whichever occurs first.

End point type	Secondary

End point timeframe:

At baseline, every 8 weeks for the first year then every 12 weeks there after untill disease progression, up to 3 years.

End point values	Adenoid cystic carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	52		
Units: percent				
median (confidence interval 95%)	8.7 (2.4 to 20.8)	3.8 (0.5 to 13.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

Overall survival was defined as the time inclusion until death of any cause, up to 3 years.

End point values	Adenoid cystic carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	52		
Units: percent				
median (confidence interval 95%)	17.2 (12.5 to 40)	11.5 (7.5 to 14.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From inclusion until 30 days after end of treatment (up to 3 years).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Adenoid Cystic Carcinoma (ACC)
Reporting group description: -	
Reporting group title	Non-Adenoid Cystic Carcinoma (Non ACC)
Reporting group description: -	

Serious adverse events	Adenoid Cystic Carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 46 (21.74%)	15 / 52 (28.85%)	
number of deaths (all causes)	26	32	
number of deaths resulting from adverse events	0	0	
Investigations			
Liver function test increased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			

subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Epistaxis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post biopsy bleeding			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oedema lower limb			

subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 46 (0.00%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory insufficiency			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration pneumonia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	1 / 46 (2.17%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Fasciitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Epiduritis			
subjects affected / exposed	1 / 46 (2.17%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 46 (2.17%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Adenoid Cystic Carcinoma (ACC)	Non-Adenoid Cystic Carcinoma (Non ACC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 46 (100.00%)	35 / 52 (67.31%)	
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 46 (2.17%)	2 / 52 (3.85%)	
occurrences (all)	1	2	
Lipase			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Eosinopenia			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	13 / 46 (28.26%)	9 / 52 (17.31%)	
occurrences (all)	13	9	
Chest pain			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 46 (15.22%)	2 / 52 (3.85%)	
occurrences (all)	7	2	
Dry mouth			
subjects affected / exposed	4 / 46 (8.70%)	2 / 52 (3.85%)	
occurrences (all)	4	2	
Nausea			
subjects affected / exposed	4 / 46 (8.70%)	1 / 52 (1.92%)	
occurrences (all)	4	1	
Skin and subcutaneous tissue disorders			

Dry skin			
subjects affected / exposed	2 / 46 (4.35%)	2 / 52 (3.85%)	
occurrences (all)	2	2	
Erythema			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	5 / 46 (10.87%)	7 / 52 (13.46%)	
occurrences (all)	5	7	
Rash			
subjects affected / exposed	6 / 46 (13.04%)	3 / 52 (5.77%)	
occurrences (all)	6	3	
Skin lesion			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	8 / 46 (17.39%)	0 / 52 (0.00%)	
occurrences (all)	8	0	
Hypothyroidism			
subjects affected / exposed	5 / 46 (10.87%)	2 / 52 (3.85%)	
occurrences (all)	5	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 46 (8.70%)	3 / 52 (5.77%)	
occurrences (all)	4	3	
Myalgia			
subjects affected / exposed	3 / 46 (6.52%)	2 / 52 (3.85%)	
occurrences (all)	3	2	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	2 / 46 (4.35%)	0 / 52 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported