Clinical trial results:
A phase II trial assessing Bintrafusp alfa, a bifunctional fusion protein targeting TGF- and PD-L1, in a pre-operative setting for resectable and untreated head and neck squamous cell carcinoma.

Summary

EudraCT number	2019-004052-11
Trial protocol	FR
Global end of trial date	07 January 2022

Results information

Result version number	v1 (current)
This version publication date	09 March 2025
First version publication date	09 March 2025

Trial information

Trial identification

Sponsor protocol code	UC-HNG/1909

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04428047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France,
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	09 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 January 2022
Global end of trial reached?	Yes
Global end of trial date	07 January 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of bintrafusp alfa, measured by pathological response (PathR), given in a pre-operative setting.

Protection of trial subjects:

This study was conducted in conformity 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 French regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	5
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 18-MAR-2021 (first inclusion) and 8-OCT-2021 (inclusion suspension), 11 patients were enrolled in the ICING study. However, only 7 patients recruited by 2 cancer centers.

Pre-assignment

Screening details:

Patients were included in the study with histologically or cytologically confirmed HNSCC of the oral cavity, oropharynx, larynx or hypopharynx, previously untreated, with indication of primary surgery. Patients with a diagnosis of HNSCC of occult primary cannot be enrolled.

Period 1

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

Arms

Arm title	COHORT A

Arm description: -

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

Dosage and administration details:

bintrafusp alfa will be administered by intravenous infusion over 60 minutes at a dose of 1200 mg on Day1 and Day15

Number of subjects in period 1	COHORT A
Started	7
Completed	6
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	COHORT A

Reporting group description: -

Reporting group values	COHORT A	Total	
Number of subjects	7	7	
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)	5	5	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
median	61		
full range (min-max)	34 to 74	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	3	3	
ECOG Units: Subjects			
ECOG 0	6	6	
ECOG 1	1	1	
The primary site of cancer Units: Subjects			
Oral cavity	5	5	
Oropharynx	2	2	
Serology for HPV Units: Subjects			
Negative	7	7	
Cancer stage T Units: Subjects			
T2	2	2	
T3	1	1	
T4	4	4	
Cancer stage N Units: Subjects			
N0	2	2	
N1	1	1	

N2	3	3	
N3	1	1	
Cancer stage M Units: Subjects			
M0	7	7	

End points

End points reporting groups

Reporting group title	COHORT A

Reporting group description: -

Primary: Pathological response (PathR)

End point title	Pathological response (PathR)[1]

End point description:

Pathological tumor response was evaluated as the percentage of the tumor area showing evidence of anti-tumor activity, such as tumor cell necrosis and/or giant cell/histolytic reaction to keratinous debris.

* and/or giant cell/histolytic reaction to keratinous debris

End point type	Primary

End point timeframe:

From inclusion to 1 month after surgery

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statiscal analyses for the primary end point.
Due to an early trial termination only 7 patients were included, such a low number of patients did not allow to evaluate Bintrafusp alfa efficacy with enough power.

End point values	COHORT A			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percent				
arithmetic mean (inter-quartile range (Q1-Q3))				
Tumor diameter (mm)	33.9 (27.5 to 45)			
Number of slides (n)	8.4 (8 to 10)			
Sum of tumor necrosis*	183.5 (58.3 to 240)			
PathR	17.8 (4.4 to 22.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of the impact of inking the tumor margins during baseline endoscopy to avoid surgical plan changes putatively induced by tumor shrinking under therapy

End point title	Evaluation of the impact of inking the tumor margins during baseline endoscopy to avoid surgical plan changes putatively induced by tumor shrinking under therapy

End point description:

Evaluation of the impact of inking the tumor margins during baseline endoscopy to avoid surgical plan

changes putatively induced by tumor shrinking under therapy.
Just before the beginning of the surgery, surgeons will answer a question (4-level: Yes, No, Not evaluable, Unknown) to indicate if their surgical plan would have been different in the absence of ink labelling.

End point type	Secondary

End point timeframe:

From inclusion to surgery, an average of 21 days

End point values	COHORT A			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Cm				
arithmetic mean (inter-quartile range (Q1-Q3))				
Tumor front to inked zone mean distance	0.83 (0.75 to 1.5)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Survival

End point title	Survival

End point description:

Number of patients alive at time of statisticals analysis.

End point type	Post-hoc

End point timeframe:

At time of statisticals analysis

End point values	COHORT A			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Number				
Alive	7			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Endoscopy to surgery interval

End point title	Endoscopy to surgery interval

End point description:

The mean time between endoscopy and surgery and the mean time between the first dose of Bintrafusp alfa and surgery

End point type	Post-hoc

End point timeframe:

At the end of study.

End point values	COHORT A			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Days				
arithmetic mean (inter-quartile range (Q1-Q3))				
Endoscopy to surgery mean time	27.4 (25 to 28.5)			
Bintrafusp alfa first dose to surgery mean time	23.3 (21.5 to 24.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion to 12 weeks after the last administration of the investigational product.

Adverse event reporting additional description:

Due to an early trial termination only 7 patients were included, such a low number of patients did not allow to evaluate Bintrafusp alfa efficacy with enough power. Similarly, Bintrafusp alfa safety data gathered from this restricted population over 6 months instead of the 36 months initially envisioned does not provide significant evidence.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	COHORT A

Reporting group description: -

Serious adverse events	COHORT A		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Postoperative hemorrhage			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	COHORT A		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hyperthermia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Mucositis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Investigations			
Weight loss			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Infusion reaction subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Tracheostomy complication subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Vascular access complication subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Nervous system disorders Dysarthria subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 5		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 3		
Hypersalivation subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Tongue pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Xerostomia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders Hyperpigmentation skin subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Intertrigo subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		

Rash vesicular subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Infections and infestations Gingivitis subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all) Surgical site infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2 1 / 7 (14.29%) 1 3 / 7 (42.86%) 4		
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2021	Amendment N°1 (Substantial; approved on 09-DEC-2021): - Study enrollment suspension. Amendment N°2 (Substantial; approved on 12-DEC-2022): - Study inclusion period reduced from 24 to 8 months - Study enrollment termination - Protocol modification: - Efficacy assessment: The assessment of disease-free survival (DFS), overall survival (OS), loco- regional disease-free survival (LR-DFS), and distant disease-free survival (D-DFS) rates that was to be conducted at 12, 18, 24 and 36 was solely performed at 6 months post-surgery. -Safety assessment: Toxicity survey were reduced from 36 to 6 months post-surgery.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 January 2022	The study ICING was suspended early on in response to the preliminary results gathered from two NSCLC randomized trials demonstrating an equivalence or slight inferiority but not superiority of Bintrafusp Alfa compared to anti-PD1/PDL1-based therapy. As a security measure, UNICANCER resorted to suspend all inclusion. At the time of suspension, seven patients had already been enrolled and given the investigational product. Due to this early termination all analyses were restricted to the data collected from those seven patients and toxicity survey was reduced from 36 to 6 months post-surgery.	-

Notes:

Limitations and caveats

None reported