



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 statistical 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 statistical analysis. | |
| End point type | Post-hoc |
| End point timeframe: | |
| At time of statistical 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

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

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|-----------------------|----------|
| 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 occurrences (all) | 1 / 7 (14.29%) 1 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Hyperthermia subjects affected / exposed occurrences (all) Mucositis subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | | |
| Investigations Weight loss subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 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 | <p>Amendment N°1 (Substantial; approved on 09-DEC-2021):</p> <ul style="list-style-type: none">- Study enrollment suspension. <p>Amendment N°2 (Substantial; approved on 12-DEC-2022):</p> <ul style="list-style-type: none">- Study inclusion period reduced from 24 to 8 months- Study enrollment termination- Protocol modification:<ul style="list-style-type: none">- 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 | <p>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.</p> <p>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.</p> | - |

Notes:

Limitations and caveats

None reported