Clinical trial results:
Phase II randomized trial comparating two concomitant administration of radiotherapy with cisplatin in patients with not operated or inoperable squamous cell carcinoma of the head and neck or with recurrence high-risk in adjuvant postoperative treatment.

Summary

EudraCT number	2015-001928-29
Trial protocol	FR
Global end of trial date	10 May 2021

Results information

Result version number	v1 (current)
This version publication date	07 April 2024
First version publication date	07 April 2024
Summary attachment (see zip file)	Summary (2015-001928-29_résumé rapport final_CisFRad.pdf)

Trial information

Trial identification

Sponsor protocol code	GORTEC 2015-02: CisFRad

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03330249
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GORTEC
Sponsor organisation address	4 Bis Rue Emile Zola, TOURS, France, 37000
Public contact	Adeline PECHERY, GORTEC, 33 (0)6 49 21 06 07, adeline.pechery@gortec.fr
Scientific contact	Dr Lionnel GEOFFROIS, GORTEC, 33 (0)3 68 76 67 67, c.borel@icans.eu

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	04 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 May 2021
Global end of trial reached?	Yes
Global end of trial date	10 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare the cumulative dose of Cisplatin administered concomitantly with radiotherapy in the reference arm A (Cisplatin 100 mg / m2 J1 every 21 days) and in the experimental B arm (Split Cisplatin 25 mg / m2 / D D1 to D4 every 21 days).

Protection of trial subjects:

Follow-up of patients according to the protocol calendar, adaptation of treatment or discontinuation of treatment according to toxicities

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 124
Worldwide total number of subjects	124
EEA total number of subjects	124

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)	88
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study is presented to patients during a standard visit by the investigator. If the patient agrees to participate and meets the eligibility criteria, then they can be included in the trial.

Pre-assignment

Screening details:

-Squamous cell carcinoma of the upper aerodigestive tract, stage III or IV
- Patient not operated on and/or not operable for reasons of non-extirpability, loco-regional extension, general state or medical condition Or Patient operated on within 8 weeks preceding radiotherapy with a high risk of recurrence

Period 1

Period 1 title	final analysis (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Standard arm

Arm type	Active comparator
Investigational medicinal product name	CISPLATINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatine : 100 mg/m2 in IV at D1, D22 and D43 of the radiotherapy

Arm title	Arm B

Arm description:

Fractionned experimental

Arm type	Experimental
Investigational medicinal product name	CISPLATINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatine : 25 mg/m2/d in IV at D1 à J4, D22 to D25 and D43 to D46 of the radiotherapy

Number of subjects in period 1	Arm A	Arm B
Started	65	59
Completed	64	58
Not completed	1	1
Consent withdrawn by subject	-	1
Under guardianship	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description: Standard arm	
Reporting group title	Arm B
Reporting group description: Fractionned experimental	

Reporting group values	Arm A	Arm B	Total
Number of subjects	65	59	124
Age categorical Units: Subjects			
Adults (18-64 years)	44	43	87
From 65-84 years	21	16	37
Age continuous Units: years			
median	61	61	
full range (min-max)	57 to 66	55 to 65	-
Gender categorical Units: Subjects			
Female	11	10	21
Male	54	49	103

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description: Standard arm	
Reporting group title	Arm B
Reporting group description: Fractionned experimental	

Primary: Cumulative dose of Cisplatin administered in the intention to treat

End point title	Cumulative dose of Cisplatin administered in the intention to treat[1]
End point description: Cumulative dose of cisplatin delivered during radiotherapy compared between the two arms	
End point type	Primary
End point timeframe: At the end of study	

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: See in the summary of report

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	58		
Units: dose mg/m2				
median (inter-quartile range (Q1-Q3))	274 (198 to 295)	291 (251 to 298)		

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative dose of Cisplatin administered in the per-protocol

End point title	Cumulative dose of Cisplatin administered in the per-protocol[2]
End point description:	
End point type	Primary
End point timeframe: At the end of study	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: See in the summary of report

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	51		
Units: dose mg/m2				
least squares mean (inter-quartile range (Q1-Q3))	280 (198 to 295)	292 (273 to 298)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

monitoring of tolerance begins when the subject is included in the study (date of signing the informed consent) until the completion of the end-of-study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B

Reporting group description: -

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 65 (32.31%)	12 / 59 (20.34%)	
number of deaths (all causes)	30	24	
number of deaths resulting from adverse events	1	0	
Blood and lymphatic system disorders			
Septic neutropenia			
subjects affected / exposed	4 / 65 (6.15%)	2 / 59 (3.39%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	4 / 4	1 / 1	
Sepsis			
subjects affected / exposed	10 / 65 (15.38%)	6 / 59 (10.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
mucositis			
subjects affected / exposed	4 / 65 (6.15%)	4 / 59 (6.78%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute renal impairment			

subjects affected / exposed	10 / 65 (15.38%)	10 / 59 (16.95%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 65 (73.85%)	44 / 59 (74.58%)	
General disorders and administration site conditions			
xerostomia			
subjects affected / exposed	26 / 65 (40.00%)	32 / 59 (54.24%)	
occurrences (all)	26	32	
Ear and labyrinth disorders			
larynx			
subjects affected / exposed	11 / 65 (16.92%)	7 / 59 (11.86%)	
occurrences (all)	11	7	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	10 / 65 (15.38%)	11 / 59 (18.64%)	
occurrences (all)	10	11	
mucositis			
subjects affected / exposed	10 / 65 (15.38%)	9 / 59 (15.25%)	
occurrences (all)	10	9	
Skin and subcutaneous tissue disorders			
subcutaneous			
subjects affected / exposed	22 / 65 (33.85%)	22 / 59 (37.29%)	
occurrences (all)	22	22	
Musculoskeletal and connective tissue disorders			
bone			
subjects affected / exposed	2 / 65 (3.08%)	3 / 59 (5.08%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2015	- Clarification of the examinations to be carried out during post-treatment follow-up - Analysis of HPV status for patients with an oropharynx tumor - Development of the research hypothesis, following the question asked by the EC during the initial submission
19 February 2016	-Clarification of the examinations to be carried out: certain examinations present in the body of the protocol have been forgotten in the table of investigations; - Modification of the duration of follow-up of the study due to topography error: In the synopsis, it is noted that the follow-up is up to one year while in the table of investigations, it is up to 3 years; - Urine samples are made optional; - Pharmacokinetics (PK) is also made optional because it requires a lot of involvement from the center. On the other hand, if the center decides to do it, it will only be carried out during the first cycle of treatment.
07 June 2016	Updated list of centers
13 September 2016	Updated list of centers
02 February 2017	Updated list of centers
10 October 2017	Increase in the number of patients to be included
15 May 2018	Extension of the inclusion period and updating of the list of centers
07 July 2020	Updated list of centers

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported