Clinical trial results:
Phase II multicentre non-randomised trial investigating the impact of radio-chemotherapy (65 Gy + cisplatin + 5FU) in combination with cetuximab in patients with locally advanced anal cancer.

Summary

EudraCT number	2007-007029-38
Trial protocol	FR
Global end of trial date	04 May 2014

Results information

Result version number	v1 (current)
This version publication date	05 January 2025
First version publication date	05 January 2025

Trial information

Trial identification

Sponsor protocol code	ACCORD 16 / 0708

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	13 April 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 May 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the objective responserate (complete and partial response) 8 weeks after the end of treatment (radio-chemotherapy + anti-EGFR + adjuvant radiotherapy) in locally advanced anal cancer.

Protection of trial subjects:

To assess the objective tumour response (complete and partial response) 8 weeks after the end of treatment (radio-chemotherapy + anti-EGFR + adjuvant radiotherapy) in locally advanced anal cancer.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	15
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment only in France,
Date of first inclusion: 01-Apr-2009
Date of last inclusion: 03-May-2010

Pre-assignment

Screening details:

All men and women 18-80 years with an histologically confirmed anal cancer, squamous cell disease, locally advanced non metastatic disease.

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	Radiochemotherapy+ cetuximab

Arm description:

Only one arm in this trial
Treatments: 65 GY+ CISPLATINUM+5FU+CETUXIMAB

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

Dosage and administration details:

Patients received cetuximab IV 400 mg/m² on day 0 and 250 mg/m² on day 7, 14, 21, 28 and 35.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

The patients received 5FU IV (800 mg/m²/d decreased to 600 mg/m²/d after amandment) on day 7-10 and 35-38.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The patients received Cisplatin IV 80 mg/m² over 2 hours on days 7 and 35.

Number of subjects in period 1	Radiochemotherapy + cetuximab
Started	16
Completed	5
Not completed	11
Consent withdrawn by subject	2
medication error	1
Toxicity	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall periode

Reporting group description: -

Reporting group values	Overall periode	Total	
Number of subjects	16	16	
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)	15	15	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	14	14	
Male	2	2	
Performance status Units: Subjects			
Performance status 0	13	13	
Performance status 1	3	3	
T Stage Units: Subjects			
T1	1	1	
T2	4	4	
T3	6	6	
T4	5	5	
N Stage Units: Subjects			
N0	3	3	
N1	5	5	
N2	5	5	
N+	3	3	
M Stage Units: Subjects			
M0	16	16	
Histological type Units: Subjects			
Well differenciated	7	7	
Moderate differenciated	2	2	
Poorly differenciated	5	5	

Without further information	2	2	

End points

End points reporting groups

Reporting group title	Radiochemotherapy+ cetuximab

Reporting group description:

Only one arm in this trial
Treatments: 65 GY+ CISPLATINUM+5FU+CETUXIMAB

Primary: Tumoral response rate

End point title	Tumoral response rate[1]

End point description:

The primary endpoint was the clinical benefit rate (CBR) defined as the percentage of patients who had a complete response (CR), partial response, or stable disease (SD), 8 weeks after the end of study treatment.comrising radiotheray , chemotheray and cetumaximab followed by additional radiotherapy, according to the RECIST criteria.

End point type	Primary

End point timeframe:

8 weeks after the end of study treatment.

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.

End point values	Radiochemotherapy+ cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Number				
Complete response	6			
Partial response	4			
Stable disease	0			
Progressive disease	1			
Non evaluable	5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Reporting from the signing of the 1st consent form, until 30 days following the last administration of the experimental treatment

Adverse event reporting additional description:

For non-serious adverse events, the number of occurrences were not recorded, the number of patient affected were the only value available. Thus, the number of patient affected was entered in both "Subjects affected number" and "Occurrence all number" fields.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11

Reporting groups

Reporting group title	all patients

Reporting group description: -

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 16 (75.00%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Anal injury			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation injury			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile aplasia			

subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Lymphopenia				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombopenia				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
General physical health deterioration				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea of presumed infectious origin				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Fistula involving female genital tract			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hemorrhage rectal			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Meningitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Perineal infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Potassium deficiency			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)		
Investigations			
Gamma-glutamyltransferase			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Potassium			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	6		
Calcium			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	6		
Sodium			
subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	7		
Albumin			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 16 (68.75%)		
occurrences (all)	11		
Fever			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Weight loss			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Anorexia			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Epithelitis			
subjects affected / exposed	10 / 16 (62.50%)		
occurrences (all)	10		
Blood and lymphatic system disorders			

Hemoglobin			
subjects affected / exposed	12 / 16 (75.00%)		
occurrences (all)	12		
Neutrophils			
subjects affected / exposed	8 / 16 (50.00%)		
occurrences (all)	8		
Platelets			
subjects affected / exposed	10 / 16 (62.50%)		
occurrences (all)	10		
Lymphocyte			
subjects affected / exposed	9 / 16 (56.25%)		
occurrences (all)	9		
Gastrointestinal disorders			
Mucitis			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Vomiting			
subjects affected / exposed	9 / 16 (56.25%)		
occurrences (all)	9		
Rectorrhagia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hemorrhoidal seizure			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Anal incontinence			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	9 / 16 (56.25%)		
occurrences (all)	9		
Constipation			
subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	7		
Proctitis			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal pain			
subjects affected / exposed	9 / 16 (56.25%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorders			
Skin dryness			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Skin eruption			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Hand and foot syndrome			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Rash acneiform			
subjects affected / exposed	12 / 16 (75.00%)		
occurrences (all)	12		
Pruritis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pruritic rash			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Radiodermatitis			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	5		
Acne			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Renal and urinary disorders			
Creatinine			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Dysuria			

subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Pollakiuria			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Cystitis/Urethritis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Urinary burning			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
Neutropenia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Localized infection			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Anitis			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 December 2008	- Correction of an error concerning the dosage for Cetuximab 5 mg/ml: The dosage at 400 mg/m² corresponds to 80 ml/m² and not 200 ml/m². The dosage of 250 mg/m² corresponds to 50 ml/m² and not 125 ml/m². - Clarification regarding renal or neurological toxicity of Cisplatin - In the information note, it is added that premedication with corticosteroids is necessary with monoclonal antibodies. - Information concerning cetuximab 5mg/ml treatment was added: Initially the formulation to be used was 5mg/ml No HT. However, the treatment used will be cetuximab HT, i.e. the one with marketing authorisation. - Investigators' list update
23 January 2009	- Investigators' list update.
15 June 2009	- Investigators' list updated
30 July 2009	- Modification of the method of administration of 5FU - Clarification of the inclusion criterea 1 - Clarification about the administration of Cetuximab if radiotherapy is stopped - The investigators list update - Information file and consent form modification
24 August 2009	- All inclusion suspended: Following the abnormal occurrence of major toxicities (grade 4 neutropenia, grade 4 thrombocytopenia, grade 3 febrile aplasia) qualified as SUSARs for patients n°01 and n°03, it was decided on 30 July 2009 between the Sponsor, the coordinating investigator and the investigators in charge of patients n°1 and n°3 to suspend inclusion in the trial. A 3 SUSAR concerning patient n°5 was notified on 06 August 2009. -Investigators' list updated
18 December 2009	- Request for resumption of inclusions: 6 New patients were included despite of 10 planned. - Protocol modification: Reduction in the 5 FU dose from 800 mg/m²/d to 600 mg/m²/d - Modification of the Cetuximab file reference (SmPC will replace BI) - Re-opening of the first inclusion centres and evaluation of toxicity in the next 10 patients included. - The investigators' list updated
19 October 2010	- All inculsions suspended on 05-May-2010. - The investigators' list updated
07 June 2011	-Permanent suspension of the inclusions following the IDMC conducted on 26 November 2010.
10 January 2012	- Amendment to information in the CT application form - Amendment to the protocol - change of sponsor's name

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 November 2010	The IDMC decided to stop the trial after reviewing the data of the fist 16 patients for a high rate of toxicity and an insufficient efficacy. 5FU+cisplatinum+cetuximab is not recommended combined with RT even in case ol locally advenced disease.	-

Notes:

Limitations and caveats

None reported