



Clinical trial results:

Etude de phase III randomisée, multicentrique comparant une chimiothérapie d'induction par TPF suivie d'une association radiothérapie Erbitux® versus une radiochimiothérapie concomitante chez des patients présentant un carcinome épidermoïde des VADS localement évolué inopérable

Summary

EudraCT number	2008-005760-14
Trial protocol	FR BE
Global end of trial date	06 November 2018

Results information

Result version number	v1 (current)
This version publication date	12 August 2023
First version publication date	12 August 2023
Summary attachment (see zip file)	Summary (202304201 ANSM rapport final.pdf)

Trial information

Trial identification

Sponsor protocol code	GORTEC 2007-02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01233843
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GORTEC
Sponsor organisation address	CHRU de Tours – Hôpital Bretonneau, 2 Boulevard Tonnellé, TOURS cedex 9, France, 37044
Public contact	Fanny LOUAT, GORTEC, 0033 02 42 06 01 85, fanny.louat@gortec.fr
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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	28 February 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Comparer la survie sans progression des patients du bras radiochimiothérapie concomitante et des patients du bras chimiothérapie d'induction (Taxotère, Cisplatine, 5 Fluorouracile) puis radiothérapie et Erbitux.

Protection of trial subjects:

Les doses de TPF devront être modifiées en cas de toxicité hématologique sévère et ou non hématologique.

Si plusieurs toxicités sont observées chez le même patient, l'adaptation de dose doit suivre la recommandation la plus restrictive. Il est également important de souligner qu'en cas de réduction de dose pour une toxicité, la dose des cures suivantes ne doit jamais être ré-escaladée.

En cas de traitement retardé de plus de deux semaines en raison de toxicités, le patient sera sorti de l'essai.

Le cetuximab doit être administré sous la surveillance d'un médecin expérimenté dans l'administration de médicaments cytotoxiques. Une surveillance étroite du patient (incluant les signes vitaux) est nécessaire pendant la perfusion et jusqu'à une heure après la fin de la perfusion afin d'observer la survenue potentielle d'événements indésirables (en particulier réaction de type allergie ou hypersensibilité). La disponibilité d'un matériel de réanimation est indispensable.

L'ensemble des traitements symptomatiques nécessaires à la gestion des effets secondaires est autorisé (anti-nauséeux, antalgiques, bains de bouche, antibiotiques...) en l'absence d'interaction connue avec le médicament à l'étude.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	France: 357
Worldwide total number of subjects	370
EEA total number of subjects	370

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)	350
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient avec Carcinome épidermoïde des VADS localement évolué. Les patients sont inclus en France et en Belgique pendant 5 ans

Pre-assignment

Screening details:

Critères d'inclusion :

-Carcinome épidermoïde histologiquement prouvé de la cavité buccale, de l'oropharynx, du larynx ou de l'hypopharynx, de stade IV non métastatique

-Stades TNM : T2-T4 et N2b-c ou N3

-Non opérable

Au moins une lésion mesurable (RECIST : unidimensionnelle)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Radio chimiothérapie concomitante

Arm description:

Radiothérapie 70 Gy, 7 semaines, fractionnement et étalement classiques

Chimiothérapie : Carboplatine 70 mg /m²/ jour J1 à J4 et 5FU 600 mg/m²/jour de J1 à J4, semaines 1-4 et 7

Arm type	Active comparator
Investigational medicinal product name	carboplatine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

0 mg /m²/ jour J1 à J4

Investigational medicinal product name	5 Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion , Injection

Dosage and administration details:

600 mg/m²/jour de J1 à J4, semaines 1-4 et 7

Arm title	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab
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Arm description:

TPF : 3 cycles

Docétaxel : 75 mg/m² J1

Cisplatine : 75 mg/m² J1

5FU : 750 mg/m²/ jour J1 à J5 Reprise à J 22 et J43

Cetuximab : à débiter à J-7 de la radiothérapie, dose de charge 400 mg/m² puis 250 mg/m² hebdomadaire sur toute la durée de la radiothérapie (pour un total de 8 doses incluant la dose de charge)

Radiothérapie (RT) : 70 Gy, fractionnement et étalement classiques

Arm type	Experimental
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Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

75 mg/m² J1 while 3 cycles

Investigational medicinal product name	Cisplatine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Concentrate for solution for injection
Routes of administration	Concentrate for solution for infusion , Injection

Dosage and administration details:

75 mg/m² J1 while 3 cycles

Investigational medicinal product name	5 Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion , Injection

Dosage and administration details:

750 mg/m²/ jour J1 à J5 Reprise à J 22 et J43 while 3 cycles

Number of subjects in period 1	Radio chimiothérapie concomitante	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab
Started	184	186
Completed	174	180
Not completed	10	6
no receive treatment	10	6

Baseline characteristics

Reporting groups

Reporting group title	Radio chimiothérapie concomitante
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Reporting group description:

Radiothérapie 70 Gy, 7 semaines, fractionnement et étalement classiques

Chimiothérapie : Carboplatine 70 mg /m²/ jour J1 à J4 et 5FU 600 mg/m²/jour de J1 à J4, semaines 1-4 et 7

Reporting group title	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab
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Reporting group description:

TPF : 3 cycles

Docétaxel : 75 mg/m² J1

Cisplatine : 75 mg/m² J1

5FU : 750 mg/m²/ jour J1 à J5 Reprise à J 22 et J43

Cetuximab : à débiter à J-7 de la radiothérapie, dose de charge 400 mg/m² puis 250 mg/m² hebdomadaire sur toute la durée de la radiothérapie (pour un total de 8 doses incluant la dose de charge)

Radiothérapie (RT) : 70 Gy, fractionnement et étalement classiques

Reporting group values	Radio chimiothérapie concomitante	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab	Total
Number of subjects	184	186	370
Age categorical			
Patient avec carcinome épidermoïde histologiquement prouvé de la cavité buccale, de l'oropharynx, du larynx ou de l'hypopharynx, de stade IV non métastatique			
Units: Subjects			
Adults (18-64 years)	162	162	324
From 65-84 years	22	24	46
Gender categorical			
Units: Subjects			
Female	27	24	51
Male	157	162	319

End points

End points reporting groups

Reporting group title	Radio chimiothérapie concomitante
Reporting group description: Radiothérapie 70 Gy, 7 semaines, fractionnement et étalement classiques Chimiothérapie : Carboplatine 70 mg /m ² / jour J1 à J4 et 5FU 600 mg/m ² /jour de J1 à J4, semaines 1-4 et 7	
Reporting group title	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab
Reporting group description: TPF : 3 cycles Docétaxel : 75 mg/m ² J1 Cisplatine : 75 mg/m ² J1 5FU : 750 mg/m ² / jour J1 à J5 Reprise à J 22 et J43 Cetuximab : à débiter à J-7 de la radiothérapie, dose de charge 400 mg/m ² puis 250 mg/m ² hebdomadaire sur toute la durée de la radiothérapie (pour un total de 8 doses incluant la dose de charge) Radiothérapie (RT) : 70 Gy, fractionnement et étalement classiques	

Primary: Efficacy

End point title	Efficacy
End point description: La survie sans progression est définie comme le délai entre la date de randomisation et la survenue d'une récurrence ou d'une poursuite évolutive clinique ou radiologique sur le site primitif ou sur les ganglions ou la survenue de métastases à distance ou la survenue d'un décès quelle qu'en soit la cause.	
End point type	Primary
End point timeframe: Le critère de jugement principal étant le taux de survie sans progression à 2 ans, un bilan endoscopique et scanographique (et/ou IRM) sera systématiquement réalisé 2 ans après la randomisation pour évaluer la réponse tumorale.	

End point values	Radio chimiothérapie concomitante	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	180		
Units: percentage	174	180		

Statistical analyses

Statistical analysis title	response to treatment
Statistical analysis description: The analysis was performed in the Intent to Treat (ITT) population according to randomized treatment group	
Comparison groups	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab v Radio chimiothérapie concomitante

Number of subjects included in analysis	354
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.4
Method	Regression, Cox

Secondary: Response rate according to RECIST

End point title	Response rate according to RECIST
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End point description:

End point type	Secondary
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End point timeframe:

Response rate according to RECIST was evaluated at week 9 or 10 in arm B and at 3 months after the end of treatment for both arms

End point values	Radio chimiothérapie concomitante	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	180		
Units: percentage	174	180		

Statistical analyses

No statistical analyses for this end point

Secondary: Metastases rate

End point title	Metastases rate
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End point description:

Le taux de métastases est défini comme le nombre de patients ayant eu une évolution avec apparition de métastase(s)

End point type	Secondary
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End point timeframe:

Metastases rate defined as the time between randomization and the first event.

End point values	Radio chimiothérapie concomitante	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	180		
Units: percentage	174	180		

Statistical analyses

No statistical analyses for this end point

Secondary: Locoregional control rate

End point title	Locoregional control rate
End point description: L'échec loco-régional est défini par la survenue d'une récurrence ou d'une poursuite évolutive clinique ou radiologique sur le site primitif ou sur les ganglions.	
End point type	Secondary
End point timeframe: Locoregional control rate defined as the time between randomization and the first event	

End point values	Radio chimiothérapie concomitante	Docetaxel, cisplatine, 5FU puis radiothérapie + cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	180		
Units: percentage	174	180		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

from the start of treatment until 1 month after the end of treatment

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11
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Reporting groups

Reporting group title	Comparator Arm
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Reporting group description: -

Reporting group title	Experimental arm
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Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There are non serious adverse events, but they did not listed in the report. There are 168 in comparator arm and 146 in experimental arm

Serious adverse events	Comparator Arm	Experimental arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	80 / 174 (45.98%)	99 / 180 (55.00%)	
number of deaths (all causes)	122	128	
number of deaths resulting from adverse events	3	12	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant dysphagia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	8 / 174 (4.60%)	8 / 180 (4.44%)	
occurrences causally related to treatment / all	8 / 8	8 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			

subjects affected / exposed	6 / 174 (3.45%)	4 / 180 (2.22%)	
occurrences causally related to treatment / all	6 / 6	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour ulceration			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial rupture			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism venous			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			

subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal haemorrhage			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			

subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	2 / 174 (1.15%)	5 / 180 (2.78%)	
occurrences causally related to treatment / all	2 / 2	5 / 5	
deaths causally related to treatment / all	2 / 2	5 / 5	
fatigue			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	25 / 174 (14.37%)	19 / 180 (10.56%)	
occurrences causally related to treatment / all	25 / 25	19 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 174 (0.57%)	2 / 180 (1.11%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 174 (0.00%)	4 / 180 (2.22%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactoid reaction			

subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial obstruction			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal necrosis			

subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal obstruction			
subjects affected / exposed	2 / 174 (1.15%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 174 (1.72%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
myocardial strain			

subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	2 / 174 (1.15%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
accident overdose			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Air embolism			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaesthetic complication			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrostomy failure			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 174 (0.00%)	2 / 180 (1.11%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation mucositis			

subjects affected / exposed	4 / 174 (2.30%)	6 / 180 (3.33%)	
occurrences causally related to treatment / all	4 / 4	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation necrosis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation skin injury			
subjects affected / exposed	1 / 174 (0.57%)	6 / 180 (3.33%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	2 / 174 (1.15%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 174 (1.15%)	3 / 180 (1.67%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of chronic disease			

subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	2 / 2	
Bone marrow failure			
subjects affected / exposed	4 / 174 (2.30%)	3 / 180 (1.67%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	4 / 174 (2.30%)	15 / 180 (8.33%)	
occurrences causally related to treatment / all	4 / 4	15 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 174 (0.00%)	9 / 180 (5.00%)	
occurrences causally related to treatment / all	0 / 0	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	2 / 2	
Neutropenia			
subjects affected / exposed	1 / 174 (0.57%)	2 / 180 (1.11%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 174 (1.15%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	2 / 174 (1.15%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic pancreatitis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Diarrhoea			
subjects affected / exposed	0 / 174 (0.00%)	7 / 180 (3.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	3 / 174 (1.72%)	2 / 180 (1.11%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			

subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal mass			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
malaena			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenic colitis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 174 (0.57%)	6 / 180 (3.33%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 174 (0.57%)	6 / 180 (3.33%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal syndrome			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	13 / 174 (7.47%)	11 / 180 (6.11%)	
occurrences causally related to treatment / all	13 / 13	11 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis infected			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation skin injury			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 174 (1.15%)	4 / 180 (2.22%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal failure			
subjects affected / exposed	0 / 174 (0.00%)	3 / 180 (1.67%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal salt-wasting syndrome			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	2 / 174 (1.15%)	4 / 180 (2.22%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 174 (0.57%)	2 / 180 (1.11%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			

subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis staphylococcal			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 174 (0.00%)	2 / 180 (1.11%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected fistula			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			

subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION PSEUDOMONAL			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal infection			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 174 (3.45%)	4 / 180 (2.22%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	2 / 2	
PNEUMONIA SEPSIS			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTIOUS COLITIS			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	1 / 174 (0.57%)	7 / 180 (3.89%)	
occurrences causally related to treatment / all	1 / 1	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 174 (0.57%)	8 / 180 (4.44%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	3 / 174 (1.72%)	4 / 180 (2.22%)	
occurrences causally related to treatment / all	3 / 3	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection bacterial			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Urinary tract infection			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	2 / 174 (1.15%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding disorder			

subjects affected / exposed	1 / 174 (0.57%)	0 / 180 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 174 (0.57%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 180 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Comparator Arm	Experimental arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	168 / 174 (96.55%)	146 / 180 (81.11%)	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	168 / 174 (96.55%)	146 / 180 (81.11%)	
occurrences (all)	168	146	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2009	Add of new investigators
02 February 2010	Add of new investigatord
06 May 2010	Add of new investigators
04 January 2011	Add of new centers
03 July 2012	Prolongation of the duration of study
02 April 2013	Add of number of subjects included in the study
04 June 2013	change of PI in a center
02 September 2014	Prolongation of the duration of follow-up after treatment
04 April 2017	Add of analyse of tumor samples

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported