Clinical trial results:
Randomised phase-III-trial of simultaneous radiochemotherapy (RCT) of locally advanced head and neck cancer in the stages III and IV A-B: Comparing dose reduced RCT (63.6 Gy) with Paclitaxel/Cisplatin to standard RCT (70.2 Gy) with 5-Fluorouracil/Cisplatin

Summary

EudraCT number	2005-003484-23
Trial protocol	DE
Global end of trial date	20 March 2019

Results information

Result version number	v1 (current)
This version publication date	08 May 2022
First version publication date	08 May 2022

Trial information

Trial identification

Sponsor protocol code	Paccis-RCT_2005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01126216
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Erlangen
Sponsor organisation address	Krankenhausstr. 12, Erlangen, Germany, 91054
Public contact	Studiensekretariat, Universitätsklinikum Erlangen, Strahlenklinik, ++49 0913185-33968, st-studiensekretariat@uk-erlangen.de
Scientific contact	Studiensekretariat, Universitätsklinikum Erlangen, Strahlenklinik, ++49 0913185-33968, st-studiensekretariat@uk-erlangen.de

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 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2019
Global end of trial reached?	Yes
Global end of trial date	20 March 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the superiority of dose reduced radiotherapy (63.6 Gy) with Paclitaxel/Cisplatin versus standard radiotherapy (70.2 Gy) with 5-FU/Cisplatin:
NED-Survival

Protection of trial subjects:

Overall Information on the trial and the possible side effects before starting therapy. Sufficient time for the decision to take part in the trial. Close monitoring of the patients by the study team.

Background therapy:

Supportive Therapy for the side effects of the therapy

Evidence for comparator:

Phase III study

Actual start date of recruitment	28 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 221
Worldwide total number of subjects	221
EEA total number of subjects	221

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)	153
From 65 to 84 years	68

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient in: 14 June 2010
Last patient out of therapy: June 2015
End of follow up: June 2019

Pre-assignment

Screening details:

Main criteria for inclusion:
• Histologically proven, locally advanced stage III-IV A-B (UICC 2002) primary squamous cell carcinoma of the oral cavity, the oropharynx, the hypopharynx, the supraglottic larynx
• Age ≥ 18
• Written informed consent for the participation in the clinical trial

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	Experimental (A)

Arm description:

63,6 Gy accelerated hyperfractionated Radiotherapy with
Paclitaxel (20 mg/m^2/d, d2,5,8,11 and d25,30,33,36) and
Cisplatin (20 mg/m^2/d, d1-4 and 29-32)
Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: d1-4 and 29-32

Arm type	Experimental
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	PR2
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/m^2/d, d1-4 and 29-32

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	PR4
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin may be replaced by Carboplatin in case of nephrotoxicity:
Investigational arm: d1-4 and 29-32

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/m^2/d, d2,5,8,11 and d25,30,33,36

Arm title	Control (B)

Arm description:

70.6 Gy accelerated hyperfractionated Radiotherapy with concomitant fluorouracil (600 mg/m^2/d, days 1-5 and 29-33 as continuous infusion) and cisplatin (20 mg/m^2/d, days 1-5 and 29-33). Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: AUC 1/d d1-5, 29-33

Arm type	Active comparator
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	PR2
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin (20 mg/m^2/d, d1-5 and 29-33)

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	PR4
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: d1-5, 29-33

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	PR3
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5-FU (600 mg/m^2/d, d1-5 and 29-33)

Number of subjects in period 1[1]	Experimental (A)	Control (B)
Started	111	105
Completed	111	105

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Enrolled per randomization were 221 patients. In the experimental arm 4 withdraw the consent and in the control arm 1 died before the treatment started. Therefore the trial started with 216 patients. These 216 patients were analysed.

Baseline characteristics

Reporting groups

Reporting group title	Experimental (A)

Reporting group description:

63,6 Gy accelerated hyperfractionated Radiotherapy with
Paclitaxel (20 mg/m^2/d, d2,5,8,11 and d25,30,33,36) and
Cisplatin (20 mg/m^2/d, d1-4 and 29-32)
Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: d1-4 and 29-32

Reporting group title	Control (B)

Reporting group description:

70.6 Gy accelerated hyperfractionated Radiotherapy with concomitant fluorouracil (600 mg/m^2/d, days 1-5 and 29-33 as continuous infusion) and cisplatin (20 mg/m^2/d, days 1-5 and 29-33). Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: AUC 1/d d1-5, 29-33

Reporting group values	Experimental (A)	Control (B)	Total
Number of subjects	111	105	216
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults 18-80 years	111	105	216
Gender categorical Units: Subjects			
Female	25	20	45
Male	86	85	171

Subject analysis sets

Subject analysis set title	3y-DFS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The primary endpoint was disease-free survival (DFS) as defined from the time of randomization to either locoregional persistant disease at re-staging or recurrent disease during follow-up, distant metastases, or death from any cause, whichever occurred first.

Reporting group values	3y-DFS		
Number of subjects	216		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over Adults 18-80 years	216		
Gender categorical Units: Subjects			
Female	45		
Male	171		

End points

End points reporting groups

Reporting group title	Experimental (A)

Reporting group description:

63,6 Gy accelerated hyperfractionated Radiotherapy with
Paclitaxel (20 mg/m^2/d, d2,5,8,11 and d25,30,33,36) and
Cisplatin (20 mg/m^2/d, d1-4 and 29-32)
Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: d1-4 and 29-32

Reporting group title	Control (B)

Reporting group description:

70.6 Gy accelerated hyperfractionated Radiotherapy with concomitant fluorouracil (600 mg/m^2/d, days 1-5 and 29-33 as continuous infusion) and cisplatin (20 mg/m^2/d, days 1-5 and 29-33). Cisplatin may be replaced by Carboplatin in case of nephrotoxicity: AUC 1/d d1-5, 29-33

Subject analysis set title	3y-DFS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The primary endpoint was disease-free survival (DFS) as defined from the time of randomization to either locoregional persistant disease at re-staging or recurrent disease during follow-up, distant metastases, or death from any cause, whichever occurred first.

Primary: 3y-DFS

End point title	3y-DFS

End point description:

The primary endpoint was disease-free survival (DFS) as defined from the time of randomization to either locoregional persistant disease at re-staging or recurrent disease during follow-up, distant metastases, or death from any cause, whichever occurred first.

End point type	Primary

End point timeframe:

Start to end of follow up

End point values	Experimental (A)	Control (B)	3y-DFS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	111	105		
Units: patients	59	43	216	

Statistical analyses

Statistical analysis title	3y-DFS

Statistical analysis description:

With a median follow-up of 3.7 years, 3y-DFS in the CisFU arm and PacCis arm was 58.2% and 48.4%, respectively (HR 0.82, 95% CI 0.56-1.21, p=0.52). The 3y-OS amounted to 64.6% in the CisFU arm, and to 59.2% in the PacCis arm (HR 0.82, 95% CI 0.54-1.24, p=0.43).

Comparison groups	Experimental (A) v Control (B)

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Logrank
Parameter estimate	Hazard ratio (HR)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Therapy and Follow up	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	Experimental as treated
Reporting group description: Patients treated with experimental regime - Randomization until 3y-Follow up	
Reporting group title	Control as treated
Reporting group description: Patients treated with control regime - Randomization until 3y-Follow up	

Serious adverse events	Experimental as treated	Control as treated	
Total subjects affected by serious adverse events			
subjects affected / exposed	73 / 106 (68.87%)	59 / 109 (54.13%)	
number of deaths (all causes)	48	39	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	2 / 106 (1.89%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flushing			
subjects affected / exposed	2 / 106 (1.89%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Resuscitation			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic fatigue syndrome			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
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	1 / 106 (0.94%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	0 / 106 (0.00%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 106 (0.94%)	3 / 109 (2.75%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 106 (0.94%)	3 / 109 (2.75%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 106 (4.72%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	4 / 106 (3.77%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 106 (2.83%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 106 (0.94%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium tremens			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 106 (0.94%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	5 / 106 (4.72%)	4 / 109 (3.67%)	
occurrences causally related to treatment / all	4 / 5	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood electrolytes abnormal			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal function test abnormal			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation skin injury			
subjects affected / exposed	0 / 106 (0.00%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Constipation			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			

subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 106 (1.89%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 106 (0.94%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 106 (0.94%)	3 / 109 (2.75%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 106 (0.00%)	3 / 109 (2.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	3 / 106 (2.83%)	4 / 109 (3.67%)	
occurrences causally related to treatment / all	2 / 3	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	4 / 106 (3.77%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 106 (2.83%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	3 / 106 (2.83%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	2 / 3	2 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	

Renal failure			
subjects affected / exposed	0 / 106 (0.00%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bone abscess			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	1 / 106 (0.94%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Clostridium difficile infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	11 / 106 (10.38%)	7 / 109 (6.42%)	
occurrences causally related to treatment / all	10 / 11	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	11 / 106 (10.38%)	3 / 109 (2.75%)	
occurrences causally related to treatment / all	6 / 11	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 106 (1.89%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acidosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	3 / 106 (2.83%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			

subjects affected / exposed	1 / 106 (0.94%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 106 (0.00%)	2 / 109 (1.83%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polydipsia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Experimental as treated	Control as treated	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 106 (100.00%)	109 / 109 (100.00%)	
Injury, poisoning and procedural complications			
Dermatitis radiation >= grade 3			
subjects affected / exposed	30 / 106 (28.30%)	37 / 109 (33.94%)	
occurrences (all)	30	37	

Blood and lymphatic system disorders			
Anemia >= grade 3	Additional description: only the highest grade of the toxicity was analysed		
subjects affected / exposed	2 / 106 (1.89%)	12 / 109 (11.01%)	
occurrences (all)	2	12	
Leucocytopenia >= grade 3			
subjects affected / exposed	17 / 106 (16.04%)	37 / 109 (33.94%)	
occurrences (all)	17	37	
Platelet count decreased >= grade 3			
subjects affected / exposed	3 / 106 (2.83%)	6 / 109 (5.50%)	
occurrences (all)	3	6	
General disorders and administration site conditions			
Vomiting >= grade 3			
subjects affected / exposed	2 / 106 (1.89%)	0 / 109 (0.00%)	
occurrences (all)	2	0	
Pain >= grade 3			
subjects affected / exposed	27 / 106 (25.47%)	28 / 109 (25.69%)	
occurrences (all)	27	28	
Immune system disorders			
Allergic reaction >= grade 3			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Dysphagia >= grade 3			
subjects affected / exposed	86 / 106 (81.13%)	84 / 109 (77.06%)	
occurrences (all)	86	84	
Mucositis oral >= grade 3			
subjects affected / exposed	63 / 106 (59.43%)	70 / 109 (64.22%)	
occurrences (all)	63	70	
Renal and urinary disorders			
Creatinine increased >= grade 3			
subjects affected / exposed	2 / 106 (1.89%)	1 / 109 (0.92%)	
occurrences (all)	2	1	
Infections and infestations			
Infections >= grade 3			
subjects affected / exposed	34 / 106 (32.08%)	18 / 109 (16.51%)	
occurrences (all)	34	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 April 2010	Changes requested by the BOB for approval
19 April 2010	Changes requested by the EC in the IC documents
15 August 2011	Addition of Carboplatin as IMP Addition of Study Centers and Changes in investigators Extension of Translational project: Changes in the IC documents
06 February 2014	Statistics: change to adaptive design Closing of a study center
17 June 2015	Stop of Recruitment 15.03.2015

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32044419