Clinical trial results:
Skin Changes in Head and Neck Cancer during Immuno-(Chemo-) and Radiotherapy with Erbitux®

Summary

EudraCT number	2010-019748-38
Trial protocol	DE
Global end of trial date	04 November 2015

Results information

Result version number	v1 (current)
This version publication date	08 September 2021
First version publication date	08 September 2021
Summary attachment (see zip file)	HICARE_Synopsis_CSR_V1.0_20161028 (HICARE_Synopsis_CSR_1.0_20161028.pdf)

Trial information

Trial identification

Sponsor protocol code	UniHD-2010-11-40-1001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01553032
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Heidelberg
Sponsor organisation address	Im Neuenheimer Feld 672, Heidelberg, Germany, 69120
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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	09 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2015
Global end of trial reached?	Yes
Global end of trial date	04 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

It was the primary objective of the study to assess the rate of radiation-induced dermatitis grade 3/4 graded by the National Cancer Institute (NCI), Common Terminology Criteria for Adverse Events (CTCAE) version 4.02.

Protection of trial subjects:

Safety and tolerability assessments: collection of adverse events, routine laboratory parameters, vital signs, ECOG; Data Safety and Monitoring Board (DSMB): assessing safety/risk profile in regular intervals

Background therapy:

Fractionated radiotherapy (3D-conventional or IMRT); total duration of treatment was 7 to 8 weeks corresponding to 30 to 35 fractions of radiotherapy

Evidence for comparator: -

Actual start date of recruitment	14 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 160
Worldwide total number of subjects	160
EEA total number of subjects	160

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)	82
From 65 to 84 years	75
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between June 2011 and July 2015. Recruitment was stopped prematurely in July 2015. Due to persistently slow recruitment and increasing application of skin prophylaxis for patients undergoing radioimmunotherapy in the clinical routine, the expected planned number of patients could not be reached.

Pre-assignment

Screening details:

Inclusion and exclusion criteria were checked by the investigators. 161 pts were screened. 1 patient was excluded due to exclusion criteria (poor general condition due to infection). Of 160 pts enrolled, 154 pts qualified for analysis. 154 pts were analyzed in the Safety Set (SAF); 140 pts were analyzed in the mITT population.

Pre-assignment period milestones

Number of subjects started	161[1]
Intermediate milestone: Number of subjects	Enrolled: 160
Number of subjects completed	154

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failure: poor condition due to infection: 1
Reason: Number of subjects	Consent withdrawn by subject: 2
Reason: Number of subjects	Limited compliance: 1
Reason: Number of subjects	No radiotherapy: 3

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 161 patients were screened for the trial. One patient was excluded due to exclusion criteria (poor general condition due to infection), 160 patients were enrolled into the trial.

Period 1

Period 1 title	Patients analyzed (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Patients analyzed - total
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Cetuximab (Erbitux®): 400 mg/m2 initial dose, 250 mg/m2 weekly for 6 to 7 weeks, intravenous (iv) infusion;
Fractionated radiotherapy (3D-conventional or IMRT): Total duration of treatment was 7 to 8 weeks corresponding to 30 to 35 fractions of radiotherapy

Number of subjects in period 1[2]	Patients analyzed - total
Started	154
Completed	154

Notes:

[2] - 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: 160 patients were enrolled into the trial. However, only 154 patients qualified for analysis, 6 subjects had to be excluded from analysis, as described in section "Subject disposition", sub-section "Pre-assignment". Baseline characteristics are only reported for patients that qualified for analysis, i.e. were included in the full analysis set (FAS) or the modiefied intention to treat population (mITT).

Baseline characteristics

Reporting groups	
Reporting group title	Patients analyzed

Reporting group description: -

Reporting group values	Patients analyzed	Total	
Number of subjects	154	154	
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)	79	79	
From 65-84 years	72	72	
85 years and over	3	3	
Age continuous Units: years			
median	63.8		
full range (min-max)	43.2 to 87.3	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	129	129	
Number of concomitant diseases Units: Subjects			
n = 0	12	12	
n = 1	11	11	
n = 2	18	18	
n > 2	113	113	
Induction chemotherapy Units: Subjects			
Yes	6	6	
No	144	144	
Missing	4	4	
Number of previous surgeries Units: Subjects			
n = 0	130	130	
n = 1	16	16	
n = 2	6	6	
n = 3	2	2	
T-stage at primary diagnosis Units: Subjects			
T1	10	10	

T2	22	22	
T3	35	35	
T4	86	86	
TX	1	1	
N-stage at primary diagnosis Units: Subjects			
N0	22	22	
N1	14	14	
N2a	7	7	
N2b	54	54	
N2c	48	48	
N3	7	7	
NX	2	2	
M-stage at primary diagnosis Units: Subjects			
M0	154	154	
UICC 2010 stage at primary diagnosis Units: Subjects			
II	5	5	
III	13	13	
IVa/b	134	134	
Unknown	2	2	
Number of previous surgeries Units: Subjects			
n = 0	130	130	
n = 1	16	16	
n = 2	6	6	
n = 3	2	2	
Time between last previous surgery and start of study treatment Units: Months			
median	1.4		
full range (min-max)	0.5 to 174.7	-	
Time from primary diagnosis to date of consent Units: Months			
median	1.0		
full range (min-max)	0.1 to 25.8	-	

Subject analysis sets

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population consisted of 140 patients. Patients that did not receive any cetuximab or radiotherapy were excluded from the efficacy analysis as well as patients for whom all lesions were surgically removed with resction outcome R0 prior to study treatment (3 patients had a surgery with resection outcome R0 but had further lesions that were not or not completely resected (resection outcome R2 or RX); these patients were not excluded from analysis).

Patients excluded from mITT:
- R0 resection (all lesions) prior to study treatment (n = 13)
- CUP syndrome (n = 1)

Patients excluded from mITT and SAF:

- No radiotherapy (n = 3)
- Withdrawal of consent (n = 2)
- Limited compliance (n = 1)

Subject analysis set title	SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of all patients who received at least 1 dose of study medication cetuximab and at least 1 fraction of radiotherapy. This population was the primary population for evaluating the rate of radiodermatitis, and the general safety profile.

Patients excluded from SAF (and mITT):
- No radiotherapy (n = 3)
- Withdrawal of consent (n = 2)
- Limited compliance (n = 1)

Reporting group values	mITT	SAF	
Number of subjects	140	154	
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)	67	79	
From 65-84 years	70	72	
85 years and over	3	3	
Age continuous Units: years			
median	66.2	63.8	
full range (min-max)	43.2 to 87.3	43.2 to 87.3	
Gender categorical Units: Subjects			
Female	24	25	
Male	116	129	
Number of concomitant diseases Units: Subjects			
n = 0	8	12	
n = 1	11	11	
n = 2	16	18	
n > 2	105	113	
Induction chemotherapy Units: Subjects			
Yes	6	6	
No	132	144	
Missing	2	4	
Number of previous surgeries Units: Subjects			
n = 0	129	130	
n = 1	6	16	
n = 2	4	6	

n = 3	1	2	
T-stage at primary diagnosis Units: Subjects			
T1	8	10	
T2	17	22	
T3	33	35	
T4	82	86	
TX	0	1	
N-stage at primary diagnosis Units: Subjects			
N0	20	22	
N1	13	14	
N2a	6	7	
N2b	48	54	
N2c	45	48	
N3	6	7	
NX	2	2	
M-stage at primary diagnosis Units: Subjects			
M0	140	154	
UICC 2010 stage at primary diagnosis Units: Subjects			
II	5	5	
III	12	13	
IVa/b	121	134	
Unknown	2	2	
Number of previous surgeries Units: Subjects			
n = 0	129	130	
n = 1	6	16	
n = 2	4	6	
n = 3	1	2	
Time between last previous surgery and start of study treatment Units: Months			
median	1.4	1.4	
full range (min-max)	0.5 to 174.7	0.5 to 174.7	
Time from primary diagnosis to date of consent Units: Months			
median	0.9	1.0	
full range (min-max)	0.1 to 25.8	0.1 to 25.8	

End points

End points reporting groups

Reporting group title	Patients analyzed - total
Reporting group description: -	
Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population consisted of 140 patients. Patients that did not receive any cetuximab or radiotherapy were excluded from the efficacy analysis as well as patients for whom all lesions were surgically removed with resction outcome R0 prior to study treatment (3 patients had a surgery with resection outcome R0 but had further lesions that were not or not completely resected (resection outcome R2 or RX); these patients were not excluded from analysis).

Patients excluded from mITT:
- R0 resection (all lesions) prior to study treatment (n = 13)
- CUP syndrome (n = 1)

Patients excluded from mITT and SAF:
- No radiotherapy (n = 3)
- Withdrawal of consent (n = 2)
- Limited compliance (n = 1)

Subject analysis set title	SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of all patients who received at least 1 dose of study medication cetuximab and at least 1 fraction of radiotherapy. This population was the primary population for evaluating the rate of radiodermatitis, and the general safety profile.

Patients excluded from SAF (and mITT):
- No radiotherapy (n = 3)
- Withdrawal of consent (n = 2)
- Limited compliance (n = 1)

Primary: Rate of radiation dermatitis NCI CTCAE grade 3 and 4

End point title	Rate of radiation dermatitis NCI CTCAE grade 3 and 4[1]

End point description:

The rate of radiation dermatitis grade 3 and 4 was defined as ratio of patients who developed radiation dermatitis of CTCAE (v 4.02) severity grade 3 or 4 until first follow-up visit after end of treatment (55-65 days after last radiation). The grading was determined weekly during therapy and once at the first follow-up visit (55-65 days after end of treatment) by the local investigator.

End point type	Primary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

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: This single-arm trial was explorative in nature with the goal to explore the side effect "radiation dermatitis". No hypothesis was stated and therefore data analysis was conducted descriptively without formal testing.

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)	36.4 (28.8 to 44.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of radiation dermatitis NCI CTCAE grade 0, 1 and 2

End point title	Rate of radiation dermatitis NCI CTCAE grade 0, 1 and 2

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)	63.6 (56.0 to 71.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of radiation dermatitis NCI CTCAE all grades

End point title	Rate of radiation dermatitis NCI CTCAE all grades

End point description:

Severity grade of radiation dermatitis according to NCI CTCAE version 4.02 as assessed by the local investigator

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 0	12.3 (7.1 to 17.5)			
CTCAE grade 1	22.1 (15.5 to 28.6)			
CTCAE grade 2	29.2 (22.0 to 36.4)			
CTCAE grade 3	35.1 (27.5 to 42.6)			
CTCAE grade 4	1.3 (0.0 to 3.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of cetuximab-induced acneiform rash NCI CTCAE grade 3/4 vs. 0/1/2

End point title	Rate of cetuximab-induced acneiform rash NCI CTCAE grade 3/4 vs. 0/1/2

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 3/4	19.5 (13.2 to 25.7)			
CTCAE grade 0/1/2	80.5 (74.3 to 86.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of cetuximab-induced acneiform rash NCI CTCAE all grades

End point title	Rate of cetuximab-induced acneiform rash NCI CTCAE all grades

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 0	8.4 (4.1 to 12.8)			
CTCAE grade 1	26.6 (19.6 to 33.6)			
CTCAE grade 2	45.5 (37.6 to 53.3)			
CTCAE grade 3	18.2 (12.1 to 24.3)			
CTCAE grade 4	1.3 (0.0 to 3.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of cetuximab-induced rhagades NCI CTCAE grade 3/4 vs. 0/1/2

End point title	Rate of cetuximab-induced rhagades NCI CTCAE grade 3/4 vs. 0/1/2

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 3/4	2.6 (0.1 to 5.1)			
CTCAE grade 0/1/2	97.4 (94.9 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of cetuximab-induced rhagades NCI CTCAE all grades

End point title	Rate of cetuximab-induced rhagades NCI CTCAE all grades

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 0	62.3 (54.7 to 70.0)			
CTCAE grade 1	22.1 (15.5 to 28.6)			
CTCAE grade 2	13.0 (7.7 to 18.3)			
CTCAE grade 3	2.6 (0.1 to 5.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of cetuximab-induced nail changes NCI CTCAE grade 3/4 vs. 0/1/2

End point title	Rate of cetuximab-induced nail changes NCI CTCAE grade 3/4 vs. 0/1/2

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 0/1/2	100.0 (100.0 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of cetuximab-induced nail changes NCI CTCAE all grades

End point title	Rate of cetuximab-induced nail changes NCI CTCAE all grades

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	154			
Units: Percentage of patients				
number (confidence interval 95%)				
CTCAE grade 0	91.6 (87.2 to 95.9)			
CTCAE grade 1	6.5 (2.6 to 10.4)			
CTCAE grade 2	1.9 (0.0 to 4.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

Objective response rate was defined as ratio of patients who achieved an objective response (CR/PR) according to RECIST 1.1 at the end of therapy (55-65 days after end of radiation)

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	140			
Units: Patients	99			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	140			
Units: Months				
median (confidence interval 95%)	15.4 (12.1 to 21.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: 12 months overall survival (OS) rate

End point title	12 months overall survival (OS) rate

End point description:

Overall survival is defined as time from first administration of study medication to death due to any cause

End point type	Secondary

End point timeframe:

First administration of study medication until end of study

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	140			
Units: Percentage of patients				
number (confidence interval 95%)	80.2 (72.0 to 86.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Locoregional control (LRC)

End point title	Locoregional control (LRC)

End point description:

The LRC is defined as the rate of patients for which neither a progression of the locoregional disease (defined as primary tumor and / or metastases of cervical lymph nodes) nor death is documented at the time of the first follow-up visit

End point type	Secondary

End point timeframe:

First dose of cetuximab until first follow-up visit after end of treatment (55-65 days after last radiation)

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	140			
Units: Patients				
Locoregional control	67			
Progression of primary tumor	8			
Progression of lymph node metastases	4			
Progression of primary tumor and lymph node metast	2			
No evaluation of locoregional disease	34			
No response evaluation because of PD at final visi	8			
Patient died	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Total dose of radiotherapy

End point title	Total dose of radiotherapy

End point description:

The dose intensity of radiation (including possible boost) was calculated based on details of applied doses, routinely documented in the medical record

End point type	Secondary

End point timeframe:

First until last dose of radiotherapy

End point values	SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	153[2]			
Units: Gy				
median (full range (min-max))	69.8 (28.0 to 78.0)			

Notes:

[2] - One patient was excluded from analysis due to implausible total dose documentation (92.4 Gy).

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC QLQ-C30: Global health status

End point title	EORTC QLQ-C30: Global health status

End point description:

Quality of life was assessed by evaluation of patient reported outcomes (PROs) at baseline, week 4 (day 22), week 7 or 8 (last treatment week) and at end of study (final visit), using the EORTC QLQ-C30 questionnaire and the EORTC QLQ Head and Neck Cancer specific module

End point type	Secondary

End point timeframe:

Baseline, week 4, week 7 or 8, and at end of study

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	140[3]			
Units: Score				
arithmetic mean (standard deviation)				
Baseline	50.8 (± 22.24)			
Day 22	51.1 (± 18.65)			
Last treatment week	46.3 (± 20.02)			
Final visit	51.7 (± 21.71)			

Notes:

[3] - Returned questionnaires: Baseline n=123; Day 22 n=120; Last treatment week n=102; Final visit n=9

Statistical analyses

No statistical analyses for this end point

Secondary: DLQI: Total score

End point title	DLQI: Total score

End point description:

Quality of life was assessed by evaluation of patient reported outcomes (PROs) at baseline, week 4 (day 22), week 7 or 8 (last treatment week) and at end of study (final visit), using the Dermatology Life Quality Index (DLQI) questionnaire

End point type	Secondary

End point timeframe:

Baseline, week 4, week 7 or 8, and at end of study

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	140[4]			
Units: Score				
arithmetic mean (standard deviation)				
Baseline	1.2 (± 2.29)			
Day 22	5.2 (± 5.82)			
Last treatment week	7.9 (± 6.64)			
Final visit	3.0 (± 5.34)			

Notes:

[4] - Returned questionnaires: Baseline n=112; Day 22 n=110; Last treatment week n=87; Final visit n=80

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose of cetuximab until 30 days after last study medication (i.e. last dose of radiotherapy)	
Adverse event reporting additional description:	
Relatedness to treatment is reported for cetuximab and/or radiotherapy	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	Safety Set - SAF
Reporting group description: -	

Serious adverse events	Safety Set - SAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 154 (35.06%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	9		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - other, specify			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Hypotension			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			

subjects affected / exposed	2 / 154 (1.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions - other, specify				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Allergic reaction				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Aspiration				
subjects affected / exposed	2 / 154 (1.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Apnea				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnea				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

Pharyngeal mucositis				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Investigations - other, specify				
subjects affected / exposed	2 / 154 (1.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Lymphocyte count decreased				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Weight loss				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Dermatitis radiation				
subjects affected / exposed	10 / 154 (6.49%)			
occurrences causally related to treatment / all	10 / 10			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications - other, specify				
subjects affected / exposed	5 / 154 (3.25%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Cardiac disorders - other, specify				

subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Asystole			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Heart failure			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial hemorrhage			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Mucositis oral			
subjects affected / exposed	11 / 154 (7.14%)		
occurrences causally related to treatment / all	11 / 11		
deaths causally related to treatment / all	0 / 0		

Dysphagia				
subjects affected / exposed	7 / 154 (4.55%)			
occurrences causally related to treatment / all	7 / 7			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal hemorrhage				
subjects affected / exposed	2 / 154 (1.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Colonic perforation				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Nausea				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral pain				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatobiliary disorders - other, specify				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash acneiform				
subjects affected / exposed	7 / 154 (4.55%)			
occurrences causally related to treatment / all	8 / 8			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				

subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations - other, specify			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 2		
Catheter related infection			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal infection			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder infection			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritoneal infection			

subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Anorexia			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalemia			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyperglycemia			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety Set - SAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 154 (99.35%)		
Investigations			
Weight loss			
subjects affected / exposed	9 / 154 (5.84%)		
occurrences (all)	9		
Investigations - other, specify			

subjects affected / exposed	8 / 154 (5.19%)		
occurrences (all)	9		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	10 / 154 (6.49%)		
occurrences (all)	13		
Injury, poisoning and procedural complications			
Dermatitis radiation			
subjects affected / exposed	127 / 154 (82.47%)		
occurrences (all)	131		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	10 / 154 (6.49%)		
occurrences (all)	10		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	54 / 154 (35.06%)		
occurrences (all)	66		
General disorders and administration site conditions - other, specify			
subjects affected / exposed	9 / 154 (5.84%)		
occurrences (all)	9		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	10 / 154 (6.49%)		
occurrences (all)	10		
Gastrointestinal disorders			
Mucositis oral			
subjects affected / exposed	102 / 154 (66.23%)		
occurrences (all)	122		
Dysphagia			
subjects affected / exposed	41 / 154 (26.62%)		
occurrences (all)	49		
Constipation			
subjects affected / exposed	29 / 154 (18.83%)		
occurrences (all)	29		
Nausea			

subjects affected / exposed	23 / 154 (14.94%)		
occurrences (all)	25		
Dry mouth			
subjects affected / exposed	16 / 154 (10.39%)		
occurrences (all)	16		
Gastrointestinal disorders - other, specify			
subjects affected / exposed	11 / 154 (7.14%)		
occurrences (all)	12		
Oral pain			
subjects affected / exposed	11 / 154 (7.14%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Rash acneiform			
subjects affected / exposed	133 / 154 (86.36%)		
occurrences (all)	138		
Skin and subcutaneous tissue disorders - other, specify			
subjects affected / exposed	58 / 154 (37.66%)		
occurrences (all)	60		
Pruritus			
subjects affected / exposed	14 / 154 (9.09%)		
occurrences (all)	16		
Nail ridging			
subjects affected / exposed	10 / 154 (6.49%)		
occurrences (all)	10		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	27 / 154 (17.53%)		
occurrences (all)	27		
Anxiety			
subjects affected / exposed	8 / 154 (5.19%)		
occurrences (all)	8		
Infections and infestations			
Infections and infestations - other, specify			
subjects affected / exposed	36 / 154 (23.38%)		
occurrences (all)	43		

Mucosal infection subjects affected / exposed occurrences (all)	24 / 154 (15.58%) 27		
Metabolism and nutrition disorders Hypokalemia subjects affected / exposed occurrences (all)	13 / 154 (8.44%) 13		
Hypomagnesemia subjects affected / exposed occurrences (all)	12 / 154 (7.79%) 14		
Hypoalbuminemia subjects affected / exposed occurrences (all)	8 / 154 (5.19%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to poor recruitment, only 160 patients were included in this trial instead of 500 planned patients. The reduced number of analyzed patients may limit the generalisability of the study results.

Notes: