



Clinical trial results:

Identification of tissue biomarkers related to late toxicity in Head and Neck Cancer Patients treated with chemoradiotherapy or bioradiotherapy

Summary

EudraCT number	2015-003012-21
Trial protocol	ES
Global end of trial date	04 March 2019

Results information

Result version number	v1 (current)
This version publication date	16 October 2024
First version publication date	16 October 2024
Summary attachment (see zip file)	Scientific manuscript (Articulo_TOX-TTCC-2015-01.pdf)

Trial information

Trial identification

Sponsor protocol code	TOX-TTCC-2015-01
-----------------------	------------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Grupo Español de Tratamiento de Tumores de Cabeza y Cuello
Sponsor organisation address	Velazquez St, 7-3o, Madrid, Spain, 28001
Public contact	Secretaria, Grupo Español de Tratamiento de Tumores de Cabeza y Cuello (TTCC), 0034 676154172, cmontalban@ttccgrupo.com
Scientific contact	Secretaria, Grupo Español de Tratamiento de Tumores de Cabeza y Cuello (TTCC), 0034 676154172, cmontalban@ttccgrupo.com

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	30 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 March 2019
Global end of trial reached?	Yes
Global end of trial date	04 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the differences in healthy tissue caused by bioradiotherapy and chemoradiotherapy

Protection of trial subjects:

This study was performed in line with the principles of the Declaration of Helsinki. The entire study was approved by Hospital Universitari de Bellvitge Ethics Committee under the approval number AC112/15. All the participants provided written informed consent prior to their inclusion in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2015
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	Spain: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	33
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	33
----------------------------	----

Number of subjects completed	31
------------------------------	----

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
----------------------------	---------------------------------

Reason: Number of subjects	Not meeting inclusion criteria: 1
----------------------------	-----------------------------------

Period 1

Period 1 title	Overall study period (overall period)
----------------	---------------------------------------

Is this the baseline period?	Yes
------------------------------	-----

Allocation method	Non-randomised - controlled
-------------------	-----------------------------

Blinding used	Not blinded
---------------	-------------

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	CRT treatment
------------------	---------------

Arm description:

Radiotherapy (RT) with concomitant cisplatin (CRT)

Arm type	Active comparator
----------	-------------------

Investigational medicinal product name	cisplatin
--	-----------

Investigational medicinal product code	
--	--

Other name	
------------	--

Pharmaceutical forms	Concentrate for solution for infusion
----------------------	---------------------------------------

Routes of administration	Intravenous use
--------------------------	-----------------

Dosage and administration details:

Standard of care (intitutional protocol)

Investigational medicinal product name	Carboplatin
--	-------------

Investigational medicinal product code	
--	--

Other name	
------------	--

Pharmaceutical forms	Concentrate for solution for infusion
----------------------	---------------------------------------

Routes of administration	Intravenous use
--------------------------	-----------------

Dosage and administration details:

Standard of care (intitutional protocol)

Switching from cisplatin to carboplatin was allowed if needed due to toxicity.

Arm title	ERT treatment
------------------	---------------

Arm description:

Radiotherapy (RT) with concomitant cetuximab (ERT)

Arm type	Active comparator
----------	-------------------

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

Dosage and administration details:

Standard of Care (Institutional protocols)

Number of subjects in period 1^[1]	CRT treatment	ERT treatment
Started	12	19
Completed	10	17
Not completed	2	2
progression	1	1
rescue surgery	-	1
prolonged admission	1	-

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: Two patients were considered not eligible (screening failures)

Baseline characteristics

Reporting groups

Reporting group title	CRT treatment
Reporting group description:	
Radiotherapy (RT) with concomitant cisplatin (CRT)	
Reporting group title	ERT treatment
Reporting group description:	
Radiotherapy (RT) with concomitant cetuximab (ERT)	

Reporting group values	CRT treatment	ERT treatment	Total
Number of subjects	12	19	31
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	60.5	63	-
full range (min-max)	45 to 69	44 to 76	-
Gender categorical			
Units: Subjects			
Female	2	1	3
Male	10	18	28
ECOG-PS			
Eastern Cooperative Oncology Group Performance Status			
Units: Subjects			
Score 0	0	1	1
Score 1	12	18	30
Tobacco consumption			
Units: Subjects			
Non smoker	0	1	1
Former smoker	3	8	11
Active smoker	9	10	19
Alcohol consumption			
Units: Subjects			
Non alcohol use	1	3	4
Former alcohol use	4	6	10
Active user	7	10	17
Pre-treatment PG-SGA			

Patient-Generated Subjective Global Assessment			
Units: Subjects			
A, well-nourished	4	11	15
B, moderate/suspected malnutrition	5	2	7
C, severely malnourished	1	2	3
Unknown	2	4	6
Tumor location			
Units: Subjects			
Oral cavity	1	2	3
Oropharynx	3	6	9
Larynx	3	6	9
Hypopharynx	4	5	9
Unknown primary location	1	0	1
Primary tumor (TNM 7th ed.)			
Units: Subjects			
Tx	1	1	2
T1	0	1	1
T2	1	1	2
T3	3	10	13
T4	7	6	13
Lymph nodes (TNM 7th ed.)			
Units: Subjects			
N0	4	8	12
N1	1	0	1
N2a	0	1	1
N2b	3	5	8
N2c	2	2	4
N3	2	3	5
Pre-treatment weight			
Units: kilogram(s)			
arithmetic mean	71.1	73.7	
standard deviation	± 12.8	± 20	-
Tumor volumes			
Units: Cubic centimetre			
median	42	47	
full range (min-max)	3 to 153	6 to 118	-
Lymph nodes volumes			
Units: Cubic centimetre			
median	300	317	
full range (min-max)	221 to 400	175 to 533	-

End points

End points reporting groups

Reporting group title	CRT treatment
-----------------------	---------------

Reporting group description:

Radiotherapy (RT) with concomitant cisplatin (CRT)

Reporting group title	ERT treatment
-----------------------	---------------

Reporting group description:

Radiotherapy (RT) with concomitant cetuximab (ERT)

Subject analysis set title	late toxicity low
----------------------------	-------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

A group of patients has been defined as "late toxicity low," which includes those patients who have experienced between 0 and 2 late adverse effects and none of them higher than or equal to RTOG grade 2, and another group, defined as "late toxicity high," which includes those patients who have experienced 3 or more late adverse events or have experienced at least one late adverse event of an RTOG grade higher than or equal to 2

Subject analysis set title	late toxicity high
----------------------------	--------------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

A group of patients has been defined as "late toxicity low," which includes those patients who have experienced between 0 and 2 late adverse effects and none of them higher than or equal to RTOG grade 2, and another group, defined as "late toxicity high," which includes those patients who have experienced 3 or more late adverse events or have experienced at least one late adverse event of an RTOG grade higher than or equal to 2.

Primary: CD34 expression before-after treatment

End point title	CD34 expression before-after treatment
-----------------	--

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Punch biopsies (4 mm) were carried out before study treatment and 2 months after the last radiotherapy dose in healthy skin from cervical node level II, homolateral to the greatest tumor burden.

End point values	CRT treatment	ERT treatment	late toxicity low	late toxicity high
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	10 ^[1]	14 ^[2]	14 ^[3]	6 ^[4]
Units: Percentage positive cells				
arithmetic mean (standard deviation)				
CD34 pre	53.53 (± 0)	49.45 (± 0)	53.05 (± 0)	38.05 (± 0)
CD34 post	59.46 (± 0)	53.67 (± 0)	57.03 (± 0)	50.49 (± 0)

Notes:

[1] - 2 patients with values missing pre or post dose

[2] - 5 patients with values missing pre or post dose

[3] - 6 missing values

[4] - 1 missing value

Attachments (see zip file)	CD34 expression/CD34.jpg
	CD34 late toxicity/CD34 late toxicity.jpg

Statistical analyses

Statistical analysis title	Paired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6162
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5484
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5031
Method	t-test, 2-sided

Statistical analysis title	Paired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.116
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high Pre
-----------------------------------	--------------------------

Statistical analysis description:

Comparison between late toxicity low and the late toxicity high subgroup in pretreatment.

Unpaired-T test

Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1171
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high Post
-----------------------------------	---------------------------

Statistical analysis description:

Comparison between late toxicity low and the late toxicity high subgroup in posttreatment.

Unpaired-T test

Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5251
Method	t-test, 2-sided

Primary: CD68 expression before-after treatment

End point title	CD68 expression before-after treatment
-----------------	--

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Punch biopsies (4 mm) were carried out before study treatment and 2 months after the last radiotherapy dose in healthy skin from cervical node level II, homolateral to the greatest tumor burden.

End point values	CRT treatment	ERT treatment	late toxicity low	late toxicity high
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	10 ^[5]	16 ^[6]	14 ^[7]	6 ^[8]
Units: Percentage of positive cells				
arithmetic mean (standard deviation)				
CD68 pre	3.538 (± 0)	3.231 (± 0)	3.628 (± 0)	1.818 (± 0)
CD68 post	11.70 (± 0)	7.443 (± 0)	8.026 (± 0)	5.901 (± 0)

Notes:

[5] - 2 patients with values missing pre or post dose

[6] - 3 patients with values missing pre or post dose

[7] - 6 missing

[8] - 1 missing

Attachments (see zip file)	A CD68 expression/CD68.jpg CD68 late toxicity/CD68 late toxicity.jpg
-----------------------------------	---

Statistical analyses

Statistical analysis title	Paired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3063
Method	t-test, 2-sided

Statistical analysis title	Paired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0535
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1161
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description: Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0117
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high Pre
Statistical analysis description: "Comparison between late toxicity low and the late toxicity high subgroup in pretreatment Unpaired-T test"	
Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.044
Method	t-test, 2-sided

Statistical analysis title	Copy of Toxicity low vs high Post
Statistical analysis description: "Comparison between late toxicity low and the late toxicity high subgroup in posttreatment Unpaired-T test"	
Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3289
Method	t-test, 2-sided

Primary: CD163 expression before-after treatment	
End point title	CD163 expression before-after treatment
End point description:	

End point type	Primary
End point timeframe:	
Punch biopsies (4 mm) were carried out before study treatment and 2 months after the last radiotherapy dose in healthy skin from cervical node level II, homolateral to the greatest tumor burden.	

End point values	CRT treatment	ERT treatment	late toxicity low	late toxicity high
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	10 ^[9]	14 ^[10]	14 ^[11]	6 ^[12]
Units: Percentage of positive cells				
arithmetic mean (standard deviation)				
CD163 pre	9.722 (± 0)	9.938 (± 0)	10.98 (± 0)	6.806 (± 0)
CD163 post	21.20 (± 0)	16.12 (± 0)	17.42 (± 0)	14.45 (± 0)

Notes:

[9] - 2 patients with values missing pre or post dose

[10] - 5 patients with values missing pre or post dose

[11] - 6 missing

[12] - 1 missing

Attachments (see zip file)	CD163 expression/CD163.jpg CD163 late toxicity/CD163 late toxicity.jpg
-----------------------------------	---

Statistical analyses

Statistical analysis title	Paired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0655
Method	t-test, 2-sided

Statistical analysis title	Paired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0993
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0431
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0181
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high Pre
Statistical analysis description:	
"Comparison between late toxicity low and the late toxicity high subgroup in pretreatment Unpaired-T test"	
Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1066
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high Post
Statistical analysis description:	
"Comparison between late toxicity low and the late toxicity high subgroup in posttreatment Unpaired-T test"	
Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.613
Method	t-test, 2-sided

Primary: CD163/CD68 Ratio

End point title	CD163/CD68 Ratio
-----------------	------------------

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Punch biopsies (4 mm) were carried out before study treatment and 2 months after the last radiotherapy dose in healthy skin from cervical node level II, homolateral to the greatest tumor burden.

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[13]	14 ^[14]		
Units: Percentage				
arithmetic mean (standard deviation)				
CD163/CD68 pre	3.768 (± 0)	2.996 (± 0)		
CD163/CD68 post	2.427 (± 0)	2.760 (± 0)		

Notes:

[13] - 2 patients with values missing pre or post dose

[14] - 5 patients with values missing pre or post dose

Statistical analyses

Statistical analysis title	Mann Whitney test
----------------------------	-------------------

Statistical analysis description:

Comparison pre-treatment and post-treatment

Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0221
Method	Mann Whitney test

Statistical analysis title	Mann Whitney test
----------------------------	-------------------

Statistical analysis description:

Comparison pre-treatment and post-treatment

Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7938
Method	Mann Whitney test

Primary: Masson Trichrome pre-treatment and post-treatment

End point title	Masson Trichrome pre-treatment and post-treatment
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Punch biopsies (4 mm) were carried out before study treatment and 2 months after the last radiotherapy dose in healthy skin from cervical node level II, homolateral to the greatest tumor burden.

End point values	CRT treatment	ERT treatment	late toxicity low	late toxicity high
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	10 ^[15]	16 ^[16]	14 ^[17]	6 ^[18]
Units: Percentage stained cells				
arithmetic mean (standard deviation)				
Masson Trichrome Pre	48.47 (± 0)	43.7 (± 0)	44 (± 0)	49.27 (± 0)
Masson Trichrome post	38.80 (± 0)	37.23 (± 0)	40.08 (± 0)	36.61 (± 0)

Notes:

[15] - 2 patients with values missing pre or post dose

[16] - 3 patients with values missing pre or post dose

[17] - 6 missing

[18] - 1 missing

Attachments (see zip file)	Collagen deposition & Mason /Collagen.jpg
	Collagen late toxicity/Collagen late toxicity.jpg

Statistical analyses

Statistical analysis title	Paired-T test
----------------------------	---------------

Statistical analysis description:

Comparison pre-treatment and post-treatment

Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0905
Method	t-test, 2-sided

Statistical analysis title	Paired-T test
----------------------------	---------------

Statistical analysis description:

Comparison pre-treatment and post-treatment

Comparison groups	ERT treatment v CRT treatment
-------------------	-------------------------------

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8908
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	CRT treatment v ERT treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1953
Method	t-test, 2-sided

Statistical analysis title	Unpaired-T test
Statistical analysis description:	
Comparison pre-treatment and post-treatment	
Comparison groups	ERT treatment v CRT treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3386
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high Pre
Statistical analysis description:	
"Comparison between late toxicity low and the late toxicity high subgroup in pretreatment Unpaired-T test"	
Comparison groups	late toxicity low v late toxicity high
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5402
Method	t-test, 2-sided

Statistical analysis title	Toxicity low vs high post
Statistical analysis description:	
"Comparison between late toxicity low and the late toxicity high subgroup in posttreatment Unpaired-T test"	
Comparison groups	late toxicity low v late toxicity high

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6917
Method	t-test, 2-sided

Primary: Frequency of patients with late toxicities

End point title	Frequency of patients with late toxicities ^[19]
End point description:	
One year after the end of radiation treatment	
End point type	Primary

End point timeframe:

Late toxicity was defined as per RTOG/EORTC late radiation morbidity scoring system as adverse events that were still experienced by the patients 90 days after the end of radiation treatment and collected one year after the end of radiation treatment.

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal comparison was done between rates of patients experiencing late toxicities. The trial describes the type of toxicities experienced in adverse events section

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[20]	17 ^[21]		
Units: Patients				
late toxicities high	4	3		
late toxicities low	6	14		

Notes:

[20] - 2 missing: 1 started further chemotherapy and 1 operated on one year after radiotherapy

[21] - 2 missing: 1 died after 4.6 months and 1 admitted for a long time because of surgical complications

Statistical analyses

No statistical analyses for this end point

Secondary: Lymph node dissection

End point title	Lymph node dissection
End point description:	
End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	19		
Units: patients				
underwent Lymph node dissection	3	4		
Did not undergo Lymph node dissection	9	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse frequency

End point title	Relapse frequency
End point description:	
End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	19		
Units: Patients				
Relapsed	3	3		
Did not relapse	9	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Requirement of nasogastric feeding tube

End point title	Requirement of nasogastric feeding tube
End point description:	
End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[22]	19		
Units: Patients				
Required	2	8		
Not required	9	11		

Notes:

[22] - 1 patient was missing

Statistical analyses

No statistical analyses for this end point

Secondary: Gastrostomy

End point title	Gastrostomy
End point description:	
End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	19		
Units: Patients				
Performed	0	3		
Not performed	12	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Tracheostomy

End point title	Tracheostomy
End point description:	
End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	19		
Units: Patients				
Performed	0	1		
Not performed	12	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
End point description:	
Number of patients who died from any cause	
End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	CRT treatment	ERT treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	19		
Units: Patients				
Alive	12	15		
Dead	0	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported throughout the study from baseline to 1 year after the end of radiation treatment.

Adverse event reporting additional description:

Late toxicity was defined as per RTOG/EORTC late radiation morbidity scoring system as adverse events that were still experienced by the patients 90 days after the end of radiation treatment and collected one year after the end of radiation treatment.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	22
--------------------	----

Reporting groups

Reporting group title	CRT treatment
-----------------------	---------------

Reporting group description:

Radiotherapy (RT) with concomitant cisplatin (CRT)

Reporting group title	ERT treatment
-----------------------	---------------

Reporting group description:

Radiotherapy (RT) with concomitant cetuximab (ERT)

Serious adverse events	CRT treatment	ERT treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	3 / 19 (15.79%)	
number of deaths (all causes)	0	4	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Neutropenia	Additional description: one G3 and one G4 events		
subjects affected / exposed	2 / 12 (16.67%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia	Additional description: Grade 1		
subjects affected / exposed	2 / 12 (16.67%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever	Additional description: Grade 3		

subjects affected / exposed	0 / 12 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oral mucositis			
subjects affected / exposed	0 / 12 (0.00%)	2 / 19 (10.53%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cheilitis			
Additional description: Grade 3			
subjects affected / exposed	0 / 12 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
Additional description: Grade 3			
subjects affected / exposed	0 / 12 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
Additional description: Grade 2			
subjects affected / exposed	2 / 12 (16.67%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Conjunctivitis			
Additional description: Grade 3			
subjects affected / exposed	0 / 12 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
Additional description: Grade 4			
subjects affected / exposed	0 / 12 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperpotassemia			
Additional description: Grade 1			

subjects affected / exposed	1 / 12 (8.33%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CRT treatment	ERT treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	19 / 19 (100.00%)	
Nervous system disorders			
Dysphonia G1			
subjects affected / exposed	1 / 12 (8.33%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Dysgeusia G1			
subjects affected / exposed	1 / 12 (8.33%)	5 / 19 (26.32%)	
occurrences (all)	1	5	
Dysgeusia G2			
subjects affected / exposed	6 / 12 (50.00%)	10 / 19 (52.63%)	
occurrences (all)	6	10	
Dysgeusia G3			
subjects affected / exposed	3 / 12 (25.00%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Neurotoxicity G1			
subjects affected / exposed	1 / 12 (8.33%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Neurotoxicity G2			
subjects affected / exposed	2 / 12 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia G1			
subjects affected / exposed	6 / 12 (50.00%)	5 / 19 (26.32%)	
occurrences (all)	6	5	
Asthenia G2			
subjects affected / exposed	6 / 12 (50.00%)	10 / 19 (52.63%)	
occurrences (all)	6	10	
Blood and lymphatic system disorders			

Febrile neutropenia G3 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 19 (5.26%) 1	
Gastrointestinal disorders			
Dysphagia G1 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	3 / 19 (15.79%) 3	
Dysphagia G2 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	8 / 19 (42.11%) 8	
Dysphagia G3 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 19 (10.53%) 2	
Oral mucositis G1 subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	3 / 19 (15.79%) 3	
Oral mucositis G2 subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	6 / 19 (31.58%) 6	
Oral mucositis G3 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	8 / 19 (42.11%) 8	
Nausea/vomiting G1 subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	0 / 19 (0.00%) 0	
Nausea/vomiting G3 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 19 (0.00%) 0	
Odynophagia G1 subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	4 / 19 (21.05%) 4	
Odynophagia G2 subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	8 / 19 (42.11%) 8	
Odynophagia G3			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 19 (0.00%) 0	
Liver toxicity G1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 19 (5.26%) 1	
Xerostomia G1 subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 6	4 / 19 (21.05%) 4	
Xerostomia G2 subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4	11 / 19 (57.89%) 11	
Xerostomia G3 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 19 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Radiodermatitis G1 subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 5	7 / 19 (36.84%) 7	
Radiodermatitis G2 subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3	7 / 19 (36.84%) 7	
Radiodermatitis G3 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	2 / 19 (10.53%) 2	
Rash G1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	8 / 19 (42.11%) 8	
Rash G2 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 19 (5.26%) 1	
Renal and urinary disorders			
Renal impairment G1 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 19 (0.00%) 0	
Renal impairment G3			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 19 (0.00%) 0	
Musculoskeletal and connective tissue disorders Trismus G1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 19 (5.26%) 1	
Metabolism and nutrition disorders Anorexia G1 subjects affected / exposed occurrences (all) Anorexia G2 subjects affected / exposed occurrences (all) Anorexia G3 subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 5 4 / 12 (33.33%) 4 0 / 12 (0.00%) 0	5 / 19 (26.32%) 5 4 / 19 (21.05%) 4 1 / 19 (5.26%) 1	

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

None reported