Clinical trial results:
A Randomized Phase II Trial for Patients with p16 Positive, Non-Smoking Associated, Locoregionally Advanced Oropharyngeal Cancer

Summary

EudraCT number	2016-002244-16
Trial protocol	IE
Global end of trial date	04 September 2025

Results information

Result version number	v2 (current)
This version publication date	12 February 2026
First version publication date	26 January 2025
Version creation reason	• Correction of full data set Global end date added: 04th Sep 2025.

Trial information

Trial identification

Sponsor protocol code	NRG-HN002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02254278
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland
Sponsor organisation address	RCSI House, Dublin, Ireland, D02 H903
Public contact	Clinical Program Leader , Irish Clinical Oncology Research Group CLG, trading as Cancer Trials Ireland, +353 16677211, info@cancertrials.ie
Scientific contact	Clinical Program Leader , Irish Clinical Oncology Research Group CLG, trading as Cancer Trials Ireland, 0876654933 16677211, info@cancertrials.ie
Sponsor organisation name	NRG Oncology
Sponsor organisation address	1818 Market Street, Suite 1720, Philadelphia, United States, PA 19103
Public contact	Clinical Project Manager, NRG Oncology, +1 267-519-6630, info@nrgoncology.org
Scientific contact	Clinical Project Manager, NRG Oncology, +1 267-519-6630, info@nrgoncology.org

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	Interim
Date of interim/final analysis	25 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 June 2019
Global end of trial reached?	Yes
Global end of trial date	04 September 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To select the arm(s) achieving a 2-year progression-free survival rate of >= 85% without unacceptable swallowing toxicity at 1 year.

Protection of trial subjects:

The Trial was conducted in accordance with International Conference on Harmonization Good Clinical Practice Guidelines and principles of the Declaration of Helsinki of 1964. An independent, unblinded data and safety monitoring committee reviewed safety and efficacy data at predefined data points. Patients provided written informed consent before undergoing any trial-related procedures.

Background therapy:

None

Evidence for comparator:

This randomized phase II trial studies the side effects and how well modestly reduced-dose intensity-modulated radiation therapy (IMRT) with or without cisplatin works in treating patients with oropharyngeal cancer that has spread to other places in the body (advanced). Radiation therapy uses high energy x rays to kill tumor cells. Drugs used in chemotherapy, such as cisplatin, work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. It is not yet known whether IMRT is more effective with or without cisplatin in treating patients with oropharyngeal cancer.

Actual start date of recruitment	01 October 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	7 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 61
Country: Number of subjects enrolled	United States: 243
Country: Number of subjects enrolled	Saudi Arabia: 1
Country: Number of subjects enrolled	Ireland: 1
Worldwide total number of subjects	306
EEA total number of subjects	1

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)	215
From 65 to 84 years	91
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From October 27th 2014 to February 7th 2017, a total of 316 patients were enrolled and 308 were randomized, of whom 2 were subsequently determined to ineligible

Pre-assignment

Screening details:

After first step registration and prior to randomization, patients were tested for p16. Only patients with p16-positive tumors continued on to randomization. In total, 316 patients were enrolled and 308 were randomized.

Pre-assignment period milestones

Number of subjects started	308[1]
Number of subjects completed	306

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 2

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: no previous justification

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	IMRT 6 Weeks + Cisplatin

Arm description:

Cisplatin: 40 mg/m2 IV (intravenously) weekly for 6 weeks
IMRT 6 weeks: Intensity-modulated radiation therapy (IMRT), 30 fractions over 6 weeks, 5 fractions per week, 2 Gray per fraction to total dose of 60 Gy

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:

40 mg/m2 IV (intravenously) weekly for 6 weeks
Radiation: IMRT 6 weeks, 30 fractions over 6 weeks, 5 fractions per week, 2 Gray per fraction to total dose of 60 Gy

Arm title	IMRT 5 weeks

Arm description:

Intensity-modulated radiation therapy (IMRT), 30 fractions over 5 weeks, 6 fractions per week, 2 Gray per fraction to total dose of 60 Gy

Arm type	Intenisty-modulated Radiotherapy

No investigational medicinal product assigned in this arm

Number of subjects in period 1	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks
Started	157	149
Completed	157	149

Baseline characteristics

Reporting groups	
Reporting group title	IMRT 6 Weeks + Cisplatin
Reporting group description:	
Cisplatin: 40 mg/m2 IV (intravenously) weekly for 6 weeks IMRT 6 weeks: Intensity-modulated radiation therapy (IMRT), 30 fractions over 6 weeks, 5 fractions per week, 2 Gray per fraction to total dose of 60 Gy	
Reporting group title	IMRT 5 weeks
Reporting group description:	
Intensity-modulated radiation therapy (IMRT), 30 fractions over 5 weeks, 6 fractions per week, 2 Gray per fraction to total dose of 60 Gy	

Reporting group values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks	Total
Number of subjects	157	149	306
Age categorical			
Randomized and eligible patients			
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)	108	107	215
From 65-84 years	49	42	91
Gender categorical Units: Subjects			
Female	24	25	49
Male	133	124	257
Ethnicity Units: Subjects			
Hispanic or Latino	3	7	10
Not Hispanic or Latino	143	130	273
Unknown or Not Reported	11	12	23
Race Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	0	4	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	3
White	151	130	281
More than one race	0	0	0
Unknown or Not Reported	4	12	16
Zubrod performance status Units: Subjects			
0: Asymptomatic	132	113	245

1: Symptomatic but completely ambulatory	25	36	61
Smoking history (pack years)			
Smoking history as measured in pack-years, calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked.			
Units: Subjects			
=0	112	101	213
>0-<5	26	32	58
5-10	19	16	35
T Stage			
Tumor stage per the American Joint Committee on Cancer (AJCC) 7th ed. refers to the size and/or extent of the main tumor. The higher the number after the T, the larger the tumor or the more it has grown into nearby tissues. T's may be further divided to provide more detail, such as T3a and T3b.			
Units: Subjects			
T1	64	51	115
T2	67	80	147
T3	26	18	44
N Stage			
Regional lymph nodes staging per American Joint Committee on Cancer (AJCC) 7th ed. refers to the number and/or extent of spread of lymph nodes that contain cancer. The higher the number after the N, the greater the involvement of regional lymph nodes.			
Units: Subjects			
N0	6	7	13
N1	28	34	62
N2a	24	19	43
N2b	99	89	188
Primary tumor site Units: Subjects			
Oropharynx NOS	4	13	17
Tonsillar fossa	83	78	161
Base of tongue	68	58	126
Pharyngeal oropharynx	1	0	1
Posterior pharyngeal wll	1	0	1
Radiation Therapy (RT) planning (as stratified)			
Radiation therapy plan included unilateral or bilateral radiation to the neck, as provided by the treating site at stratification.			
Units: Subjects			
Unilateral	52	47	99
Bilateral	105	102	207
RT planning (per central review)			
Radiation therapy plan included unilateral or bilateral radiation to the neck, as provided by central review by the study radiation oncologist.			
Units: Subjects			
Unilateral	16	21	37
Bilateral	136	125	261
Unknown	5	3	8

End points

End points reporting groups

Reporting group title	IMRT 6 Weeks + Cisplatin
Reporting group description:	
Cisplatin: 40 mg/m2 IV (intravenously) weekly for 6 weeks IMRT 6 weeks: Intensity-modulated radiation therapy (IMRT), 30 fractions over 6 weeks, 5 fractions per week, 2 Gray per fraction to total dose of 60 Gy	
Reporting group title	IMRT 5 weeks
Reporting group description:	
Intensity-modulated radiation therapy (IMRT), 30 fractions over 5 weeks, 6 fractions per week, 2 Gray per fraction to total dose of 60 Gy	
Subject analysis set title	Both Arms Combined
Subject analysis set type	Per protocol
Subject analysis set description:	
IMRT 6 Weeks + Cisplatin (Arm 1)and IMRT 5 weeks (Arm 2) combined	
Subject analysis set title	Both Arms Combined
Subject analysis set type	Full analysis
Subject analysis set description:	
IMRT 6 Weeks + Cisplatin (Arm 1)and IMRT 5 weeks (Arm 2) combined This subject set is created as a workaround for reporting statistical analysis.	
Subject analysis set title	IMRT 6 Weeks + Cisplatin (Arm 1)
Subject analysis set type	Per protocol
Subject analysis set description:	
This subject analysis set is being set up for a workaround for reporting statistical analysis	
Subject analysis set title	IMRT 5 Weeks (Arm 2)
Subject analysis set type	Per protocol
Subject analysis set description:	
This subject analysis set is set up as a workaround to report statistical analysis	
Subject analysis set title	IMRT 6 Weeks + Cisplatin (Arm 1) 1 month post-RT
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subject analysis set Arm 1 - 1 month post RT	
Subject analysis set title	IMRT 5 Weeks (Arm 2) 1 month post RT
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subject analysis set - Arm 2 1 month Post RT	
Subject analysis set title	IMRT 6 Weeks + Cisplatin (Arm 1) 6 months post-RT
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
6 months after end of radiation therapy (RT)	
Subject analysis set title	IMRT 5 weeks (Arm 2) 6 months post RT
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
6 months after end of radiation therapy (RT)	
Subject analysis set title	IMRT 6 Weeks + Cisplatin (Arm 1) 1 year post-RT
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
1 year after end of Radiation therapy (RT)	
Subject analysis set title	IMRT 5 weeks (Arm 2) 1 year post RT
Subject analysis set type	Sub-group analysis

Subject analysis set description: 1 year after end of radiation therapy (RT)	
Subject analysis set title	IMRT 6 Weeks + Cisplatin (Arm 1) 2 years post-RT
Subject analysis set type	Sub-group analysis
Subject analysis set description: 2 years after end of radiation therapy (RT)	
Subject analysis set title	IMRT 5 weeks (Arm 2) 2 years post RT
Subject analysis set type	Sub-group analysis
Subject analysis set description: 2 years after end of radiation therapy (RT)	

Primary: Percentage of Participants Alive Without Progression at Two Years (Progression-free Survival)

End point title	Percentage of Participants Alive Without Progression at Two Years (Progression-free Survival)

End point description:

Progression is defined as local, regional, or distant disease progression or death due to any cause.
Percentage is estimated using the binomial distribution.
Two-year data was available for 147/157 (Arm 1) and 145/149 (Arm 2) randomized and eligible participants.
One-side confidence interval

End point type	Primary
End point timeframe: From randomization to 2 years	

End point values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	145		
Units: Percentage of Participants				
number (not applicable)	90.5	87.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Assuming a binomial distribution, 140 eligible patients per arm were required for 80% power and 1-sided type I error rate of 10% to test the null hypothesis of 2-year progression-free survival (PFS) rate ≤ 85% against the alternative hypothesis of > 85% with a binomial test. The arms are not compared to each other; they are each tested separately against the null hypothesis.

Comparison groups	IMRT 6 Weeks + Cisplatin v IMRT 5 weeks
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04 [1]
Method	Binomial

Notes:

[1] - One-sided significance level=0.10

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Assuming a binomial distribution, 140 eligible patients per arm were required for 80% power and 1-sided type I error rate of 10% to test the null hypothesis of 2-year PFS rate ≤ 85% against the alternative hypothesis of > 85% with a binomial test. The arms are not compared to each other; they are each tested separately against the null hypothesis.

Comparison groups	IMRT 5 weeks v IMRT 6 Weeks + Cisplatin
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23
Method	Binomial
Confidence interval	
level	Other: 10 %
sides	1-sided

Secondary: Percentage of Participants With Local-regional Failure

End point title	Percentage of Participants With Local-regional Failure

End point description:

Local-regional failure is defined as local or regional progression, salvage surgery of the primary tumor with tumor present/unknown, salvage neck dissection with tumor present/unknown > 20 weeks after the end of radiation therapy, death due to study cancer without documented progression, or death due to unknown causes without documented progression. Distant metastasis and death due to other causes are considered competing risks. Local-regional failure time is defined as time from randomization to the date of first progression/death or last known follow-up (censored). Rates are estimated by the cumulative incidence method.

End point type	Secondary

End point timeframe:

From randomization to 2 years

End point values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	149		
Units: percentage of participants				
number (confidence interval 95%)				
Six months	0.7 (0.1 to 3.3)	2.0 (0.6 to 5.4)		
Two Years	3.3 (1.2 to 7.1)	9.5 (5.5 to 15.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	IMRT 5 weeks v IMRT 6 Weeks + Cisplatin
Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.9

Notes:

[2] - Two-sided significance level = 0.05

Secondary: Percentage of Participants With Distant Metastasis

End point title	Percentage of Participants With Distant Metastasis

End point description:

Distant metastasis is defined as distant progression. Local-regional failure and death due to any cause are considered competing risks. Distant metastasis time is defined as time from randomization to the date of progression/death or last known follow-up (censored). Rates are estimated by the cumulative incidence method.

End point type	Secondary

End point timeframe:

From randomization to 2 years

End point values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	149		
Units: Percentage of participants				
number (confidence interval 95%)				
Six months	0 (0 to 0)	0 (0 to 0)		
Two years	4 (1.6 to 8.0)	2.1 (0.6 to 5.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	IMRT 6 Weeks + Cisplatin v IMRT 5 weeks

Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.58 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	5.08

Notes:

[3] - Estimation Comments Reference level = IMRT 5 weeks

[4] - Two-sided significance level = 0.05

Secondary: Percentage of Participants Alive

End point title	Percentage of Participants Alive

End point description:

Overall survival time is defined as time from randomization to the date of death or last known follow-up (censored). Overall survival rates are estimated by the Kaplan-Meier method.

End point type	Secondary

End point timeframe:

From randomization to 2 years

End point values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	149		
Units: Percentage of participants				
number (confidence interval 95%)				
Six months	99.3 (98.1 to 100)	98.0 (95.7 to 100)		
Two years	96.7 (93.9 to 99.5)	97.3 (94.6 to 99.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	IMRT 6 Weeks + Cisplatin v IMRT 5 weeks
Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.93 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	2.95

Notes:

[5] - Estimation Comments Reference level = IMRT 5 weeks

[6] - Two-side significance level = 0.05

Secondary: Percentage of Participants With Grade 3+ Adverse Events (End of RT)

End point title	Percentage of Participants With Grade 3+ Adverse Events (End of RT)

End point description:

Adverse events were graded using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Grade refers to the severity of the AE. The CTCAE v4.0 assigns Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline: Grade 1 Mild, Grade 2 Moderate, Grade 3 Severe, Grade 4 Life-threatening or disabling, Grade 5 Death related to AE.

End point type	Secondary

End point timeframe:

End of radiation therapy (RT) (approximately 6 weeks for Arm 1 and 5 weeks for Arm 2).

End point values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	147		
Units: Percentage of Participants				
number (confidence interval 95%)	73.7 (65.9 to 80.5)	46.3 (38.0 to 54.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

End of RT

Comparison groups	IMRT 6 Weeks + Cisplatin v IMRT 5 weeks
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001 [8]
Method	Fisher exact

Notes:

[7] - End of RT

[8] - Two-sided significance level = 0.05

Secondary: Mean One-year Total MD Anderson Dysphagia Inventory (MDADI) Score (Patient-reported Swallowing Outcome)

End point title	Mean One-year Total MD Anderson Dysphagia Inventory (MDADI) Score (Patient-reported Swallowing Outcome)

End point description:

The MDADI is a 20-item tool with each item scored as Strongly agree; Agree; No opinion; Disagree; or Strongly disagree. There is 1 global item (G1), 6 emotional subscale items (E2-E7), 5 functional subscale items (F1-F5), and 8 physical subscale items (P1-P8). For all items except E7 and F2, Strongly agree corresponds to a score of 1, Agree 2, No opinion 3, Disagree 4, and Strongly disagree 5. For E7 and F2, the scores are reversed; these 2 items are rescored to match the others before calculating summary scores. The composite (total) score is the mean of the 19 items (other than G1) X 20. Composite scores range from 20 to 100 with higher scores indicating less dysphagia.

End point type	Secondary

End point timeframe:

One year post-RT. Radiation therapy (RT) ends at approximately 6 weeks for Arm 1 and 5 weeks for Arm 2

End point values	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[9]	106[10]		
Units: Score on scale				
arithmetic mean (confidence interval 95%)	85.3 (82.5 to 88.1)	81.8 (79.0 to 84.5)		

Notes:

[9] - 121 Arm 1 participants had one year post-RT data.

[10] - 106 Arm 2 participants had one year post-RT data

Statistical analyses

No statistical analyses for this end point

Secondary: Negative Predictive Value (NPV) of Post-treatment FDG-PET/CT Scan [Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT)] for Progression-free Survival and Local-regional Control at Two Years

End point title	Negative Predictive Value (NPV) of Post-treatment FDG-PET/CT Scan [Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT)] for Progression-free Survival and Local-regional Control at Two Years

End point description:

NPV is the percentage of participants alive and failure-free at 2 years among those with a negative post-treatment scan, as evaluated by central review. Negative scan determined as follows: primary site, right neck, left neck evaluated using a 5-point ordinal scale: 1-Definite complete metabolic response (CMR), 2-Likely CMR, 3-Likely inflammatory, 4-Likely residual metabolic disease (RMD), and 5-Definite RMD. 'Negative'= 1 or 2, 'Indeterminate'=3, 'Positive' = 4 or 5. 'Negative' for all three evaluation sites = overall score of 'Negative.' Progression (failure) is defined as local, regional, or distant disease progression (PR) or any death. Local-regional progression (failure) is defined as local or regional PR, salvage surgery of the primary tumor with tumor present/unknown, salvage neck dissection with tumor present/unknown > 20 weeks post RT, death due to study cancer or unknown causes without documented PR. The protocol specified that both arms would be combined for analysis.

End point type	Secondary

End point timeframe:

3 months (scan) and two years after the end of RT (approximately 6 weeks for Arm 1 and 5 weeks for Arm 2)

End point values	Both Arms Combined			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: Percentage of participants				
number (not applicable)				
Progression-free Survival	92.0			
Local-regional failure	94.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Grade 3+ Adverse Events (1 month Post RT)

End point title	Percentage of Participants With Grade 3+ Adverse Events (1 month Post RT)

End point description:

Adverse events were graded using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Grade refers to the severity of the AE. The CTCAE v4.0 assigns Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline: Grade 1 Mild, Grade 2 Moderate, Grade 3 Severe, Grade 4 Life-threatening or disabling, Grade 5 Death related to AE.

End point type	Secondary

End point timeframe:

1 month post radiation therapy (RT)

End point values	IMRT 6 Weeks + Cisplatin (Arm 1) 1 month post-RT	IMRT 5 Weeks (Arm 2) 1 month post RT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	142		
Units: Percentage of Participants				
number (confidence interval 95%)	36.1 (28.3 to 44.5)	28.2 (21.0 to 36.3)		

Statistical analyses

Statistical analysis title	One month after end of RT
Comparison groups	IMRT 6 Weeks + Cisplatin (Arm 1) 1 month post-RT v IMRT 5 Weeks (Arm 2) 1 month post RT

Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17 [11]
Method	Fisher exact

Notes:

[11] - Two-sided significance level = 0.05

Secondary: Percentage of Participants With Grade 3+ Adverse Events (6 months Post RT)

End point title	Percentage of Participants With Grade 3+ Adverse Events (6 months Post RT)

End point description:

Adverse events were graded using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Grade refers to the severity of the AE. The CTCAE v4.0 assigns Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline: Grade 1 Mild, Grade 2 Moderate, Grade 3 Severe, Grade 4 Life-threatening or disabling, Grade 5 Death related to AE.

End point type	Secondary

End point timeframe:

6 months post Radiation therapy (RT)

End point values	IMRT 6 Weeks + Cisplatin (Arm 1) 6 months post-RT	IMRT 5 weeks (Arm 2) 6 months post RT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	126		
Units: Percentage of participants				
number (confidence interval 95%)	17.9 (11.9 to 25.2)	11.1 (6.2 to 17.9)		

Statistical analyses

Statistical analysis title	6 months after end of RT
Comparison groups	IMRT 6 Weeks + Cisplatin (Arm 1) 6 months post-RT v IMRT 5 weeks (Arm 2) 6 months post RT
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.16
Method	Fisher exact

Notes:

[12] - Two-side significance level = 0.05

Secondary: Percentage of Participants With Grade 3+ Adverse Events (1 year Post RT)

End point title	Percentage of Participants With Grade 3+ Adverse Events (1 year Post RT)

End point description:

Adverse events were graded using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Grade refers to the severity of the AE. The CTCAE v4.0 assigns Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline: Grade 1 Mild, Grade 2 Moderate, Grade 3 Severe, Grade 4 Life-threatening or disabling, Grade 5 Death related to AE.

End point type	Secondary

End point timeframe:

1 year after end of radiation therapy (RT)

End point values	IMRT 6 Weeks + Cisplatin (Arm 1) 1 year post-RT	IMRT 5 weeks (Arm 2) 1 year post RT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	134		
Units: Percentage of Participants				
number (confidence interval 95%)	14.0 (8.8 to 20.8)	9.0 (4.7 to 15.1)		

Statistical analyses

Statistical analysis title	1 year after end of RT
Comparison groups	IMRT 6 Weeks + Cisplatin (Arm 1) 1 year post-RT v IMRT 5 weeks (Arm 2) 1 year post RT
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.26
Method	Fisher exact

Notes:

[13] - Two-sided significance level =0.05

Secondary: Percentage of Participants With Grade 3+ Adverse Events (2 years Post RT)

End point title	Percentage of Participants With Grade 3+ Adverse Events (2 years Post RT)

End point description:

Adverse events were graded using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Grade refers to the severity of the AE. The CTCAE v4.0 assigns Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline: Grade 1 Mild, Grade 2 Moderate, Grade 3 Severe, Grade 4 Life-threatening or disabling, Grade 5 Death related to AE.

End point type	Secondary

End point timeframe:

2 years after end of radiation therapy (RT)

End point values	IMRT 6 Weeks + Cisplatin (Arm 1) 2 years post-RT	IMRT 5 weeks (Arm 2) 2 years post RT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	128	122		
Units: Percentage of participants				
number (confidence interval 95%)	8.6 (4.4 to 14.9)	7.4 (3.4 to 13.5)		

Statistical analyses

Statistical analysis title	2 years after end of RT
Comparison groups	IMRT 6 Weeks + Cisplatin (Arm 1) 2 years post-RT v IMRT 5 weeks (Arm 2) 2 years post RT
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.82
Method	Fisher exact

Notes:

[14] - Two-side significance level = 0.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Weekly during treatment, 1 & 3 months after EOT, then every 3 months from end of treatment for 2 years, every 6 months from end of treatment for 3 years, then annually until study completion. Maximum follow-up at time of reporting was 4.1 years.

Adverse event reporting additional description:

The Assessment type for the Adverse Events documented was both Systematic and Non-Systematic.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	IMRT 6 Weeks + Cisplatin

Reporting group description:

IMRT 6 weeks: Intensity-modulated radiation therapy (IMRT), 30 fractions over 6 weeks, 5 fractions per week, 2 Gray per fraction to total dose of 60 Gy

Reporting group title	IMRT 5 weeks

Reporting group description:

Intensity-modulated radiation therapy (IMRT), 30 fractions over 5 weeks, 6 fractions per week, 2 Gray per fraction to total dose of 60 Gy

Serious adverse events	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 152 (20.39%)	11 / 147 (7.48%)	
number of deaths (all causes)	6	6	
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboemboloic event			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 152 (3.95%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	3 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flu like symptoms			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 152 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pharyngeal mucositis			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 152 (1.97%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngolaryngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sore throat			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 152 (1.97%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine increased			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Heart failure			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dysarthria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysgeusia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 152 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 152 (0.66%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 152 (2.63%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 152 (0.66%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry mouth			
subjects affected / exposed	1 / 152 (0.66%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	4 / 152 (2.63%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Esophagitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Neck soft tissue necrosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 152 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (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			
Anorexia			
subjects affected / exposed	4 / 152 (2.63%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypocalcaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 152 (1.32%)	0 / 147 (0.00%)	
occurrences causally related to treatment / all	2 / 2	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	IMRT 6 Weeks + Cisplatin	IMRT 5 weeks	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	152 / 152 (100.00%)	147 / 147 (100.00%)	
Vascular disorders			
Hypertension			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 152 (6.58%)	11 / 147 (7.48%)	
occurrences (all)	25	21	
Lymphoedema			
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 152 (7.24%)	11 / 147 (7.48%)	
occurrences (all)	13	13	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	138 / 152 (90.79%)	117 / 147 (79.59%)	
occurrences (all)	280	245	
Fever			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 152 (5.92%)	2 / 147 (1.36%)	
occurrences (all)	9	2	
Neck edema			

alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 152 (2.63%)	10 / 147 (6.80%)	
occurrences (all)	6	12	
Pain			
subjects affected / exposed	115 / 152 (75.66%)	121 / 147 (82.31%)	
occurrences (all)	226	262	
General disorders and administration site conditions - Other			
subjects affected / exposed	6 / 152 (3.95%)	11 / 147 (7.48%)	
occurrences (all)	13	14	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	38 / 152 (25.00%)	37 / 147 (25.17%)	
occurrences (all)	62	57	
Hiccups			
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 152 (7.24%)	0 / 147 (0.00%)	
occurrences (all)	11	0	
Hoarseness			
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 152 (11.84%)	19 / 147 (12.93%)	
occurrences (all)	25	25	
Respiratory, thoracic and mediastinal disorders - Other			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 152 (5.26%)	8 / 147 (5.44%)	
occurrences (all)	9	9	
Sore throat			
alternative assessment type: Non-systematic			
subjects affected / exposed	42 / 152 (27.63%)	28 / 147 (19.05%)	
occurrences (all)	55	39	
Voice alteration			
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 152 (7.24%)	13 / 147 (8.84%)	
occurrences (all)	11	14	
Pharyngeal mucosistis			

subjects affected / exposed	29 / 152 (19.08%)	44 / 147 (29.93%)	
occurrences (all)	39	61	
Psychiatric disorders			
Anxiety			
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 152 (7.24%)	15 / 147 (10.20%)	
occurrences (all)	12	18	
Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 152 (7.89%)	7 / 147 (4.76%)	
occurrences (all)	20	9	
Insomnia			
subjects affected / exposed	44 / 152 (28.95%)	34 / 147 (23.13%)	
occurrences (all)	62	55	
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 152 (9.21%)	7 / 147 (4.76%)	
occurrences (all)	15	8	
Aspartate aminotransferase increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 152 (7.89%)	7 / 147 (4.76%)	
occurrences (all)	12	9	
Blood bilirubin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 152 (5.92%)	5 / 147 (3.40%)	
occurrences (all)	13	7	
Creatinine increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	26 / 152 (17.11%)	3 / 147 (2.04%)	
occurrences (all)	28	3	
Lymphocyte count decreased			
subjects affected / exposed	118 / 152 (77.63%)	87 / 147 (59.18%)	
occurrences (all)	248	158	
Neutrophil count decreased			

alternative assessment type: Non-systematic			
subjects affected / exposed	33 / 152 (21.71%)	3 / 147 (2.04%)	
occurrences (all)	40	3	
Platelet count decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	53 / 152 (34.87%)	8 / 147 (5.44%)	
occurrences (all)	70	12	
Weight loss			
subjects affected / exposed	119 / 152 (78.29%)	101 / 147 (68.71%)	
occurrences (all)	235	186	
White blood cell count decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	56 / 152 (36.84%)	13 / 147 (8.84%)	
occurrences (all)	90	14	
Injury, poisoning and procedural complications			
Dermatitis radiation			
subjects affected / exposed	113 / 152 (74.34%)	109 / 147 (74.15%)	
occurrences (all)	147	135	
Nervous system disorders			
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 152 (9.87%)	8 / 147 (5.44%)	
occurrences (all)	17	8	
Dysgeusia			
subjects affected / exposed	142 / 152 (93.42%)	132 / 147 (89.80%)	
occurrences (all)	312	281	
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 152 (7.89%)	11 / 147 (7.48%)	
occurrences (all)	13	14	
Peripheral sensory neuropathy			
subjects affected / exposed	29 / 152 (19.08%)	15 / 147 (10.20%)	
occurrences (all)	51	29	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	92 / 152 (60.53%)	35 / 147 (23.81%)	
occurrences (all)	172	49	
Ear and labyrinth disorders			
Ear pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 152 (5.26%)	4 / 147 (2.72%)	
occurrences (all)	10	4	
Hearing impaired			
subjects affected / exposed	43 / 152 (28.29%)	34 / 147 (23.13%)	
occurrences (all)	95	72	
Tinnitus			
subjects affected / exposed	65 / 152 (42.76%)	41 / 147 (27.89%)	
occurrences (all)	119	75	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	92 / 152 (60.53%)	53 / 147 (36.05%)	
occurrences (all)	118	75	
Diarrhoea			
subjects affected / exposed	26 / 152 (17.11%)	14 / 147 (9.52%)	
occurrences (all)	30	17	
Dry mouth			
subjects affected / exposed	150 / 152 (98.68%)	142 / 147 (96.60%)	
occurrences (all)	391	365	
Dyspepsia			
subjects affected / exposed	42 / 152 (27.63%)	31 / 147 (21.09%)	
occurrences (all)	57	52	
Dysphagia			
subjects affected / exposed	124 / 152 (81.58%)	119 / 147 (80.95%)	
occurrences (all)	259	282	
Gastrooesophageal reflux disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 152 (5.26%)	3 / 147 (2.04%)	
occurrences (all)	9	6	
Gastrointestinal disorder			
alternative assessment type: Non-systematic			

subjects affected / exposed	16 / 152 (10.53%)	13 / 147 (8.84%)	
occurrences (all)	29	19	
Mucositis oral			
subjects affected / exposed	131 / 152 (86.18%)	121 / 147 (82.31%)	
occurrences (all)	193	172	
Nausea			
subjects affected / exposed	109 / 152 (71.71%)	62 / 147 (42.18%)	
occurrences (all)	145	84	
Oral pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 152 (5.92%)	9 / 147 (6.12%)	
occurrences (all)	11	13	
Vomiting			
subjects affected / exposed	51 / 152 (33.55%)	30 / 147 (20.41%)	
occurrences (all)	61	37	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	28 / 152 (18.42%)	25 / 147 (17.01%)	
occurrences (all)	34	34	
Dry skin			
subjects affected / exposed	36 / 152 (23.68%)	35 / 147 (23.81%)	
occurrences (all)	54	45	
Skin and subcutaneous tissue disorders - Other			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 152 (7.89%)	10 / 147 (6.80%)	
occurrences (all)	15	13	
Skin hyperpigmentation			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 152 (1.97%)	9 / 147 (6.12%)	
occurrences (all)	3	9	
Endocrine disorders			
Hypothyroidism			
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 152 (11.84%)	16 / 147 (10.88%)	
occurrences (all)	28	23	

Musculoskeletal and connective tissue disorders			
Neck pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 152 (4.61%)	11 / 147 (7.48%)	
occurrences (all)	7	15	
Trismus			
subjects affected / exposed	22 / 152 (14.47%)	25 / 147 (17.01%)	
occurrences (all)	31	36	
Infections and infestations			
Infections and infestations - Other			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 152 (7.89%)	7 / 147 (4.76%)	
occurrences (all)	12	9	
Mucosal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 152 (6.58%)	10 / 147 (6.80%)	
occurrences (all)	11	14	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	81 / 152 (53.29%)	69 / 147 (46.94%)	
occurrences (all)	116	96	
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed	23 / 152 (15.13%)	11 / 147 (7.48%)	
occurrences (all)	28	12	
Hyperglycaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	27 / 152 (17.76%)	13 / 147 (8.84%)	
occurrences (all)	35	16	
Hyperkalaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 152 (5.92%)	4 / 147 (2.72%)	
occurrences (all)	11	5	
Hypoalbuminaemia			
alternative assessment type: Non-systematic			

subjects affected / exposed	23 / 152 (15.13%)	11 / 147 (7.48%)	
occurrences (all)	26	11	
Hypocalcaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 152 (9.21%)	4 / 147 (2.72%)	
occurrences (all)	14	4	
Hypokalaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	16 / 152 (10.53%)	4 / 147 (2.72%)	
occurrences (all)	22	8	
Hypomagnesaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	31 / 152 (20.39%)	3 / 147 (2.04%)	
occurrences (all)	40	3	
Hyponatraemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	33 / 152 (21.71%)	9 / 147 (6.12%)	
occurrences (all)	44	11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 September 2016	SA01 Protocol Amendment 2 24-May-2016 which included the addition of an optional modified barium swallow sub study and changes to the open eligibility checklist.
12 February 2018	Protocol Amendment 3 20-Dec-2017 was submitted as a non-substantial amendment.

Notes:

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.

None

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33507809