Clinical trial results:
Preoperative combined radiochemotherapy for patients with newly diagnosed, primary operable and locally advanced rectal carcinoma (cT3, Nx, M0) of the lower and middle rectum

Summary

EudraCT number	2004-002358-72
Trial protocol	AT
Global end of trial date	19 December 2013

Results information

Result version number	v2 (current)
This version publication date	23 October 2021
First version publication date	10 September 2021
Version creation reason	• New data added to full data set Adding/updating information for Final Analysis (v1 included Interim Analysis as defined by EudraCT)

Trial information

Trial identification

Sponsor protocol code	ABCSG R02 (95)/TAKO 05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00297141
WHO universal trial number (UTN)	-
Other trial identifiers	Roche: ML18560

Notes:

Sponsors

Sponsor organisation name	ABCSG (Austrian Breast & Colorectal Cancer Study Group)
Sponsor organisation address	Nußdorfer Platz 8/12, Vienna, Austria, 1190
Public contact	Hannes Fohler (Trial Office Director), ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsg.at
Scientific contact	Prof. Dietmar Oefner-Velano, ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsg.at

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	19 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Rate of T-downstaging (Reduction of the T-stadium) at the time of final surgery following the preoperative combined radiochemotherapy (chemotherapy: Oxaliplatin, Capecitabine)

Protection of trial subjects:

A Data Monitoring Committee (DMC) was established to obtain Patient Safety. The responsibility of the DMC was to evaluate deviations of medical relevance and safety issues. The DMC decided on whether or not the patient should continue the study treatment due to safety issues. Major protocol deviations include all deviations endangering the basal medical concept of the study jeopardizing the safety of the patient. Minor protocol deviations include all other protocol deviations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 December 2004
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	7 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	38
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 8 trial sites participated and had the possibility to recruit patients in this trial in Austria. A total of 60 patients were enrolled between Dec 2004 and Dec 2005.

Pre-assignment

Screening details:

Time period of max. 21 days for screening (from diagnosis to therapy start) in which inclusion and exclusion criteria were assessed and clinical laboratory tests were performed.

Pre-assignment period milestones

Number of subjects started	60
Number of subjects completed	60

Period 1

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

Arms

Arm title	Combined radio chemotherapy

Arm description:

Preoperative Chemoradiation with therapy start within 21 days after MRI. Radiotherapy: 5 x 5 days 1.8 Gy; total dose 45 Gy; Chemotherapy: Capecitabine 825mg/m² bid, on radiotherapy days (week 1-4), Oxaliplatin 50mg/m² iv., d 1, 8, 15, 22.

Arm type	Experimental
Investigational medicinal product name	Xeloda
Investigational medicinal product code	RO 09-1978
Other name	Capecitabine
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

825 mg/m2/bid, on radiotherapy days (week 1-4)

Investigational medicinal product name	Eloxatin
Investigational medicinal product code	SR 96669
Other name	Oxaliplatin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50mg/m2 BSA per day (d1, d8, d15, d22)

Number of subjects in period 1	Combined radio chemotherapy
Started	60
Completed	58
Not completed	2
retrospectively stated ineligible	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	60	60	
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)	38	38	
From 65-84 years	22	22	
85 years and over	0	0	
Age continuous Units: years			
median	61		
full range (min-max)	34 to 76	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	41	41	
WHO Performance Status Units: Subjects			
0 (Zero)	55	55	
1 (One)	5	5	
Tumor differentiation Units: Subjects			
G1-2	42	42	
G3	9	9	
not classified	9	9	
Histologic type Units: Subjects			
adenocarcinoma	51	51	
mucinous	5	5	
others	4	4	
Tumor stage Units: Subjects			
cT2	1	1	
cT3	59	59	

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat population (ITT) consisted of all patients who received at least one dose of study medication. All efficacy and safety analyses were performed on this population.

Subject analysis set title	Survival
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The survival population consisted of all ITT patients with available long-term follow-up. All survival analyses were performed on this population.

Reporting group values	ITT	Survival	
Number of subjects	59	58	
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)	38		
From 65-84 years	22		
85 years and over	0		
Age continuous Units: years			
median	61		
full range (min-max)	34 to 76		
Gender categorical Units: Subjects			
Female	19		
Male	40		
WHO Performance Status Units: Subjects			
0 (Zero)	54		
1 (One)	5		
Tumor differentiation Units: Subjects			
G1-2	41		
G3	9		
not classified	9		
Histologic type Units: Subjects			
adenocarcinoma	50		
mucinous	5		
others	4		
Tumor stage Units: Subjects			
cT2	0		

cT3	59		

End points

End points reporting groups

Reporting group title	Combined radio chemotherapy

Reporting group description:

Preoperative Chemoradiation with therapy start within 21 days after MRI. Radiotherapy: 5 x 5 days 1.8 Gy; total dose 45 Gy; Chemotherapy: Capecitabine 825mg/m² bid, on radiotherapy days (week 1-4), Oxaliplatin 50mg/m² iv., d 1, 8, 15, 22.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat population (ITT) consisted of all patients who received at least one dose of study medication. All efficacy and safety analyses were performed on this population.

Subject analysis set title	Survival
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The survival population consisted of all ITT patients with available long-term follow-up. All survival analyses were performed on this population.

Primary: Tumor down-categorization

End point title	Tumor down-categorization[1]

End point description:

The primary efficacy variable was the rate of tumor down-categorization (defined as a decrease of ≥ 1 point(s)) at the T level. The extent of residual tumor in the resected specimen was classified according to the TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC). In case of a complete pathological response (pCR; i.e., ypT0ypN0M0), an independent pathologist re-evaluated the tumor tissue. All efficacy parameters were analyzed descriptively.

End point type	Primary

End point timeframe:

At the time of final surgery following the preoperative combined radio chemotherapy (chemotherapy: Oxaliplatin, Capecitabine).

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: Single arm study based on descriptive analysis only.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Subjects	31			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Pathological Complete Response (pCR)

End point title	Pathological Complete Response (pCR)

End point description:

The extent of residual tumor in the resected specimen was classified according to the TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC). In

case of a complete pathological response (pCR; i.e., ypT0ypN0M0), an independent pathologist re-evaluated the tumor tissue. All efficacy parameters were analyzed descriptively.

End point type	Other pre-specified

End point timeframe:

At the time of final surgery following the preoperative combined radio chemotherapy (chemotherapy: Oxaliplatin, Capecitabine).

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Subjects	6			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Confirmed Pathological Complete Response (pCR)

End point title	Confirmed Pathological Complete Response (pCR)

End point description:

The extent of residual tumor in the resected specimen was classified according to the TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC). In case of a complete pathological response (pCR; i.e., ypT0ypN0M0), an independent pathologist re-evaluated the tumor tissue. All efficacy parameters were analyzed descriptively.

End point type	Other pre-specified

End point timeframe:

At the time of final surgery following the preoperative combined radio chemotherapy (chemotherapy: Oxaliplatin, Capecitabine).

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Subjects	4			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Tumor status

End point title	Tumor status

End point description:

The extent of residual tumor in the resected specimen was classified according to the TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC). In case of a complete pathological response (pCR; i.e., ypT0ypN0M0), an independent pathologist re-

evaluated the tumor tissue. All efficacy parameters were analyzed descriptively.

End point type	Other pre-specified

End point timeframe:

At the time of final surgery following the preoperative combined radio chemotherapy (chemotherapy: Oxaliplatin, Capecitabine).

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Subjects				
0 (Zero)	6			
1 (One)	2			
2 (Two)	23			
3 (Three)	26			
4 (Four)	2			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Nodal status

End point title	Nodal status

End point description:

The extent of residual tumor in the resected specimen was classified according to the TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC). In case of a complete pathological response (pCR; i.e., ypT0ypN0M0), an independent pathologist re-evaluated the tumor tissue. All efficacy parameters were analyzed descriptively.

End point type	Other pre-specified

End point timeframe:

At the time of final surgery following the preoperative combined radio chemotherapy (chemotherapy: Oxaliplatin, Capecitabine).

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Subjects				
0 (Zero)	43			
1 (One)	10			
2 (Two)	6			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Metastasis

End point title	Metastasis

End point description:

The extent of residual tumor in the resected specimen was classified according to the TNM staging system of the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC). In case of a complete pathological response (pCR; i.e., ypT0ypN0M0), an independent pathologist re-evaluated the tumor tissue. All efficacy parameters were analyzed descriptively.

End point type	Other pre-specified

End point timeframe:

At the time of final surgery following the preoperative combined radio chemotherapy (chemotherapy: Oxaliplatin, Capecitabine).

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Subjects				
0 (Zero)	59			
1 (One)	0			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Relapse-free survival

End point title	Relapse-free survival

End point description:

Relapse-free survival was defined as the interval between surgery and the first evidence of locoregional recurrence, distant metastasis or death from any cause. Patients without relapse or death were right-censored at the last date when they were known to be alive (date of their last assessment). 5-year survival estimates (%) for relapse-free survival were presented based on Kaplan-Meier method.

End point type	Other pre-specified

End point timeframe:

During follow-up

End point values	Combined radio chemotherapy	Survival		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: percent				
number (not applicable)	65.5	65.5		

Statistical analyses

Statistical analysis title	Tumor down-categorization

Statistical analysis description:

Relapse-free survival was compared for patients with different chemotherapy response (without vs. with tumor down-categorization) at surgery. Comparison was done using Log-rank test with two-sided p-values. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression.

Comparison groups	Combined radio chemotherapy v Survival
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.0478 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	6.03

Notes:

[2] - Subjects in analysis actually are 58 - but the number of subjects was counted twice due to the necessary workaround for single arm studies given by EudraCT to accomodate reporting of statistical analysis.
[3] - Cox p=0.0556

Statistical analysis title	Pathological Complete Response (pCR)

Statistical analysis description:

Relapse-free survival was compared for patients with different chemotherapy response (without vs. with pCR) at surgery. Comparison was done using Log-rank test with two-sided p-values. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression.

Comparison groups	Combined radio chemotherapy v Survival
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.2591 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	22.4

Notes:

[4] - Subjects in analysis actually are 58 - but the number of subjects was counted twice due to the necessary workaround for single arm studies given by EudraCT to accomodate reporting of statistical analysis.
[5] - Cox p=0.2833

Statistical analysis title	Nodal status

Statistical analysis description:

Relapse free survival was compared for patients with different nodal status (yPN+ vs yPN-) at surgery. Comparison was done using Log-rank test with two-sided p-values. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression.

Comparison groups	Combined radio chemotherapy v Survival
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	< 0.0001 [7]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	8.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.29
upper limit	20.12

Notes:

[6] - Subjects in analysis actually are 58 - but the number of subjects was counted twice due to the necessary workaround for single arm studies given by EudraCT to accomodate reporting of statistical analysis.
[7] - Cox p<0.0001

Other pre-specified: Overall survival

End point title	Overall survival

End point description:

Overall survival was defined as the interval between surgery and death from any cause. Patients without death were right-censored at the last date when they were known to be alive (date of their last assessment). 5-year survival estimates (%) for overall survival were presented based on Kaplan-Meier method.

End point type	Other pre-specified

End point timeframe:

During follow-up

End point values	Combined radio chemotherapy	Survival		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: percent				
number (not applicable)	74.4	74.4		

Statistical analyses

Statistical analysis title	Tumor down-categorization

Statistical analysis description:

Overall survival was compared for patients with different chemotherapy response (without vs. with tumor down-categorization) at surgery. Comparison was done using Log-rank test with two-sided p-values. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression.

Comparison groups	Combined radio chemotherapy v Survival
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.3246 [9]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	4.26

Notes:

[8] - Subjects in analysis actually are 58 - but the number of subjects was counted twice due to the necessary workaround for single arm studies given by EudraCT to accomodate reporting of statistical analysis.
[9] - Cox p=0.3292

Statistical analysis title	Pathological Complete Response (pCR)

Statistical analysis description:

Overall survival was compared for patients with different chemotherapy response (without vs. with pCR) at surgery. Comparison was done using Log-rank test with two-sided p-values. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression.

Comparison groups	Combined radio chemotherapy v Survival
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.4318 [11]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	16.63

Notes:

[10] - Subjects in analysis actually are 58 - but the number of subjects was counted twice due to the necessary workaround for single arm studies given by EudraCT to accomodate reporting of statistical analysis.
[11] - Cox p=0.4437

Statistical analysis title	Nodal status

Statistical analysis description:

Overall survival was compared for patients with different nodal status (yPN+ vs yPN-) at surgery. Comparison was done using Log-rank test with two-sided p-values. Hazard ratios (HRs) and their

corresponding 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression.

Comparison groups	Combined radio chemotherapy v Survival
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	< 0.0001 [13]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.36
upper limit	17.85

Notes:

[12] - Subjects in analysis actually are 58 - but the number of subjects was counted twice due to the necessary workaround for single arm studies given by EudraCT to accomodate reporting of statistical analysis.
[13] - Cox p<0.0001

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of radiochemotherapy until surgery

Adverse event reporting additional description:

Adverse events were reported until the Interim Analysis (according to EudraCT definition) only - no adverse events were captured during follow-up and hence, there is no update on adverse events for the Final Analysis (according to EudraCT definition).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Combined radiochemotherapy

Reporting group description: -

Serious adverse events	Combined radiochemotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 59 (20.34%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertensive crisis	Additional description: Hypertensive crisis		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	3 / 59 (5.08%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper	Additional description: Abdominal pain upper		

subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	5 / 59 (8.47%)		
occurrences causally related to treatment / all	12 / 13		
deaths causally related to treatment / all	0 / 0		
Proctitis	Additional description: Proctitis		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Erythema		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Renal failure	Additional description: Renal failure		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Combined radiochemotherapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 59 (94.92%)		
Injury, poisoning and procedural complications			
Radiation skin injury	Additional description: Radiation skin injury		
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	8		
Vascular disorders			
Hypertension	Additional description: Hypertension		
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	13		
Nervous system disorders			

Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	22 / 59 (37.29%)		
occurrences (all)	57		
Blood and lymphatic system disorders			
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	17		
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	10		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	9		
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	8		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	6		
Constipation	Additional description: Constipation		
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	11		
Gastrointestinal toxicity	Additional description: Gastrointestinal toxicity		
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	8		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	26 / 59 (44.07%)		
occurrences (all)	69		
Nausea	Additional description: Nausea		
subjects affected / exposed	19 / 59 (32.20%)		
occurrences (all)	37		
Painful defaecation	Additional description: Painful defaecation		
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	11		

Vomiting	Additional description: Vomiting		
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Skin toxicity	Additional description: Skin toxicity		
subjects affected / exposed	7 / 59 (11.86%)		
occurrences (all)	11		
Psychiatric disorders			
Mental disorder	Additional description: Mental disorder		
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
Renal and urinary disorders			
Micturition urgency	Additional description: Micturition urgency		
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	8		
Dysuria	Additional description: Dysuria		
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	16		
Infections and infestations			
Infection	Additional description: Infection		
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	6		
Metabolism and nutrition disorders			
Weight fluctuation	Additional description: Weight fluctuation		
subjects affected / exposed	12 / 59 (20.34%)		
occurrences (all)	21		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 April 2010	According to Protocol Amendment #1, collection of prolonged (after surgery) follow up survival data was done. This data should enable estimation of survival curves for overall survival, cancer specific survival and relapse-free survival. Additionally, relationship between study primary endpoints tumor stage downstaging and yPCR and survival endpoints was examined. It should be stated that study was not powered for comparison between chemotherapy response and survival endpoint.

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.

Limitation of a nonrandomized design.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29127435