



Clinical trial results:

Preoperative induction chemotherapy in combination with Bevacizumab followed by combined chemoradiotherapy in locally advanced rectal cancer with high risk of recurrence - a phase II pilot study with preoperative administration of Capecitabine (Xeloda), Oxaliplatin and Bevacizumab (Avastin) followed by Capecitabine (Xeloda) plus radiotherapy (RTx)

Summary

EudraCT number	2010-024354-11
Trial protocol	AT
Global end of trial date	26 August 2013

Results information

Result version number	v1 (current)
This version publication date	26 August 2021
First version publication date	26 August 2021

Trial information

Trial identification

Sponsor protocol code	ABCSGR05
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01434147
WHO universal trial number (UTN)	-

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 1408 92 30, info@abcg.at
Scientific contact	Prof. Dietmar Oefner-Velano, ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 1408 92 30, info@abcg.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	26 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 August 2013
Global end of trial reached?	Yes
Global end of trial date	26 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate feasibility and tolerance of an induction chemotherapy (Capecitabine/Oxaliplatin) in combination with Bevacizumab (Avastin®) followed by combined radiochemotherapy with Capecitabine (Xeloda®) in patients with locally advanced rectal carcinoma

Protection of trial subjects:

The study specific patient information and informed consent form included language to encourage study participants to reach out to the Study Doctor / Study Team in case they have any questions, concerns or doubts. Section 14 specifically referenced a 24/7 contact person to reach out to and the ICF contained a reference to the local ombudsman / patient advocacy. A dedicated IDMC was established to ensure patient safety throughout the trial.

Background therapy:

Oxaliplatin was administered as part of the induction chemotherapy in a dose of 130 mg/m² bid, for 3 cycles, on day 1, 22 and 43 (+/- 2 days). Oxaliplatin was no study medication – it was used in this study as non-investigational product (NIMP).

Evidence for comparator: -

Actual start date of recruitment	11 October 2011
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	Austria: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	14
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment phase for this study was from 11.10.2011 to 27.02.2013. No extended follow up period was done for this study.

Pre-assignment

Screening details:

A careful check of inclusion and exclusion criteria had to be performed by the Investigators / Site Teams during a pre-defined "screening period". They then completed a "Registration Form" which was sent to ABCSG for registering a new patient on the study and in the eCRF.

Pre-assignment period milestones

Number of subjects started	25
Number of subjects completed	25

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	Induction chemo + Bevacizumab
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Arm description:

Induction chemotherapy (Capecitabine/Oxaliplatin) in combination with Bevacizumab (Avastin) followed by combined radiochemotherapy with Capecitabine (Xeloda)

Arm type	Experimental
Investigational medicinal product name	Avastin
Investigational medicinal product code	RO487-6646
Other name	Bevacizumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bevacizumab (Avastin®), 25mg/ml, a concentrate for solution for infusion. 100 mg or 400 mg vial diluted with 0.9% NaCl to 100 ml. First infusion during 90 minutes, in case of good tolerability the further infusions can be administered during 60 minutes and then 30 minutes. 7.5 mg Bevacizumab/kg body weight every 21 days. Bevacizumab was administered at day 1 (+/- 2 days), 22 (+/- 2 days) and 43 (+/- 2 days). Patients take a dose of 7.5 mg/kg body weight (diluted with NaCl 0.9% to 100ml) of Bevacizumab on day 1 of each cycle.

Investigational medicinal product name	Xeloda
Investigational medicinal product code	RO009-1978
Other name	Capecitabine
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Capecitabine (Xeloda®) is an approved treatment and therefore was no study treatment (NIMP).

Dosage was calculated according to the respective body surface: 1000 mg/m²/bid p.o.. Patients were administered Capecitabine in the form of tablets according to the following scheme:

- day 1 – 14, followed by 1 week off treatment
- day 22 – 35 followed by 1 week off treatment
- day 43 – 56 followed by 1 week off treatment

Capecitabine was taken twice a day with 12 hours between each intake, 30 minutes after a meal.

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

Dosage and administration details:

Oxaliplatin is an approved treatment and therefore was no study treatment (NIMP). 130mg/m²/d (on d1 of each cycle of 3-weekly treatment cycles), in combination with Bevacizumab and Capecitabine.

Number of subjects in period 1	Induction chemo + Bevacizumab
Started	25
Completed	19
Not completed	6
Adverse event, non-fatal	5
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	Induction chemo + Bevacizumab
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Reporting group description:

Induction chemotherapy (Capecitabine/Oxaliplatin) in combination with Bevacizumab (Avastin) followed by combined radiochemotherapy with Capecitabine (Xeloda)

Reporting group values	Induction chemo + Bevacizumab	Total	
Number of subjects	25	25	
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)	14	14	
From 65-84 years	11	11	
85 years and over	0	0	
Age continuous			
Units: years			
median	62		
full range (min-max)	24 to 78	-	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	16	16	
ECOG			
ECOG performance status			
Units: Subjects			
Status 0	25	25	
T-stage			
Units: Subjects			
cTis	1	1	
cT3	20	20	
cT4	4	4	
N-stage			
Units: Subjects			
cN0	5	5	
cN1	10	10	
cN2	8	8	
cNx	2	2	

End points

End points reporting groups

Reporting group title	Induction chemo + Bevacizumab
Reporting group description:	
Induction chemotherapy (Capecitabine/Oxaliplatin) in combination with Bevacizumab (Avastin) followed by combined radiochemotherapy with Capecitabine (Xeloda)	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT analysis set was defined as all patients who started preoperative treatment. Post resection for inconclusive histology showed on one patient no tumour invasion. This patient did not take any doses of Bevacizumab chemotherapy or any other study therapy and was as such, according to protocol, not included in the ITT analysis set.	

Primary: Feasibility - dose modifications - Capecitabine

End point title	Feasibility - dose modifications - Capecitabine ^[1]
End point description:	
For the primary objective feasibility, the number of patients with dose modification, therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Capecitabine . Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.	
End point type	Primary
End point timeframe:	
After induction chemotherapy	

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	24			
Units: Subjects	5			

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility - therapy delays - Capecitabine

End point title	Feasibility - therapy delays - Capecitabine ^[2]
End point description:	
For the primary objective feasibility, the number of patients with dose modification, therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Capecitabine. Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.	
End point type	Primary

End point timeframe:

After induction chemotherapy

Notes:

[2] - 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	24			
Units: Subjects	10			

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility - therapy interruptions - Capecitabine

End point title	Feasibility - therapy interruptions - Capecitabine ^[3]
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End point description:

For the primary objective feasibility, the number of patients with dose modification, therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Capecitabine. Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.

End point type	Primary
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End point timeframe:

After induction chemotherapy

Notes:

[3] - 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	24			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility - early end of therapy - Capecitabine

End point title	Feasibility - early end of therapy - Capecitabine ^[4]
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End point description:

For the primary objective feasibility, the number of patients with dose modification, therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Capecitabine. Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.

End point type	Primary
End point timeframe:	
After induction chemotherapy	
Notes:	
[4] - 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	24			
Units: Subjects	5			

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility - therapy delays - Bevacizumab

End point title	Feasibility - therapy delays - Bevacizumab ^[5]
End point description:	
For the primary objective feasibility, the number of patients with therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Bevacizumab. Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.	
End point type	Primary
End point timeframe:	
After induction chemotherapy	
Notes:	
[5] - 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	24			
Units: Subjects	9			

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility - therapy interruptions - Bevacizumab

End point title	Feasibility - therapy interruptions - Bevacizumab ^[6]
End point description:	
For the primary objective feasibility, the number of patients with therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Bevacizumab. Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.	

End point type	Primary
End point timeframe:	
After induction chemotherapy	
Notes:	
[6] - 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	24			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility - early end of therapy - Bevacizumab

End point title	Feasibility - early end of therapy - Bevacizumab ^[7]
End point description:	
For the primary objective feasibility, the number of patients with therapy delay, therapy interruption and early end of therapy, as appropriate, was given for the investigational medical product (IMP) Bevacizumab. Based on similar studies more than 17% of patients (hence, more than 4 patients from ITT in this study) experiencing therapy breaks or therapy discontinuations were defined as critical.	
End point type	Primary
End point timeframe:	
After induction chemotherapy	
Notes:	
[7] - 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	24			
Units: Subjects	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Response rate - T-stage downstaging

End point title	Response rate - T-stage downstaging
End point description:	
For the secondary objective response rate, the number of patients with T-stage downstaging, N-stage downstaging and complete pathologic remission (pCR) was given.	
End point type	Secondary

End point timeframe:

After surgery

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Response rate - N-stage downstaging

End point title	Response rate - N-stage downstaging
End point description: For the secondary objective response rate, the number of patients with T-stage downstaging, N-stage downstaging and complete pathologic remission (pCR) was given.	
End point type	Secondary
End point timeframe: After surgery	

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Repsonse rate - pCR

End point title	Repsonse rate - pCR
End point description: For the secondary objective response rate, the number of patients with T-stage downstaging, N-stage downstaging and complete pathologic remission (pCR) was given.	
End point type	Secondary
End point timeframe: After surgery	

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Postoperative morbidity

End point title	Postoperative morbidity
End point description:	
For the secondary objective postoperative morbidity, the number of patients with postoperative morbidity according to Accordion was given.	
End point type	Secondary
End point timeframe:	
At discharge	

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of study drug until 30 days after last therapy (radiotherapy or capecitabine, whatever is performed or administered later).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	Induction chemo + Bevacizumab
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Reporting group description: -

Serious adverse events	Induction chemo + Bevacizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 24 (58.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis	Additional description: Thrombosis		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arteriosclerosis coronary artery	Additional description: Arteriosclerosis coronary artery		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia	Additional description: Febrile neutropenia		

subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Enterocolitis	Additional description: Enterocolitis		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ileal perforation	Additional description: Ileal perforation		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus	Additional description: Ileus		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngospasm	Additional description: Laryngospasm		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema	Additional description: Angioedema		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erythema	Additional description: Erythema		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure	Additional description: Renal failure		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute	Additional description: Renal failure acute		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess	Additional description: Abscess		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis	Additional description: Oral candidiasis		

subjects affected / exposed	1 / 24 (4.17%)		
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	Induction chemo + Bevacizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)		
Vascular disorders			
Hypertension	Additional description: Hypertension		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
General disorders and administration site conditions			
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	9		
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Pain	Additional description: Pain		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Investigations			

Weight decreased subjects affected / exposed occurrences (all)	Additional description: Weight decreased		
	2 / 24 (8.33%) 2		
Injury, poisoning and procedural complications			
	Additional description: Infusion related reaction		
	2 / 24 (8.33%) 2		
	Additional description: Radiation skin injury		
Radiation skin injury subjects affected / exposed occurrences (all)	4 / 24 (16.67%) 4		
Nervous system disorders			
	Additional description: Dizziness		
	2 / 24 (8.33%) 2		
	Additional description: Polyneuropathy		
Polyneuropathy subjects affected / exposed occurrences (all)	10 / 24 (41.67%) 11		
Blood and lymphatic system disorders			
	Additional description: Thrombocytopenia		
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Ear and labyrinth disorders			
	Additional description: Vertigo		
Vertigo subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Gastrointestinal disorders			
	Additional description: Abdominal pain		
	3 / 24 (12.50%) 5		
	Additional description: Constipation		
	3 / 24 (12.50%) 3		
	Additional description: Defaecation urgency		
	2 / 24 (8.33%) 2		
Diarrhoea	Additional description: Diarrhoea		

subjects affected / exposed	8 / 24 (33.33%)		
occurrences (all)	11		
Nausea	Additional description: Nausea		
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	13		
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Proctitis	Additional description: Proctitis		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorders			
Dry skin	Additional description: Dry skin		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Palmar-plantar erythrodysesthesia syndrome	Additional description: Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	6 / 24 (25.00%)		
occurrences (all)	7		
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Infections and infestations			
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2011	The protocol amendment was due to changes in the Capecitabine dosage scheme.

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.

Limitations are the nonrandomized design and the short interval between neoadjuvant treatment and surgery (median=29 days).

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28476845>