Clinical trial results:
Cetuximab (Erbitux®), capecitabine and radiotherapy in neoadjuvant treatment of patients with locally advanced resectable rectal cancer: A phase II Pilot Study

Summary

EudraCT number	2006-001371-38
Trial protocol	SI
Global end of trial date	30 September 2013

Results information

Result version number	v1 (current)
This version publication date	21 December 2021
First version publication date	21 December 2021
Summary attachment (see zip file)	XERT final report (XERT final report.pdf)

Trial information

Trial identification

Sponsor protocol code	EMR 62202-688

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00689702
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institute of Oncology
Sponsor organisation address	Zaloška cesta 2, Ljubljana, Slovenia, 1000
Public contact	Vaneja Velenik, Ljubljana Institute of Oncology, vvelenik@onko-i.si
Scientific contact	Vaneja Velenik, Ljubljana Institute of Oncology, vvelenik@onko-i.si

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The pathological complete response rate.

Protection of trial subjects:

Patients undergoing the study had extra health insurance.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovenia: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	37
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible patients had a histologically verified stage II or III adenocarcinoma of the rectum, (International Union against Cancer [UICC] TNM classification 2002). Other inclusion criteria were; ≥18 years of age at diagnosis; World Health Organization (WHO) performance status ≤2.

Pre-assignment

Screening details:

Out of 43 patients, one patient did not receive study treatment due to the detection of metastatic disease during the pretreatment work-up. One patient withdrew consent, and another was excluded due to protocol violation. Other three patients were discontinued from the study. Thus 37 patients received Cetuximab and completed the treatment protocol.

Period 1

Period 1 title	Feb 2007-Sep 2008 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	XERT

Arm description:

Patients with resectable LARC received capecitabine (1250 mg/m2 twice daily, orally) for 2 weeks followed by cetuximab alone (400 mg/m2 for 1 week) and then with CRT (250 mg/m2/week) comprising capecitabine (825 mg/m2 twice daily) and radiotherapy to the small pelvis (45 Gy in 25 1.8-Gy fractions), five days a week for five weeks. Surgery was conducted six weeks following CRT, with post-operative chemotherapy with capecitabine (1250 mg/m2 twice daily for 14 days every 21 days) three weeks later.

Arm type	Active comparator
Investigational medicinal product name	cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients with resectable LARC received capecitabine (1250 mg/m2 twice daily, orally) for 2 weeks followed by cetuximab alone (400 mg/m2 for 1 week) and then with CRT (250 mg/m2/week) comprising capecitabine (825 mg/m2 twice daily) and radiotherapy to the small pelvis (45 Gy in 25 1.8-Gy fractions), five days a week for five weeks. Surgery was conducted six weeks following CRT, with post-operative chemotherapy with capecit- abine (1250 mg/m2 twice daily for 14 days every 21 days) three weeks later

Number of subjects in period 1	XERT
Started	43
Completed	36
Not completed	7
Chest pain of unknown origin	2
Consent withdrawn by subject	1
Physician decision	1

Adverse event, non-fatal	1
Protocol violation	1
Accidental death	1

Baseline characteristics

Reporting groups	
Reporting group title	Feb 2007-Sep 2008

Reporting group description: -

Reporting group values	Feb 2007-Sep 2008	Total	
Number of subjects	43	43	
Age categorical			
37 subjects aged between 33 and 72 years			
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
from 33 to 72	43	43	
Gender categorical Units: Subjects			
Female	10	10	
Male	33	33	

End points

End points reporting groups

Reporting group title	XERT

Reporting group description:

Patients with resectable LARC received capecitabine (1250 mg/m2 twice daily, orally) for 2 weeks followed by cetuximab alone (400 mg/m2 for 1 week) and then with CRT (250 mg/m2/week) comprising capecitabine (825 mg/m2 twice daily) and radiotherapy to the small pelvis (45 Gy in 25 1.8-Gy fractions), five days a week for five weeks. Surgery was conducted six weeks following CRT, with post-operative chemotherapy with capecitabine (1250 mg/m2 twice daily for 14 days every 21 days) three weeks later.

Primary: Complete pathological remission rate

End point title	Complete pathological remission rate[1]

End point description:

End point type	Primary

End point timeframe:

6 weeks after the preoperative therapy conclusion

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: Statistical analysis was performed using SPSS programme. The data is available in the Final Study Report.

End point values	XERT			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: 37	37			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During treatment, patients were evaluated weekly. Clinical examinations and complete blood counts were performed and body weight was measured. Toxic side effects were assessed according to National Cancer Institute Common Toxicity Criteria (NCI-CTC V.3.0)

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTC
Dictionary version	3.0

Reporting groups

Reporting group title	Eligible subjects

Reporting group description:

Reporting group includes all eligible patients.

Serious adverse events	Eligible subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 37 (40.54%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	0		
Immune system disorders			
Allergy			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Radiodermatitis			

subjects affected / exposed	6 / 37 (16.22%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Eligible subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 37 (86.49%)		
Blood and lymphatic system disorders			
Leukocytopenia			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	5		
Anemia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Immune system disorders			
Allergic hypersensitivity			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed[1]	8 / 8 (100.00%)		
occurrences (all)	8		
Nausea			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	7 / 37 (18.92%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Acneiform rash			
subjects affected / exposed	32 / 37 (86.49%)		
occurrences (all)	32		
Radiodermatitis			
subjects affected / exposed	15 / 37 (40.54%)		
occurrences (all)	15		
Hand and foot syndrome			
subjects affected / exposed	14 / 37 (37.84%)		
occurrences (all)	14		
Dry skin			
subjects affected / exposed	10 / 37 (27.03%)		
occurrences (all)	10		
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Infections and infestations			
infection			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Hypoalbuminaemia			

subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Hypokalemia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: More than one adverse event were present per patient.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/20042310

http://www.ncbi.nlm.nih.gov/pubmed/23077464