Clinical trial results:
A phase II trial of combination chemotherapy with intravenous oxaliplatin combined with tablet capecitabin in patients with recidivant breastcancer

Summary

EudraCT number	2012-005329-56
Trial protocol	DK
Global end of trial date	01 December 2015

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019
Summary attachment (see zip file)	CAPOX_article (CAPOX.pdf)

Trial information

Trial identification

Sponsor protocol code	MA1229

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Herlev University Hospital
Sponsor organisation address	Herlev Ringvej 75, Herlev, Denmark, 2730
Public contact	Dept of oncology, Dept of oncology, Herlev Hospital, 0045 38682344, Dorte.nielsen.01@regionh.dk
Scientific contact	Dept of oncology, Dept of Oncology, Herlev Hospital, 0045 38682344, Dorte.nielsen.01@regionh.dk

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	01 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2015
Global end of trial reached?	Yes
Global end of trial date	01 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Clinical Benefit rate (Number of patients with complete or partial response or stable disease >= 6 months (Recist 1.1)

Protection of trial subjects:

The study was approved by the Regional Scientific Ethics Committee (VEK no. H-4-2013-034), the Danish Medicine Agency (EudraCT no 2012-005329-56) and signed informed consent was obtained from all patients included. The study was conducted in accordance with the principles of good clinical practice and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	12
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients recruited at single site at Herlev Hospital, Department of Oncology, Denmark, Recruitment was open from Dec 2013 to Aug 2015

Pre-assignment

Screening details:

Eligible women were required to have locally advanced or metastatic, histologically or cytologically confirmed breast cancer as well as a HER-2 negative tumor.Previous adjuvant treatment with taxane and epirubicin or with taxane and cyclophosphamide followed by first line treatment with epirubicin was required.

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	CapOx

Arm description:

Capecitabine and Oxaliplatin (CapOx)

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

Dosage and administration details:

1300 mg/m2 daily divided into two doses

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 was administered intravenously at 85 mg/m2 as a 30-minute infusion on day 1 of each 2-weeks cycle

Number of subjects in period 1	CapOx
Started	18
Completed	15
Not completed	3
Consent withdrawn by subject	2
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	57.5		
full range (min-max)	42 to 74	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	0	0	

End points

End points reporting groups

Reporting group title	CapOx
Reporting group description:	
Capecitabine and Oxaliplatin (CapOx)	

Primary: Clinical Benefit Rate

End point title	Clinical Benefit Rate[1]
End point description:	
Patients with SD >= 6 months or partial response or complete response	
End point type	Primary
End point timeframe:	
Disease status assessed by CT scan every 8th week from treatment start to progression of disease	
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: Simon two-stage design -stage 1 analyse: The Clinical Benefit Rate (CBR; complete response, partial remission and stable disease ≥ 6 months) limit of > 50% was not met and the study was closed.	

End point values	CapOx			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: number of patients	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response

End point title	Best Overall Response
End point description:	
End point type	Secondary
End point timeframe:	
Disease status assessed by CT scan every 8th week from treatment start to progression of disease	

End point values	CapOx			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: number of patients				
CR	1			
PR	4			
SD	7			
PD	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free Survival

End point title	Progression free Survival

End point description:

End point type	Secondary

End point timeframe:

PFS was calculated as the period from the first treatment to disease progression or death of any cause.

End point values	CapOx			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: months				
median (confidence interval 95%)	5.2 (4.8 to 5.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

OS was calculated as the time from the first treatment to death from any cause or until May 1st 2017

End point values	CapOx			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: months				
median (confidence interval 95%)	12.9 (4.1 to 21.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment to 28 days after last treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	CapOx
Reporting group description:	
Capecitabine and Oxaliplatin (CapOx)	

Serious adverse events	CapOx		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 18 (27.78%)		
number of deaths (all causes)	17		
number of deaths resulting from adverse events	1		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			

subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
vena cava syndrome			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Paresis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CapOx		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	6		
Alanine aminotransferase increased			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	5		
Platelet count decreased			
subjects affected / exposed	9 / 18 (50.00%)		
occurrences (all)	9		
Neutrophil count decreased			

subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Cardiac disorders Chest pain subjects affected / exposed occurrences (all)	 4 / 18 (22.22%) 4		
Nervous system disorders Dysaesthesia subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 17 / 18 (94.44%) 18 15 / 18 (83.33%) 16 2 / 18 (11.11%) 2		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) flu like symptoms subjects affected / exposed occurrences (all) Infusion related reaction subjects affected / exposed occurrences (all)	 12 / 18 (66.67%) 14 2 / 18 (11.11%) 2 2 / 18 (11.11%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all)	 5 / 18 (27.78%) 6 14 / 18 (77.78%) 16 12 / 18 (66.67%) 13		

Vomiting subjects affected / exposed occurrences (all)	7 / 18 (38.89%) 8		
Constipation subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Gastritis subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Musculoskeletal and connective tissue disorders Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	10 / 18 (55.56%) 13		
Infections and infestations Paronychia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA, Trial was stopped after analyses of first stage in Simon´s two stage design.

Notes: