Clinical trial results:
Intra-hepatic chemotherapy with oxaliplatin every second week in combination with systemic capecitabine and in patients with a HER2-positive tumour in combination with trastuzumab (Herceptin®) in patient with non-resectable liver metastases from breast cancer.

A phase II trial in patients with limited extrahepatic disease.

Summary

EudraCT number	2009-014821-17
Trial protocol	DK
Global end of trial date	01 May 2017

Results information

Result version number	v1 (current)
This version publication date	05 October 2019
First version publication date	05 October 2019

Trial information

Trial identification

Sponsor protocol code	MA0918

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01387295
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Herlev Ringvej 75, Herlev, Denmark, 2730
Public contact	Dorte Nielsen, Department of Oncology Herlev Hospital, +45 38682344, dorte.nielsen.01@regionh.dk
Scientific contact	Dorte Nielsen, Department of Oncology Herlev Hospital, +45 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 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 May 2017
Global end of trial reached?	Yes
Global end of trial date	01 May 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Response rate
Number of patients with complete or partial response in the liver (RECIST version 1.1)

Protection of trial subjects:

Eligibility criteria, Dose modification
no additional measures

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	01 October 2009
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: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	30
From 65 to 84 years	8

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 October 2009 to September 2016

Pre-assignment

Screening details:

Patients with histologically confirmed adenocarcinoma of the breast with main metastases in liver and limited extrahepatic disease were allowed. Liver metastases evaluated not suitable for local ablation by RFA, SBRT, or surgery and had <70% of the liver affected. Extra-hepatic metastasis without progression within past 6 months.

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	Protocol treatment

Arm description:

Single Arm study

Arm type	Experimental
Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intrahepatic use , Intravenous use

Dosage and administration details:

Patients received oxaliplatin every two weeks alternating between hepatic arterial and systemic administration. Dose was at 85 mg/m2.

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:

Capecitabine was given at a daily dose of 1300 mg/m2 on a continuous schedule

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

Dosage and administration details:

Patients with HER-2 positive tumors received additional trastuzumab 8 mg/kg on day 1 followed by 6 mg/kg every third week.

Number of subjects in period 1	Protocol treatment
Started	38
Completed	38

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	38	38	
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	54.5		
full range (min-max)	31 to 72	-	
Gender categorical Units: Subjects			
Female	38	38	
Male	0	0	

End points

End points reporting groups

Reporting group title	Protocol treatment
Reporting group description:	
Single Arm study	

Primary: Response rate (hepatic)

End point title	Response rate (hepatic)[1]
End point description:	

End point type	Primary
End point timeframe:	
treatment start to progression of disease or death	

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 trial

End point values	Protocol treatment			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: number of patients				
CR	2			
PR	13			
SD	21			
PD	1			
Not evaluable	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall reponse rate

End point title	Overall reponse rate
End point description:	

End point type	Secondary
End point timeframe:	
treatment start to progression of disease or death	

End point values	Protocol treatment			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: number of patients				
CR	0			
PR	15			
SD	21			
PD	2			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS

End point title	PFS

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	Protocol treatment			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: months				
median (full range (min-max))	12.8 (6.9 to 18.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS

End point title	OS

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	Protocol treatment			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: months				
median (full range (min-max))	24.0 (17.2 to 30.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Informed consent to 30 days after last treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	3.0
Reporting groups	
Reporting group title	Protocol treatment
Reporting group description: Single Arm study	

Serious adverse events	Protocol treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 38 (21.05%)		
number of deaths (all causes)	33		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Morphine toxication			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
gallbladder stone			

subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	3 / 38 (7.89%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 38 (2.63%)		
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	Protocol treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 38 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 38 (39.47%)		
occurrences (all)	54		
Aspartate aminotransferase increased			
subjects affected / exposed	19 / 38 (50.00%)		
occurrences (all)	77		
Alkaline phosphatase increased			
subjects affected / exposed	17 / 38 (44.74%)		
occurrences (all)	46		
Amylase increased			
subjects affected / exposed	14 / 38 (36.84%)		
occurrences (all)	35		
Hyperbilirubinaemia			
subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	8		

Thrombocytopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 17 / 38 (44.74%) 82 15 / 38 (39.47%) 25		
Nervous system disorders Dysaesthesia subjects affected / exposed occurrences (all) Peripheral motor neuropathy subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	 35 / 38 (92.11%) 304 11 / 38 (28.95%) 41 29 / 38 (76.32%) 179		
General disorders and administration site conditions Allergic reaction subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) pain subjects affected / exposed occurrences (all)	 3 / 38 (7.89%) 6 30 / 38 (78.95%) 159 9 / 38 (23.68%) 12 23 / 38 (60.53%) 59		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 9 / 38 (23.68%) 12		
Gastrointestinal disorders Diarrhoea			

subjects affected / exposed	21 / 38 (55.26%)		
occurrences (all)	55		
Stomatitis			
subjects affected / exposed	21 / 38 (55.26%)		
occurrences (all)	62		
Nausea			
subjects affected / exposed	34 / 38 (89.47%)		
occurrences (all)	119		
Vomiting			
subjects affected / exposed	20 / 38 (52.63%)		
occurrences (all)	36		
Dyspepsia			
subjects affected / exposed	5 / 38 (13.16%)		
occurrences (all)	12		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	33 / 38 (86.84%)		
occurrences (all)	184		
Alopecia			
subjects affected / exposed	6 / 38 (15.79%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	5 / 38 (13.16%)		
occurrences (all)	12		
Arthralgia			
subjects affected / exposed	4 / 38 (10.53%)		
occurrences (all)	8		
Infections and infestations			
infection			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	24 / 38 (63.16%)		
occurrences (all)	91		

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.

recruitment goal not reached

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30544058