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 (R)) in patients with non-resectable liver metasatses from breast cancer
A phase II trial in patients without extrahepatic disease.

Summary

EudraCT number	2009-014863-37
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	MA0919

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01387373
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, +45 38682344, dorte.nielsen.01@regionh.dk
Scientific contact	Dorte Nielsen, Department of Oncology, +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:

not applicable

Background therapy:

none

Evidence for comparator:

not applicable

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: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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	2
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 metastases in liver only were allowed. Patients were included if the liver metastases were not eligible for local ablation by RFA, SBRT, or surgery evaluated at a MDT conference and had <70% of the liver affected.

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	Arm 1

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	Arm 1
Started	14
Completed	14

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	14	14	
Age categorical			
median age			
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			
median age			
Units: years			
median	52		
full range (min-max)	36 to 67	-	
Gender categorical			
female only			
Units: Subjects			
Female	14	14	
Male	0	0	

Subject analysis sets

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

Subject analysis set description:

All patients that received at least 1 intrahepatic infusion of oxaliplatin

Reporting group values	Intent to treat		
Number of subjects	14		
Age categorical			
median age			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
median age			
Units: years median full range (min-max)	 52 36 to 67		
Gender categorical			
female only			
Units: Subjects			
Female Male	14 0		

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description:	
single arm study	
Subject analysis set title	Intent to treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients that received at least 1 intrahepatic infusion of oxaliplatin	

Primary: Overall reponse rate

End point title	Overall reponse rate[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	Arm 1	Intent to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: number of patients				
CR	4	4		
PR	3	3		
SD	5	5		
PD	2	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	Arm 1	Intent to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: months				
median (full range (min-max))	10.8 (8.0 to 13.6)	10.8 (8.0 to 13.6)		

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	Arm 1	Intent to treat		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: months				
median (full range (min-max))	44.7 (22.0 to 67.4)	44.7 (22.0 to 67.4)		

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	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	0		
Vascular disorders			
Thrombosis	Additional description: Portal thrombosis		
subjects affected / exposed	1 / 14 (7.14%)		
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	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 14 (42.86%)		
occurrences (all)	12		
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 14 (50.00%)		
occurrences (all)	21		
Alkaline phosphatase increased			

subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	8 / 14 (57.14%) 26 4 / 14 (28.57%) 21 6 / 14 (42.86%) 10 7 / 14 (50.00%) 19		
Nervous system disorders Peripheral motor neuropathy subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Dysaesthesia subjects affected / exposed occurrences (all)	 2 / 14 (14.29%) 3 6 / 14 (42.86%) 25 13 / 14 (92.86%) 122		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all)	 11 / 14 (78.57%) 72 2 / 14 (14.29%) 3 10 / 14 (71.43%) 28		
Immune system disorders Allergic reaction subjects affected / exposed occurrences (all)	 2 / 14 (14.29%) 2		
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	7 / 14 (50.00%)		
occurrences (all)	14		
Nausea			
subjects affected / exposed	12 / 14 (85.71%)		
occurrences (all)	71		
Diarrhoea			
subjects affected / exposed	8 / 14 (57.14%)		
occurrences (all)	22		
Stomatitis			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	10 / 14 (71.43%)		
occurrences (all)	86		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	15		
Arthralgia			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	11		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	6 / 14 (42.86%)		
occurrences (all)	14		

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