Clinical trial results:
Chemotherapy with gemcitabine, capecitabine, irinotecan and bevacizumab to patients with cholangiocarcinoma after progression on first line treatment.

Summary

EudraCT number	2013-001559-11
Trial protocol	DK
Global end of trial date	01 March 2017

Results information

Result version number	v1 (current)
This version publication date	02 January 2020
First version publication date	02 January 2020

Trial information

Trial identification

Sponsor protocol code	1312

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Herlev Ringvej 75, Herlev, Denmark, 2730
Public contact	Oncology Department, Herlev University Hospital, 45 36682329, Ole.larsen@regionh.dk
Scientific contact	Oncology Department, Herlev University Hospital, 45 36682329, Ole.larsen@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	31 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2017
Global end of trial reached?	Yes
Global end of trial date	01 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary endpoint

Progression free survival

Protection of trial subjects:

Standard Safety Monitoring

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 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: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	23
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was open from Nov 2013 til Jan 2016, all patients recruited at single site (Herlev University Hospital)

Pre-assignment

Screening details:

Patients with biliary tract cancer with progression from 1st-line treatment.

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	Trial Treatment

Arm description:

Capecitabine, Gemcitabine, Irinotecan and Bevacizumab

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:

650 mg/m2 twice a day, continuously

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

Dosage and administration details:

1000 mg/m2 every 2nd week

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

Dosage and administration details:

110 mg/m2 every 2nd week

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

Dosage and administration details:

5 mg/kg every 2nd week

Number of subjects in period 1	Trial Treatment
Started	48
Completed	37
Not completed	11
Lack of efficacy	11

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	48	48	
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	66		
full range (min-max)	34 to 83	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	22	22	

End points

End points reporting groups

Reporting group title	Trial Treatment

Reporting group description:

Capecitabine, Gemcitabine, Irinotecan and Bevacizumab

Primary: Progression free survival

End point title	Progression free survival[1]

End point description:

End point type	Primary

End point timeframe:

Time from treatment start to progression 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 phase II trial

End point values	Trial Treatment			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: months				
median (confidence interval 95%)	3.6 (3.0 to 4.2)			

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:

Time from treatment start to death (censoring at time of analysis)

End point values	Trial Treatment			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: months				
median (confidence interval 95%)	6.4 (3.8 to 8.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: treatment start to progression	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	3.1

Reporting groups	
Reporting group title	Trial Treatment
Reporting group description: Capecitabine, Gemcitabine, Irinotecan and Bevacizumab	

Serious adverse events	Trial Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 48 (39.58%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Contrast fluid in abdomen			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
arterial fibriliation			

subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
transient cerebral ischemia				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Malaise				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic failure				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ascites				
subjects affected / exposed	1 / 48 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Infection			
subjects affected / exposed	10 / 48 (20.83%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Trial Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 48 (100.00%)		
Investigations			
Thrombocytopenia			
subjects affected / exposed	7 / 48 (14.58%)		
occurrences (all)	7		
Neutropenia			
subjects affected / exposed	4 / 48 (8.33%)		
occurrences (all)	4		
liver enzymes increased			
subjects affected / exposed	6 / 48 (12.50%)		
occurrences (all)	6		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	12 / 48 (25.00%)		
occurrences (all)	12		
Thromboembolic event			
subjects affected / exposed	6 / 48 (12.50%)		
occurrences (all)	6		
Cardiac disorders			
Hypertension			
subjects affected / exposed	4 / 48 (8.33%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	30 / 48 (62.50%)		
occurrences (all)	30		
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	5 / 48 (10.42%) 5		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all)	 36 / 48 (75.00%) 36 15 / 48 (31.25%) 15 20 / 48 (41.67%) 20 21 / 48 (43.75%) 21		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	 8 / 48 (16.67%) 8		
Hepatobiliary disorders Cholangitis subjects affected / exposed occurrences (all)	 4 / 48 (8.33%) 4		
Skin and subcutaneous tissue disorders Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	 20 / 48 (41.67%) 20		

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/28930749