Clinical trial results:
Randomized phase II trial of combination chemotherapy with panitumumab or bevacizumab for patients with inoperable cholangiocarcinoma without KRAS mutations

Summary

EudraCT number	2010-020385-13
Trial protocol	DK SE
Global end of trial date	31 March 2016

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	52702928

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01206049
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vejle Hospital
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark,
Public contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.dk
Scientific contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.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 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2016
Global end of trial reached?	Yes
Global end of trial date	31 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the rate of progression free survival at 6 months in a comparable population of patients with inoperable cholangiocarcinoma treated with either GOC and panitumumab or GOC and bevacizumab.

Protection of trial subjects:

Antiemetics and other supportive treatment offered as necessary

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2010
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: 85
Country: Number of subjects enrolled	Sweden: 3
Worldwide total number of subjects	88
EEA total number of subjects	88

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)	38
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment from 15 October 2010 to 7 January 2015

Pre-assignment

Screening details:

Patients referred for first line treatment of inoperable cholangiocarcinoma without KRAS mutations.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A, panitumumab

Arm description:

Combination chemotherapy (institutional practice) + panitumumab

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

Dosage and administration details:

6 mg/kg day 1 every two weeks

Arm title	Arm B, Bevacizumab

Arm description:

Combination chemotherapy (institutional guidelines) + bevacizumab

Arm type	Experimental
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:

10 mg/kg every two weeks

Number of subjects in period 1	Arm A, panitumumab	Arm B, Bevacizumab
Started	45	43
Completed	45	43

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	88	88	
Age categorical 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)	38	38	
From 65-84 years	50	50	
85 years and over	0	0	
Age continuous Units: years			
median	66		
full range (min-max)	35 to 84	-	
Gender categorical Units: Subjects			
Female	55	55	
Male	33	33	

End points

End points reporting groups

Reporting group title	Arm A, panitumumab
Reporting group description: Combination chemotherapy (institutional practice) + panitumumab	
Reporting group title	Arm B, Bevacizumab
Reporting group description: Combination chemotherapy (institutional guidelines) + bevacizumab	

Primary: Fraction of patients alive and without progression at 6 months

End point title	Fraction of patients alive and without progression at 6 months
End point description:	
End point type	Primary
End point timeframe: 6 month after randomization	

End point values	Arm A, panitumumab	Arm B, Bevacizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	43		
Units: Fraction				
arithmetic mean (confidence interval 95%)	42 (29 to 58)	53 (40 to 70)		

Statistical analyses

Statistical analysis title	Simon's Two Stage
Statistical analysis description: Our study was based on Simon's two-stage design27 and two parallel Phase II trials with a primary endpoint of the fraction of PFS at 6 months. In both treatment arms, a PFS at 6 months of 65% was considered clinically relevant. The regimens were uninteresting if less than 45% of the patients reached a PFS of ≥6 months.	
Comparison groups	Arm A, panitumumab v Arm B, Bevacizumab
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Fisher exact

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Every four weeks

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Toxicity

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Focus was on SAE and the primary endpoint releated to efficacy. Standard drugs with well-known toxicity profile was used.

Serious adverse events	Toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 88 (53.41%)		
number of deaths (all causes)	87		
number of deaths resulting from adverse events	0		
Investigations			
Reduced general condition			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thromboembolic event, Pulmonary embolism			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			

subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ischemia cerebrovascular			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	7 / 88 (7.95%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Fatique			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Anal haemorrhage				
subjects affected / exposed	2 / 88 (2.27%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	7 / 88 (7.95%)			
occurrences causally related to treatment / all	3 / 10			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	3 / 88 (3.41%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	6 / 88 (6.82%)			
occurrences causally related to treatment / all	3 / 7			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal perforation				
subjects affected / exposed	2 / 88 (2.27%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Oral hemorrhage				
subjects affected / exposed	2 / 88 (2.27%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	3 / 88 (3.41%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			

Cough			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Metastatic spinal cord compression			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever			
subjects affected / exposed	19 / 88 (21.59%)		
occurrences causally related to treatment / all	18 / 37		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			

subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hyperkalemia			
subjects affected / exposed	1 / 88 (1.14%)		
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	Toxicity		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)		

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