Clinical trial results:
FOLFIRI + Erbitux versus alternating FOLFIRI + Erbitux/FOLFOX + Erbitux to patients with RAS wild type metastatic colorectalcancer

Summary

EudraCT number	2011-004188-65
Trial protocol	SE DK
Global end of trial date	29 March 2019

Results information

Result version number	v1 (current)
This version publication date	15 May 2021
First version publication date	15 May 2021

Trial information

Trial identification

Sponsor protocol code	KFE 11.17

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J. B. Winsløws Vej 4, entrance 140, basement, Odense C, Denmark, 5000
Public contact	Ida Coordt Elle, Odense University Hospital, +45 29335922, ida.coordt.elle@rsyd.dk
Scientific contact	Per Pfeiffer, Odense University Hospital, +45 26283844, per.pfeiffer@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	11 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Response rate (RR) estimated by the investigator.

Protection of trial subjects:

Pre-medication to minimize AEs was administered when appropriate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 49
Country: Number of subjects enrolled	Sweden: 41
Country: Number of subjects enrolled	Denmark: 83
Worldwide total number of subjects	173
EEA total number of subjects	173

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)	95
From 65 to 84 years	78
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between May 2012 and May 2018, 173 patients with RAS and BRAF wildtype metastatic colorectal cancer were included.

Pre-assignment

Screening details:

RAS and BRAF wildtype mCRC, non-resectable mCRC, 1st line therapy, PS 0-1

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	FOLFIRI + Cetuximab

Arm description:

FOLFIRI + Cetuximab every two weeks.

Arm type	Active comparator
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mg/m2 i.v. every two weeks.

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg/m2 i.v.

Investigational medicinal product name	5'-fluorouracil
Investigational medicinal product code	
Other name	5FU
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intravenous bolus use

Dosage and administration details:

400 mg/m2 i.v. bolus

Investigational medicinal product name	5'-fluorouracil
Investigational medicinal product code	
Other name	5FU
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

2400 mg/m2 i.v. 46 hours.

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

Dosage and administration details:
180 mg/m2 i.v.

Arm title	FOLFIRI + Cetuximab/FOLFOX + Cetuximab

Arm description:
Cetuximab every two weeks with alternating FOLFOX/FOLFIRI

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

Dosage and administration details:
500 mg/m2 i.v. every two weeks.

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
400 mg/m2 i.v.

Investigational medicinal product name	5'-fluorouracil
Investigational medicinal product code	
Other name	5FU
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intravenous bolus use

Dosage and administration details:
400 mg/m2 i.v. bolus

Investigational medicinal product name	5'-fluorouracil
Investigational medicinal product code	
Other name	5FU
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
2400 mg/m2 i.v. 46 hours.

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

Dosage and administration details:
180 mg/m2 i.v.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

85 mg/m2 i.v.

Number of subjects in period 1	FOLFIRI + Cetuximab	FOLFIRI + Cetuximab/FOLFOX + Cetuximab
Started	86	87
Completed	86	87

Baseline characteristics

Reporting groups	
Reporting group title	Trial period

Reporting group description: -

Reporting group values	Trial period	Total	
Number of subjects	173	173	
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)	95	95	
From 65-84 years	78	78	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	59	59	
Male	114	114	

End points

End points reporting groups

Reporting group title	FOLFIRI + Cetuximab
Reporting group description: FOLFIRI + Cetuximab every two weeks.	
Reporting group title	FOLFIRI + Cetuximab/FOLFOX + Cetuximab
Reporting group description: Cetuximab every two weeks with alternating FOLFOX/FOLFIRI	
Subject analysis set title	FOLFIRI + Cetuximab
Subject analysis set type	Full analysis
Subject analysis set description: Patients in the active comparator arm.	
Subject analysis set title	Cetuximab + FOLFOX/FOLFIRI
Subject analysis set type	Full analysis
Subject analysis set description: Patients in the experimental arm.	

Primary: Response rate

End point title	Response rate[1]
End point description:	
End point type	Primary
End point timeframe: 60 months	

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: Please see attached poster for additional analyses and information.

End point values	FOLFIRI + Cetuximab	FOLFIRI + Cetuximab/FOLFOX + Cetuximab	FOLFIRI + Cetuximab	Cetuximab + FOLFOX/FOLFIRI
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	86	87	86	87
Units: percent				
number (not applicable)	11.9	11.8	68	78

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 42 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	FOLFIRI + Cetuximab
Reporting group description: FOLFIRI + Cetuximab every two weeks.	
Reporting group title	FOLFIRI + Cetuximab/FOLFOX + Cetuximab
Reporting group description: Cetuximab every two weeks with alternating FOLFOX/FOLFIRI	

Serious adverse events	FOLFIRI + Cetuximab	FOLFIRI + Cetuximab/FOLFOX + Cetuximab	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 86 (3.49%)	1 / 87 (1.15%)	
number of deaths (all causes)	86	87	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 86 (3.49%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	FOLFIRI + Cetuximab	FOLFIRI + Cetuximab/FOLFOX + Cetuximab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 86 (100.00%)	87 / 87 (100.00%)	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	21 / 86 (24.42%)	21 / 87 (24.14%)	
occurrences (all)	21	21	
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	25 / 86 (29.07%)	37 / 87 (42.53%)	
occurrences (all)	25	37	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	19 / 86 (22.09%)	23 / 87 (26.44%)	
occurrences (all)	19	23	
Vomiting			
subjects affected / exposed	8 / 86 (9.30%)	7 / 87 (8.05%)	
occurrences (all)	8	7	
Diarrhoea			
subjects affected / exposed	22 / 86 (25.58%)	26 / 87 (29.89%)	
occurrences (all)	22	26	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	43 / 86 (50.00%)	50 / 87 (57.47%)	
occurrences (all)	43	50	

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