Clinical trial results:
FLOX + Erbitux. 1. line treatment to patients with metastatic colorectal cancer and wild type K-RAS tumor. A phase II study.

Summary

EudraCT number	2007-007834-21
Trial protocol	DK SE
Global end of trial date	01 May 2011

Results information

Result version number	v1 (current)
This version publication date	11 March 2021
First version publication date	11 March 2021
Summary attachment (see zip file)	ASCO 2012 NORDIC 7.5 poster (ASCO 2012 N75 PP Final LT.ppt)

Trial information

Trial identification

Sponsor protocol code	08.04

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 2, 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	28 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim was to complement the data of the NORDIC VII trial, arm C (Tveit et al, JCO 2012). Specifically, the goal was to substantiate efficacy and safety of biweekly cetuximab as maintenance therapy and to assess time to failure of strategy (TFS) as an end-point in maintenance therapy studies.

The NORDIC-7.5 trial was an investigator-initiated, multicenter single-arm phase II trial to evaluate intermittent chemotherapy and
cetuximab every second week14 followed by maintenance cetuximab every second week in first-line treatment of mCRC. Results of the NORDIC-7.5 should add to the aims of the NORDIC-VII trial12 to investigate how cetuximab every second week might safely and
conveniently be added to an intermittent treatment strategy.

Protection of trial subjects:

Pre-medication to minimize nausea, allergic reactions etc.
Use of heating pad when administering i.v. chemotherapy.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2010
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: 28
Country: Number of subjects enrolled	Sweden: 66
Country: Number of subjects enrolled	Denmark: 58
Worldwide total number of subjects	152
EEA total number of subjects	152

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)	130
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

July 2008-September 2010.

Pre-assignment

Screening details:

The inclusion criteria were as in NORDIC-VII except that only patients with KRAS (exon 2) wild type tumors were included.
Patients eligible for inclusion were 18 to 75 years of age, had previously untreated mCRC, at least 1 measurable lesion according
to RECIST criteria, and Performance status 0-2.

Period 1

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

Arms

Arm title	Experimental
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 8 courses of Nordic FLOX (oxaliplatin 85 mg/m(2) over 1 hour on day 1, and 5-fluorouracil 500 mg/m(2) as a bolus injection, followed 30 minutes later with bolus folinic acid 60 mg/m(2) on days 1 and 2). Cetuximab was administered every 2 weeks at a dose of 500 mg/m(2) for 16 weeks followed by cetuximab as maintenance therapy until disease progression.

Number of subjects in period 1	Experimental
Started	152
Completed	152

Baseline characteristics

Reporting groups

Reporting group title	Trial period

Reporting group description: -

Reporting group values	Trial period	Total	
Number of subjects	152	152	
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)	130	130	
From 65-84 years	22	22	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	61	61	
Male	91	91	

Subject analysis sets

Subject analysis set title	Patients
Subject analysis set type	Full analysis

Subject analysis set description:

All patients included in the trial.

Reporting group values	Patients		
Number of subjects	152		
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)	130		
From 65-84 years	22		
85 years and over	0		

Gender categorical Units: Subjects			
Female	61		
Male	91		

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description: -	
Subject analysis set title	Patients
Subject analysis set type	Full analysis
Subject analysis set description: All patients included in the trial.	

Primary: Response rate

End point title	Response rate[1]
End point description:	
End point type	Primary
End point timeframe: 24 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 publication for analysis.

End point values	Experimental	Patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	152	152		
Units: %				
number (confidence interval 95%)	62 (54 to 69)	62 (54 to 69)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Last drug administration + 30 days.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1
Reporting groups	
Reporting group title	Patients

Reporting group description: -

Serious adverse events	Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 152 (3.95%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	6 / 152 (3.95%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	152 / 152 (100.00%)		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	89 / 152 (58.55%)		
occurrences (all)	89		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	52 / 152 (34.21%)		
occurrences (all)	52		
Neutropenia			

subjects affected / exposed	60 / 152 (39.47%)		
occurrences (all)	60		
Thrombocytopenia			
subjects affected / exposed	40 / 152 (26.32%)		
occurrences (all)	40		
General disorders and administration site conditions			
Nail toxicity			
subjects affected / exposed	47 / 152 (30.92%)		
occurrences (all)	47		
Fatigue			
subjects affected / exposed	84 / 152 (55.26%)		
occurrences (all)	84		
Immune system disorders			
Allergic reaction to excipient			
subjects affected / exposed	18 / 152 (11.84%)		
occurrences (all)	18		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	59 / 152 (38.82%)		
occurrences (all)	59		
Nausea			
subjects affected / exposed	71 / 152 (46.71%)		
occurrences (all)	71		
Vomiting			
subjects affected / exposed	31 / 152 (20.39%)		
occurrences (all)	31		
Skin and subcutaneous tissue disorders			
Skin reaction			
subjects affected / exposed	91 / 152 (59.87%)		
occurrences (all)	91		
Infections and infestations			
Infection			
subjects affected / exposed	33 / 152 (21.71%)		
occurrences (all)	33		
Stomatitis			

subjects affected / exposed occurrences (all)	53 / 152 (34.87%) 53		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2008	1. New information about participating departments/investigators. 2. Elaboration of the section about biomarkers. 3. Definition of events not to be treated as SAEs. 4. Correction of dose modifications at skin reactions. 5. Sanofi Avensis deleted from the protocol. 6. In section 4.2.2 we added a possible correlation between AE grade and treatment efficacy, as well as a possible correlation between serum magnesium and treatment efficacy. 7. Grammatical/spelling errors corrected.
13 October 2009	Inclusion of 120 patients instead of the originally planned 86.
23 April 2010	Inclusion of 150 patients instead of 120.

Notes:

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/25956187