Clinical trial results:
A randomized investigation of side effects to FOLFOXIRI in combination with tocotrienol or placebo as first line treatment of metastatic colorectal cancer.

Summary

EudraCT number	2015-004850-17
Trial protocol	DK
Global end of trial date	27 March 2024

Results information

Result version number	v1 (current)
This version publication date	05 April 2025
First version publication date	05 April 2025

Trial information

Trial identification

Sponsor protocol code	FOLFOXIRI-Toco

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02705300
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vejle Hospital
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark, 7100
Public contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.dk
Scientific contact	Clinical Trial Unit, Vejle Hospital, 45 79406038, 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	15 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2024
Global end of trial reached?	Yes
Global end of trial date	27 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate toxicity of FOLFOXIRI in combination with tocotrienol or placebo as first line treatment of metastatic colorectal cancer

Protection of trial subjects:

Antiemetics and other supportive treatment as necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 May 2016
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: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	43
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment between May 2016 and December 2018.

Pre-assignment

Screening details:

Patients referred for first line treatment of metastatic colorectal cancer

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

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

Arm description:

FOLFOXIRI + tocotrienol

Arm type	Experimental
Investigational medicinal product name	Tocotrienol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

300 mg x 3 daily

Arm title	Arm B, placebo

Arm description:

FOLFOXIRI + placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

300 mg x 3 daily

Number of subjects in period 1	Arm A, tocotrienol	Arm B, placebo
Started	36	34
Completed	36	34

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	70	70	
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)	43	43	
From 65-84 years	27	27	
85 years and over	0	0	
Age continuous Units: years			
median	64		
full range (min-max)	40 to 75	-	
Gender categorical Units: Subjects			
Female	27	27	
Male	43	43	

End points

End points reporting groups	
Reporting group title	Arm A, tocotrienol
Reporting group description: FOLFOXIRI + tocotrienol	
Reporting group title	Arm B, placebo
Reporting group description: FOLFOXIRI + placebo	

Primary: Time to first serious adverse event	
End point title	Time to first serious adverse event
End point description:	
End point type	Primary
End point timeframe: From date of first treatment to first hospital admission	

End point values	Arm A, tocotrienol	Arm B, placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Months				
median (confidence interval 99%)	10 (1.87 to 99)	3.7 (1.93 to 99)		

Statistical analyses

Statistical analysis title	Randomized phase II screening trial statistics
Comparison groups	Arm A, tocotrienol v Arm B, placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Every two weeks

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Toxicity

Reporting group description: -

Serious adverse events	Toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 70 (77.14%)		
number of deaths (all causes)	62		
number of deaths resulting from adverse events	1		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Fatique				
subjects affected / exposed	3 / 70 (4.29%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anemia				
subjects affected / exposed	6 / 70 (8.57%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	8 / 70 (11.43%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	36 / 70 (51.43%)			
occurrences causally related to treatment / all	0 / 36			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Nausea				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrea				
subjects affected / exposed	4 / 70 (5.71%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			

Ileus			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolus			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences causally related to treatment / all	0 / 24		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
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	70 / 70 (100.00%)		
Vascular disorders			
Thrombocytopenia			
subjects affected / exposed	34 / 70 (48.57%)		
occurrences (all)	102		
Nervous system disorders			

Sensory neuropathy subjects affected / exposed occurrences (all) Motor neuropathy subjects affected / exposed occurrences (all)	 65 / 70 (92.86%) 216 19 / 70 (27.14%) 29		
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all) Fatique subjects affected / exposed occurrences (all)	 43 / 70 (61.43%) 73 60 / 70 (85.71%) 272		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 57 / 70 (81.43%) 192 13 / 70 (18.57%) 54		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrea subjects affected / exposed occurrences (all)	 52 / 70 (74.29%) 168 34 / 70 (48.57%) 82 37 / 70 (52.86%) 102 34 / 70 (48.57%) 72 50 / 70 (71.43%) 132		

Skin and subcutaneous tissue disorders PPE subjects affected / exposed occurrences (all)	 13 / 70 (18.57%) 33		

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