



Clinical trial results:

Repurposing disulfiram as treatment for metastatic colorectal cancer An investigator initiated clinical phase II trial

Summary

EudraCT number	2019-002748-25
Trial protocol	DK
Global end of trial date	05 August 2024

Results information

Result version number	v1 (current)
This version publication date	31 December 2025
First version publication date	31 December 2025
Summary attachment (see zip file)	Synopsis_EudraCT 2019-002748-25 (ICH E3 SYNOPSIS_EudraCT 2019-002748-25.pdf)

Trial information

Trial identification

Sponsor protocol code	KFE19.17
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Odense Universitetshospital (OUH)
Sponsor organisation address	Klørvænget 19, Odense C, Denmark, 5000
Public contact	PI Line Schmidt Tarpgaard, Department of Oncology, Odense Universitetshospital, +45 2251 1616, line.tarpgaard@rsyd.dk
Scientific contact	PI Line Schmidt Tarpgaard, Department of Oncology, Odense Universitetshospital, +45 2251 1616, line.tarpgaard@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 August 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2024
Global end of trial reached?	Yes
Global end of trial date	05 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective:

Disease-control rate (complete response, partial response and/or stable disease \geq 18 weeks
To investigate efficacy and safety of the treatment combination irinotecan, disulfiram and copper in patients with metastatic colorectal cancer having developed resistance to irinotecan.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and GCP; all patients provided written informed consent, and all data were handled confidentially and pseudonymised in compliance with applicable data protection legislation.

Background therapy:

All patients had previously received standard systemic therapy for metastatic colorectal cancer, including fluoropyrimidine-, oxaliplatin- and irinotecan-based regimens, with anti-EGFR or anti-VEGF antibodies when indicated. During the trial, patients were allowed best supportive care, but no concomitant anti-cancer systemic therapy was permitted.

Evidence for comparator:

Not applicable – this was a single-arm, non-randomised phase II trial with no active or placebo comparator.

Actual start date of recruitment	01 October 2019
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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	9
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place from January 2020 to May 2022. Patients were recruited consecutively at Odense University Hospital, during routine outpatient visits and screened for eligibility as they developed irinotecan-resistant metastatic colorectal cancer.

Pre-assignment

Screening details:

Patients were screened for eligibility during routine outpatient visits. The treating oncologist identified potential candidates with irinotecan-resistant metastatic colorectal cancer and verified inclusion and exclusion criteria before obtaining written informed consent.

Period 1

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

Arms

Arm title	Irinotecan + disulfiram + copper
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Arm description:

Single treatment arm. Patients receive irinotecan 250 mg/m² as a 30-minute intravenous infusion every 3 weeks, with the possibility of intra-patient dose escalation if tolerated. Oral disulfiram and copper are given concomitantly according to the phase II schedule (disulfiram 400 mg/day plus copper 2 mg/day around the irinotecan infusion, followed by a lower maintenance dose of disulfiram in the second week of each cycle). Treatment continues until disease progression, unacceptable toxicity or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

250 mg/m² administered as a 30-minute intravenous infusion on day 1. every 3 weeks

Investigational medicinal product name	Disulfiram
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg orally once daily on days 1–7, followed by 100–400 mg orally once daily on days 8–14 of each 21-day cycle, given concomitantly with irinotecan and copper.

Investigational medicinal product name	Kobber
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg orally once daily on days 1–14 of each 21-day cycle, given concomitantly with disulfiram.

Number of subjects in period 1	Irinotecan + disulfiram + copper
Started	22
No of patients started: 22	22
Completed	22

Baseline characteristics

Reporting groups

Reporting group title	Treatment period
Reporting group description:	
Single treatment arm: irinotecan 250 mg/m ² IV every 3 weeks with the option for intra-patient dose escalation, combined with continuous oral disulfiram and copper according to the phase II schedule.	

Reporting group values	Treatment period	Total	
Number of subjects	22	22	
Age categorical			
All patients were adults (N=22). Age was categorised as 18–64 years (n=9), 65–84 years (n=13) and ≥85 years (n=0).			
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)	0	0	
From 65-84 years	9	9	
85 years and over	13	13	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	13	13	

Subject analysis sets

Subject analysis set title	Intention-to-treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who signed informed consent and received at least one cycle of study treatment. This set was used for all efficacy analyses, including disease-control rate, progression-free survival and overall survival.

Reporting group values	Intention-to-treat population		
Number of subjects	22		
Age categorical			
All patients were adults (N=22). Age was categorised as 18–64 years (n=9), 65–84 years (n=13) and ≥85 years (n=0).			
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)	9		
From 65-84 years	13		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	9		
Male	13		

End points

End points reporting groups

Reporting group title	Irinotecan + disulfiram + copper
Reporting group description: Single treatment arm. Patients receive irinotecan 250 mg/m ² as a 30-minute intravenous infusion every 3 weeks, with the possibility of intra-patient dose escalation if tolerated. Oral disulfiram and copper are given concomitantly according to the phase II schedule (disulfiram 400 mg/day plus copper 2 mg/day around the irinotecan infusion, followed by a lower maintenance dose of disulfiram in the second week of each cycle). Treatment continues until disease progression, unacceptable toxicity or withdrawal of consent.	
Subject analysis set title	Intention-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients who signed informed consent and received at least one cycle of study treatment. This set was used for all efficacy analyses, including disease-control rate, progression-free survival and overall survival.	

Primary: Disease-control rate at 18 weeks

End point title	Disease-control rate at 18 weeks ^[1]
End point description: From date of inclusion until 18 weeks after inclusion.	
End point type	Primary
End point timeframe: From date of inclusion until 18 weeks after inclusion.	

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: This is a single-arm, non-comparative phase II trial. The primary end point (18-week disease-control rate) was summarised descriptively as a proportion in the intention-to-treat population, and no formal statistical hypothesis test was specified in the protocol.

End point values	Irinotecan + disulfiram + copper	Intention-to- treat population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	22	22 ^[2]		
Units: %	22	22		

Notes:

[2] - 22

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan–Meier analysis of progression free survival

End point title	Kaplan–Meier analysis of progression free survival
End point description:	
End point type	Secondary
End point timeframe: Progression-free survival (PFS) was analysed in the intention-to-treat population using the Kaplan–Meier method. PFS was defined as the time from inclusion to radiological or clinical disease progression or death from any cause, whichever occurred first.	

End point values	Intention-to-treat population			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: months				
median (confidence interval 95%)	2.3 (1.9 to 3.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan–Meier analysis of overall survival

End point title	Kaplan–Meier analysis of overall survival
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End point description:

End point type	Secondary
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End point timeframe:

Overall survival (OS) was analysed in the intention-to-treat population using the Kaplan–Meier method. OS was defined as the time from inclusion to death from any cause. Patients alive at the time of analysis were censored at the date they were last known

End point values	Intention-to-treat population			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: months				
median (confidence interval 95%)	6.5 (4.7 to 14.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first administration of irinotecan, disulfiram or copper until 28 days after the last dose of any study drug; serious adverse events considered related to study treatment were collected beyond this period if reported.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
Dictionary version	5

Reporting groups

Reporting group title	All treated patients
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Reporting group description:

Adverse events were collected from the first administration of study treatment until 28 days after the last dose of any study drug. Events were coded using MedDRA and graded according to NCI CTCAE version 5.0; relationship to study treatment was assessed by the investigator.

Serious adverse events	All treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All treated patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)		
Cardiac disorders			
Hypertension			
subjects affected / exposed	9 / 22 (40.91%)		
occurrences (all)	9		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 22 (86.36%)		
occurrences (all)	19		
Headache			

subjects affected / exposed occurrences (all)	10 / 22 (45.45%) 10		
Anorexia subjects affected / exposed occurrences (all)	9 / 22 (40.91%) 9		
Malaise subjects affected / exposed occurrences (all)	6 / 22 (27.27%) 6		
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	13 / 22 (59.09%) 13		
Vomiting subjects affected / exposed occurrences (all)	10 / 22 (45.45%) 10		
Diarrhoea subjects affected / exposed occurrences (all)	6 / 22 (27.27%) 6		
Abdominal pain subjects affected / exposed occurrences (all)	6 / 22 (27.27%) 6		
Constipation subjects affected / exposed occurrences (all)	12 / 22 (54.55%) 12		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 5		
Hepatobiliary disorders			
Increased ALAT subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Infections and infestations			
Infection subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2020	Due to unexpectedly high toxicity with continuous treatment with disulfiram and copper (in particular pronounced fatigue and neurological adverse events), the protocol was amended so that the dose and dosing schedule of disulfiram and copper were modified to a shorter, pulsed administration around the irinotecan infusion. The aim of this amendment was to reduce toxicity while maintaining the expected antitumour effect.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported