Clinical trial results:
Preoperative chemosensitivity testing as Predictor of Treatment benefit in Adjuvant stage III colon cancer (PEPITA)

Summary

EudraCT number	2009-011445-13
Trial protocol	BE
Global end of trial date	27 November 2023

Results information

Result version number	v1 (current)
This version publication date	18 April 2025
First version publication date	18 April 2025
Summary attachment (see zip file)	Final Report (2009-011445-13_Final_study_report.pdf)

Trial information

Trial identification

Sponsor protocol code	IJB-BGDO-2009-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00994864
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut Jules Bordet
Sponsor organisation address	Rue Meylemeersch 90, Anderlecht, Belgium, 1070
Public contact	Alain Hendlisz, Institut Jules Bordet, 32 2541 31 96, alain.hendlisz@gmail.com
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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	03 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Examine the predictive value of PET-assessed tumour FDG uptake response after one course of preoperative chemotherapy on the outcome of adjuvant therapy, measured by 3-year DFS.

Protection of trial subjects:

The protection of trial subjects was ensured through several measures. Eligibility criteria were designed to minimize the risk of severe adverse events, and subjects had the right to withdraw at any time. Investigators were required to make clinical decisions based on their best judgment. The study team verified data to guarantee that subjects' rights and well-being were safeguarded, that trial data was accurate and verifiable, and that the trial complied with ICH-GCP guidelines, regulatory requirements, and the study protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 January 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 235
Worldwide total number of subjects	235
EEA total number of subjects	235

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)	110

From 65 to 84 years	123
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study was opened in September 2009. The recruitment period started on 05/01/2010 and ended on 18/12/2017. The principal investigators were in charge of identifying patients susceptible to be eligible for the study. They were responsible for the eligibility assessment.

Pre-assignment

Screening details:

Screening was done by the local investigators. In case the coordinating centre received an inclusion form corresponding to a non-eligible patient, the study PI was informed.

Period 1

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

Blinding implementation details:

Roles blinded : Nuclearists in charge of assessing metabolic response.

Arms

Arm title	Overall trial

Arm description:

Overall trial

Arm type	Experimental
Investigational medicinal product name	FOLFOX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

The FOLFOX regimen was under the PI’s discretion.
The possible regimens in neoadjuvant and adjuvant settings were the same and were either:
FOLFOX4: A two-hour infusion of leucovorin 200 mg/m2 followed by a 400 mg/m² bolus 5-fluorouracil (5-FU) followed by a 22-hour infusion of 5-FU 600 mg/m2 given on two consecutive days plus a two-hour infusion of 85 mg/m² oxaliplatin, on day 1, simultaneously with leucovorin.
Or
Modified FOLFOX6: Oxaliplatin 85 mg/m2 intravenous (IV) infusion with leucovorin 400 mg/m2 over two hours, followed by 400 mg/m2 bolus 5-FU followed by an IV infusion of 5-FU 2400 mg/m2 for 46 hours

Number of subjects in period 1	Overall trial
Started	235
Completed	216
Not completed	19
Early AE before treatment	2
Second cancer	4
Stage IV clinically documented	2
Stage IV documented at baseline PET scan	9

Baseline hyperglycaemia	2

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	235	235	
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)	110	110	
From 65-84 years	123	123	
85 years and over	2	2	
Age continuous Units: years			
median	65		
inter-quartile range (Q1-Q3)	57 to 70	-	
Gender categorical Units: Subjects			
Female	95	95	
Male	140	140	
ECOG PS Units: Subjects			
Zero	209	209	
One	26	26	
Grade of differentiation Units: Subjects			
Well	68	68	
Moderately	116	116	
Poorly	15	15	
Unknown	36	36	

Subject analysis sets

Subject analysis set title	Patients evaluable (primary obj) - with metabolic response
Subject analysis set type	Per protocol

Subject analysis set description:

Patients evaluable for the primary objective : To validate the PET-assessed tumour FDG uptake response of the primary tumour after one course of preoperative chemotherapy as a predictor of outcome of adjuvant therapy, measured by 3-year DFS. The endpoint was calculated from the date of second PET scan until disease progression or death.

Subject analysis set title	Patients evaluable (primary obj) - without metabolic response

Subject analysis set type	Per protocol

Subject analysis set description:

Patients evaluable for the primary objective : To validate the PET-assessed tumour FDG uptake response of the primary tumour after one course of preoperative chemotherapy as a predictor of outcome of adjuvant therapy, measured by 3-year DFS. The endpoint was calculated from the date of second PET scan until disease progression or death.

Reporting group values	Patients evaluable (primary obj) - with metabolic response	Patients evaluable (primary obj) - without metabolic response	
Number of subjects	45	45	
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)	46		
From 65-84 years	44		
85 years and over	0		
Age continuous Units: years			
median	64		
inter-quartile range (Q1-Q3)	58 to 70		
Gender categorical Units: Subjects			
Female	26		
Male	64		
ECOG PS Units: Subjects			
Zero	76		
One	14		
Grade of differentiation Units: Subjects			
Well	31		
Moderately	45		
Poorly	4		
Unknown	10		

End points

End points reporting groups

Reporting group title	Overall trial

Reporting group description:

Overall trial

Subject analysis set title	Patients evaluable (primary obj) - with metabolic response
Subject analysis set type	Per protocol

Subject analysis set description:

Patients evaluable for the primary objective : To validate the PET-assessed tumour FDG uptake response of the primary tumour after one course of preoperative chemotherapy as a predictor of outcome of adjuvant therapy, measured by 3-year DFS. The endpoint was calculated from the date of second PET scan until disease progression or death.

Subject analysis set title	Patients evaluable (primary obj) - without metabolic response
Subject analysis set type	Per protocol

Subject analysis set description:

Patients evaluable for the primary objective : To validate the PET-assessed tumour FDG uptake response of the primary tumour after one course of preoperative chemotherapy as a predictor of outcome of adjuvant therapy, measured by 3-year DFS. The endpoint was calculated from the date of second PET scan until disease progression or death.

Primary: Primary endpoint

End point title	Primary endpoint

End point description:

Rate disease free at 36 months

End point type	Primary

End point timeframe:

The endpoint was calculated from the date of second PET scan until disease progression or death

End point values	Patients evaluable (primary obj) - with metabolic response	Patients evaluable (primary obj) - without metabolic response		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45	45		
Units: patients				
Number of patients disease free at 36 months	37	29		

Attachments (see zip file)	PEPITA_FSR_chart1.png

Statistical analyses

Statistical analysis title	Distribution of disease-free survival

Statistical analysis description:

Distribution of disease-free survival according to metabolic response. Distributions for each of the 2

groups defined according to the relative evolution of SUV between baseline and after 1 cycle of chemotherapy.

Comparison groups	Patients evaluable (primary obj) - without metabolic response v Patients evaluable (primary obj) - with metabolic response
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.06 [2]
Method	Unadjusted Cox regression analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.07
Variability estimate	Standard deviation
Dispersion value	0.31

Notes:

[1] - Per protocol, the goal of this analysis was to assess whether metabolic response could be associated with higher disease-free survival.

[2] - The primary analysis was unadjusted for other covariates

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The investigators had to report all adverse events (related and unrelated) on the CRF from the pre-operative chemotherapy until 30 days after the last administration of the adjuvant chemotherapy

Adverse event reporting additional description:

Exceptions to AE/SAE reporting. See full document for details

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Safety assessed on all patients who started treatment

Reporting group description:

All patients who did not withdraw consent and started treatment with the first chemotherapy cycle before surgery were analysed for adverse event. Seven of the included patients were not analysed (5 patients who withdrew consent and 2 patients who did not start treatment)

Serious adverse events	Safety assessed on all patients who started treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 233 (13.30%)		
number of deaths (all causes)	27		
number of deaths resulting from adverse events	2		
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anastomotic fistula			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anastomotic leak			

subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal anastomotic leak			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Phlebitis superficial			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Neutropenia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic haematoma				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Administration site inflammation				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Extravasation				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal hernia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Colitis ischaemic				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colonic fistula				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal fistula				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal ischaemia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				

subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritoneal necrosis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumatosis intestinalis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome				
subjects affected / exposed	3 / 233 (1.29%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Genital infection fungal			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonitis			

subjects affected / exposed	3 / 233 (1.29%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Prostatitis Escherichia coli			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Septic shock			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic abscess			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	Safety assessed on all patients who started treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	164 / 233 (70.39%)		
Investigations			
Weight decreased			
subjects affected / exposed	11 / 233 (4.72%)		
occurrences (all)	40		
Protein total			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	30		
White blood celle count decreased			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	17		
Blood magnesium decreased			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	9		
Weight increased			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	7		
Gamma-glutamyl transferase increased			
subjects affected / exposed	5 / 233 (2.15%)		
occurrences (all)	24		
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	35		
Alanine aminotransferase increased			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	23		
Blood bilirubin increased			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			

subjects affected / exposed	3 / 233 (1.29%)		
occurrences (all)	21		
Alkaline phosphatase increase			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	16		
White blood cell count increased			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	104 / 233 (44.64%)		
occurrences (all)	669		
Peripheral motor neuropathy			
subjects affected / exposed	14 / 233 (6.01%)		
occurrences (all)	47		
Paraesthesia			
subjects affected / exposed	10 / 233 (4.29%)		
occurrences (all)	46		
Dysgeusia			
subjects affected / exposed	12 / 233 (5.15%)		
occurrences (all)	39		
Headache			
subjects affected / exposed	10 / 233 (4.29%)		
occurrences (all)	17		
Taste disorder			
subjects affected / exposed	3 / 233 (1.29%)		
occurrences (all)	14		
Memory impariment			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	9		
Neuropathy peripheral			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	9		
Neurotoxicity			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	8		

Ageusia			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	5		
Balance disorder			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	52 / 233 (22.32%)		
occurrences (all)	311		
Anaemia			
subjects affected / exposed	42 / 233 (18.03%)		
occurrences (all)	210		
Neutropenia			
subjects affected / exposed	63 / 233 (27.04%)		
occurrences (all)	204		
Febrile neutropenia			
subjects affected / exposed	5 / 233 (2.15%)		
occurrences (all)	5		
Splenic haematoma			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	99 / 233 (42.49%)		
occurrences (all)	509		
Pyrexia			

subjects affected / exposed	6 / 233 (2.58%)		
occurrences (all)	9		
Asthenia			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	6		
Chest pain			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	3		
Influenza like illness			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	2		
Catheter site pain			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Extravasation			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Injection site inflammation			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	80 / 233 (34.33%)		
occurrences (all)	265		

Nausea				
subjects affected / exposed	78 / 233 (33.48%)			
occurrences (all)	231			
Stomatitis				
subjects affected / exposed	24 / 233 (10.30%)			
occurrences (all)	91			
Vomiting				
subjects affected / exposed	18 / 233 (7.73%)			
occurrences (all)	35			
Dyspepsia				
subjects affected / exposed	10 / 233 (4.29%)			
occurrences (all)	30			
Oesophagitis				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences (all)	13			
Abdominal pain				
subjects affected / exposed	10 / 233 (4.29%)			
occurrences (all)	12			
Abnormal faeces				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	10			
Dysphagia				
subjects affected / exposed	3 / 233 (1.29%)			
occurrences (all)	6			
Dry mouth				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	5			
Salivary gland pain				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	4			
Angular cheilitis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	3			
Aphthous ulcer				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences (all)	2			

Colitis				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences (all)	2			
Flatulence				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences (all)	2			
Gastrointestinal pain				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences (all)	2			
Rectal haemorrhage				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences (all)	2			
Abdominal discomfort				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Abdominal pain upper				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Barrett's oesophagus				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Colonic fistula				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Faecaloma				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Gastrointestinal disorder				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Gingival erythema				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			
Intestinal ischaemia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences (all)	1			

Mouth ulceration subjects affected / exposed occurrences (all)	1 / 233 (0.43%) 1		
Periodontal disease subjects affected / exposed occurrences (all)	1 / 233 (0.43%) 1		
Swollen tongue subjects affected / exposed occurrences (all)	1 / 233 (0.43%) 1		
Mucosal inflammation subjects affected / exposed occurrences (all)	4 / 233 (1.72%) 9		
Oedema subjects affected / exposed occurrences (all)	2 / 233 (0.86%) 2		
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	13 / 233 (5.58%) 54		
Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	6 / 233 (2.58%) 19		
Prurit subjects affected / exposed occurrences (all)	4 / 233 (1.72%) 8		
Rash subjects affected / exposed occurrences (all)	4 / 233 (1.72%) 7		
Erythema subjects affected / exposed occurrences (all)	2 / 233 (0.86%) 6		
Urticaria subjects affected / exposed occurrences (all)	2 / 233 (0.86%) 6		
Dry skin			

subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	4		
Eczema			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	3		
Photosensitivity reaction			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Skin disorder			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Skin hyperpigmentation			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	29 / 233 (12.45%)		
occurrences (all)	78		
Hypokalaemia			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	17		
Hypoalbuminaemia			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	10		
Hyperglyceamia			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	7		
Vitamin D deficiency			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	5		
Carbohydrate intolerance			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	4		
Hypomagnesaemia			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences (all)	1		

Hyponatraemia subjects affected / exposed occurrences (all)	1 / 233 (0.43%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2009	Modifications dates : SA1 - V1.1 27/10/2009 + EC 26/11/2009 The assessment of the predictive value of diffusion MRI on DFS has been dropped. Some minor changes in the study timeline have been made. The EuroQoL quality of life questionnaire will be additionally used. Antibodies for erbB-2 protein will also be used in circulating tumour cells and correlated with study outcomes. Addition of an exclusion criterion at screening Minor changes in study timelines Addition of Joint Study Management Team section Modification of section 18. Publication policy section: addition of the Publication Committee and authorship sections
19 March 2010	Modifications dates : SA2 - V2.0 18/01/2010 + EC 19/03/2010 + CA 09/02/2010 Update of study personnel on the first protocol page.
03 May 2011	Modifications dates : SA3 - V3.0 21/02/2011 + EC 03/05/2011 New version of the protocol but no modification in this protocol amendment (only a change of PI and addition of 2 new sites).
29 June 2011	Modifications dates : SA4 - V4.0 24/05/2011 + EC 29/06/2011 Suppression of the MRI sub-study FOLFOX regimen let at the investigator’s discretion
28 May 2013	Modifications dates : SA5 - V5.0 19/02/2013 + EC 28/05/2013 A new sentence clarifying the follow up for stage IV patients discovered at baseline or during the surgical removal of the primitive tumour has been added Change of end date of the trial due to lower than expected accrual Change of the patients’ number due to low accrual and longer follow up for these patients Adding of new translational research endpoints - To assess genomic rearrangements associated with response or resistance to FOLFOX treatment. - To identify an immunologic signature associated with metabolic tumour response to FOLFOX therapy.
03 October 2016	Modifications dates : SA8 - V6.0 05/09/2016 + EC 15/09/2016 + CA 03/10/2016 Increasing of sample size (but decrease of required number of events for the primary analysis) AE reporting section added Translational research corrections Administrative corrections
23 December 2019	Modifications dates : SA13 - V7.0 26/11/2019 + EC 23/12/2019 The translational part of the study was amended.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

There were no limitations and caveats.

Notes: