Clinical trial results:
An Open-Label, Multi-Center, Randomized Phase 1B/2 Study of PF-05212384 Plus 5-Fluorouracil-Leucovorin- Irinotecan (FOLFIRI) Versus Bevacizumab Plus FOLFIRI in Metastatic Colorectal Cancer

Summary

EudraCT number	2013-002096-18
Trial protocol	BE IT ES
Global end of trial date	05 August 2015

Results information

Result version number	v1 (current)
This version publication date	30 July 2016
First version publication date	30 July 2016

Trial information

Trial identification

Sponsor protocol code	B2151007

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClincialTrials.gov Call Center, Pfizer Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClincialTrials.gov Call Center, Pfizer Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

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	05 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2015
Global end of trial reached?	Yes
Global end of trial date	05 August 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives were to assess safety and to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of the combination of PF-05212384 plus Folfiri (Phase 1B) and to demonstrate that the combination of PF-05212384 plus FOLFIRI is superior to the combination of bevacizumab plus FOLFIRI in prolonging progression-free survival (PFS) in patients with metastatic colorectal cancer (mCRC) who have progressed on prior oxaliplatin-containing regimen (Phase 2).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2014
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	Spain: 2
Country: Number of subjects enrolled	United States: 13
Country: Number of subjects enrolled	Canada: 3
Worldwide total number of subjects	18
EEA total number of subjects	2

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)	12
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 190 patients were planned to be enrolled to the study.

Pre-assignment

Screening details:

Patients >=18 years were required to have histologically proven diagnosis of colorectal cancer and evidence of metastatic disease not amenable to potentially curative treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1

Arm description:

Subjects received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 150 mg/m^2, leucovorin 320 mg/m^2, 5- fluorouracil (FU) 1920 mg/m^2, and IV bolus of 5-FU 320 mg/m^2 on Days 1 and 15 of each cycle.

Arm type	Experimental
Investigational medicinal product name	PF-05212384 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of PF-05212384 90 mg weekly

Arm title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A

Arm description:

Subjects received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Arm type	Experimental
Investigational medicinal product name	PF-05212384 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of PF-05212384 90 mg weekly

Arm title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B

Arm description:

Subjects received intravenous (IV) infusion of PF-05212384 110 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Arm type	Experimental

Investigational medicinal product name	PF-05212384 110 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of PF-05212384 110 mg weekly

Arm title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3

Arm description:

Subjects received intravenous (IV) infusion of PF-05212384 130 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Arm type	Experimental
Investigational medicinal product name	PF-05212384 130 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of PF-05212384 130 mg weekly

Arm title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4

Arm description:

Subjects received intravenous (IV) infusion of PF-05212384 150 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Arm type	Experimental
Investigational medicinal product name	PF-05212384 150 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of PF-05212384 150 mg weekly

Number of subjects in period 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B
Started	3	4	3
Completed	3	3	3
Not completed	0	1	0
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	1	-
Unspecified	-	-	-

Number of subjects in period 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4
Started	5	3

Completed	1	1
Not completed	4	2
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	2
Unspecified	3	-

Baseline characteristics

Reporting groups	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 150 mg/m^2, leucovorin 320 mg/m^2, 5- fluorouracil (FU) 1920 mg/m^2, and IV bolus of 5-FU 320 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 110 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 130 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 150 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	

Reporting group values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B
Number of subjects	3	4	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	1
From 65-84 years	0	1	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	41.7	54.3	63.3
standard deviation	± 11.7	± 10.1	± 11.6
Gender, Male/Female Units: Participants			
FEMALE	1	3	0

MALE	2	1	3

Reporting group values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4	Total
Number of subjects	5	3	18
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	3	12
From 65-84 years	3	0	6
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	65.8	54.3	
standard deviation	± 9	± 5.5	-
Gender, Male/Female Units: Participants			
FEMALE	0	3	7
MALE	5	0	11

End points

End points reporting groups

Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 150 mg/m^2, leucovorin 320 mg/m^2, 5- fluorouracil (FU) 1920 mg/m^2, and IV bolus of 5-FU 320 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 110 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 130 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	
Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4
Reporting group description:	
Subjects received intravenous (IV) infusion of PF-05212384 150 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.	

Primary: Percentage of Subjects with Dose-Limiting Toxicities (DLTs) in First Cycle of Therapy

End point title	Percentage of Subjects with Dose-Limiting Toxicities (DLTs) in First Cycle of Therapy[1]
End point description:	
DLTs were classified according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 and defined as any of the following events judged to be attributed to the combination of PF-05212384 plus FOLFIRI: hematologic (febrile neutropenia or a sustained temperature >=38 degrees Celcius for >1 hour, grade >=3 neutropenic infection, grade 3 thrombocytopenia with bleeding, grade 4 thrombocytopenia); non-hematologic (grade >=2 pneumonitis, grade >=3 toxicities, toxicities which resulted in failure to deliver at least 75% of the planned total dose of PF-05212384 and/or 50% of the planned total dose of FOLFIRI during the first cycle, toxicities which resulted in delay of start of Cycle 2 by >2 weeks of scheduled day (Day 43 of study), Grade 3 QTc prolongation).	
End point type	Primary
End point timeframe:	
Day 1 up to Day 28	

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: No statistical analyses were planned for this primary endpoint. For the Phase 1b, the number of subjects with a DLT was summarized by dose level.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: percentage of subjects				
number (not applicable)	0	0	0	20

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage of subjects				
number (not applicable)	66.7			

Statistical analyses

No statistical analyses for this end point

Primary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)[2]

End point description:

Progression-free survival was the time from randomization date to the date of first documentation of progression or death due to any cause, whichever occurred first. Documentation of progression was by objective disease assessment as defined by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

End point type	Primary

End point timeframe:

Baseline (Day 1) up to disease progression or death whichever occurred first (up to 18 months)

Notes:

[2] - 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: PFS was only to be assessed in the Phase 2 portion of the study. As this study was terminated prior to the Phase 2 portion, there are no efficacy evaluations for Phase 2.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[3]	0[4]	0[5]	0[6]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[3] - Study was terminated prior to the Phase 2 portion and no data were collected.

[4] - Study was terminated prior to the Phase 2 portion and no data were collected.

[5] - Study was terminated prior to the Phase 2 portion and no data were collected.

[6] - Study was terminated prior to the Phase 2 portion and no data were collected.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[7] - Study was terminated prior to the Phase 2 portion and no data were collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Best Overall Response (Phase 1B)

End point title	Number of Subjects With Best Overall Response (Phase 1B)

End point description:

Best overall response is defined as the best response recorded from randomization (or first dose for patients in the Phase 1B) until disease progression, death, start of new anti-cancer treatment or end of study. The categories for best overall response include: complete response (CR) (complete disappearance of all target lesions with the exception of nodal disease and all target nodes must decrease to normal size (short axis <10 millimeters (mm)); partial response (PR) (at least a 30 percent (%) decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters); stable disease (SD) (not qualify for CR, PR or Progression); progressive disease (PD) (20% increase in the sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm); indeterminate (IND) (progression has not been documented).

End point type	Secondary

End point timeframe:

Every 8 weeks from Cycle 1 Day 1 until 28 days of last dose

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	4	3	5
Units: subjects				
PD	2	2	0	1
SD	0	2	2	3
PR	0	0	1	0
Indeterminant	0	0	0	1

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
PD	1			
SD	0			
PR	0			
Indeterminant	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with All Causalities Treatment-Emergent Adverse Events (AEs), Serious Adverse Events (SAEs), and Discontinuations by Relationship and Seriousness

End point title	Number of Subjects with All Causalities Treatment-Emergent Adverse Events (AEs), Serious Adverse Events (SAEs), and Discontinuations by Relationship and Seriousness

End point description:

An AE was any untoward medical occurrence without regard to causality in a subject who received study drug. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. An AE was considered treatment emergent if the event occurred for the first time after the start of study treatment and within 28 days after final dose of study treatment and was not seen prior to the start of treatment; or the event was seen prior to the start of treatment but increased in CTCAE version 4.0 grade after the start of study treatment and within 28 days after final dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline up to final study evaluation (within 28 days of last dose)

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects				
Number (#) of Subjects with AEs	3	4	3	5
# of Subjects with SAEs	0	0	2	2
# of Subjects with Grade 3 or 4 AEs	0	3	3	3
# of Subjects with Grade 5 AEs	0	0	0	0

# of Subjects D/C'd Study Due to AEs	0	0	0	0
# of Subjects D/C'd PF-05212384 Due to AEs	0	0	0	0
Number of Subjects D/C'd FOLFIRI Due to AEs	0	0	0	0

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
Number (#) of Subjects with AEs	3			
# of Subjects with SAEs	3			
# of Subjects with Grade 3 or 4 AEs	3			
# of Subjects with Grade 5 AEs	0			
# of Subjects D/C'd Study Due to AEs	0			
# of Subjects D/C'd PF-05212384 Due to AEs	1			
Number of Subjects D/C'd FOLFIRI Due to AEs	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with All Causalities AEs by System Organ Class (SOC)

End point title	Number of Subjects with All Causalities AEs by System Organ Class (SOC)

End point description:

An AE was any untoward medical occurrence without regard to causality in a subject who received study drug.

End point type	Secondary

End point timeframe:

Baseline up to final study evaluation (within 28 days of last dose)

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects				
Blood and lymphatic system disorders	0	2	0	1

Eye disorders	0	1	0	0
Gastrointestinal disorders	3	4	3	5
General disorders & administration site conditions	2	2	2	4
Hepatobiliary disorders	0	0	0	1
Immune system disorders	0	0	1	0
Infections and infestations	1	3	1	1
Injury, poisoning and procedural complications	0	3	0	0
Investigations	1	4	1	2
Metabolism and nutrition disorders	2	3	1	3
Musculoskeletal and connective tissue disorders	1	4	1	1
Nervous system disorders	0	2	3	2
Psychiatric disorders	3	2	0	0
Renal and urinary disorders	0	2	0	1
Respiratory, thoracic and mediastinal disorders	1	1	3	3
Skin and subcutaneous tissue disorders	1	3	2	2
Vascular disorders	0	1	1	1

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
Blood and lymphatic system disorders	0			
Eye disorders	1			
Gastrointestinal disorders	3			
General disorders & administration site conditions	2			
Hepatobiliary disorders	0			
Immune system disorders	0			
Infections and infestations	1			
Injury, poisoning and procedural complications	0			
Investigations	2			
Metabolism and nutrition disorders	2			
Musculoskeletal and connective tissue disorders	1			
Nervous system disorders	1			
Psychiatric disorders	2			
Renal and urinary disorders	0			
Respiratory, thoracic and mediastinal disorders	1			
Skin and subcutaneous tissue disorders	3			
Vascular disorders	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent AEs by Worst On-Study Grade

End point title	Number of Subjects with Treatment-Emergent AEs by Worst On-Study Grade

End point description:

An AE was any untoward medical occurrence without regard to causality in a subject who received study drug. AEs were defined according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 criteria.

End point type	Secondary

End point timeframe:

Baseline up to final study evaluation (within 28 days of last dose)

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects				
Any AEs, Grade 1	0	0	0	1
Any AEs, Grade 2	3	1	0	1
Any AEs, Grade 3	0	3	3	2
Any AEs, Grade 4	0	0	0	1
Any AEs, Grade 5	0	0	0	0
Any AEs, total	3	4	3	5

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
Any AEs, Grade 1	0			
Any AEs, Grade 2	0			
Any AEs, Grade 3	3			
Any AEs, Grade 4	0			

Any AEs, Grade 5	0			
Any AEs, total	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Hematological Test Abnormalities

End point title	Number of Subjects with Hematological Test Abnormalities

End point description:

Number of subjects with NCI CTCAE version 4.0 grade 1 to 4 hematological test abnormalities.

End point type	Secondary

End point timeframe:

Day 1 and Day 15 of each cycle

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects				
Anemia	3	4	3	5
Hemoglobin increased	0	0	0	0
Lymphocyte count increased	0	1	0	0
Lymphopenia	2	2	2	3
Neutrophils (Absolute)	0	4	2	2
Platelets	0	2	0	2
White blood cells	1	3	3	3

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: subjects				
Anemia	2			
Hemoglobin increased	0			
Lymphocyte count increased	0			
Lymphopenia	0			
Neutrophils (Absolute)	2			
Platelets	0			

White blood cells	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Coagulation Test Abnormalities

End point title	Number of Subjects with Coagulation Test Abnormalities

End point description:

Number of subjects with NCI CTCAE version 4.0 grade 1 to 4 Coagulation test abnormalities.

End point type	Secondary

End point timeframe:

Day 1 and Day 15 of Cycle 1, Day 1 of Cycle 2 and subsequent cycles

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects				
Partial thromboplastin time (N=3, 2, 3, 5, 2)	1	0	1	2
Prothrombin time (PT) (N=3, 1,2, 5, 1)	1	0	2	1
PT INR (N=3, 2, 3, 5, 2)	1	0	2	0

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
Partial thromboplastin time (N=3, 2, 3, 5, 2)	2			
Prothrombin time (PT) (N=3, 1,2, 5, 1)	1			
PT INR (N=3, 2, 3, 5, 2)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Chemistry Test Abnormalities

End point title	Number of Subjects with Chemistry Test Abnormalities
End point description:	
Number of subjects with NCI CTCAE version 4.0 grade 1 to 4 Chemistry test abnormalities.	
End point type	Secondary
End point timeframe:	
Day 1 and Day 15 of each cycle	

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	3	5
Units: subjects				
Alanine aminotransferase	0	1	1	3
Alkaline phosphatase	3	2	0	3
Aspartate aminotransferase	2	2	2	4
Bilirubin (total)	0	2	0	1
Creatinine	1	2	3	4
Hyperglycemia	2	3	1	5
Hypermagnesemia	0	0	1	0
Hypoalbuminemia	2	2	0	3
Hypocalcemia	0	0	0	2
Hypoglycemia	1	0	0	0
Hypokalemia	2	2	1	0
Hypomagnesemia	0	1	1	1
Hyponatremia	3	2	1	4
Hypohphosphatemia	1	0	0	1
Hyperkalemia	0	1	0	0

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: subjects				
Alanine aminotransferase	1			
Alkaline phosphatase	1			
Aspartate aminotransferase	1			
Bilirubin (total)	0			
Creatinine	2			
Hyperglycemia	2			

Hypermagnesemia	0			
Hypoalbuminemia	1			
Hypocalcemia	0			
Hypoglycemia	0			
Hypokalemia	1			
Hypomagnesemia	0			
Hyponatremia	0			
Hypohphosphatemia	0			
Hyperkalemia	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Urinalysis Test Abnormalities

End point title	Number of Subjects with Urinalysis Test Abnormalities
End point description:	
Number of subjects with NCI CTCAE version 4.0 grade 1 to 4 Urinalysis test abnormalities.	
End point type	Secondary
End point timeframe:	
Day 1 and Day 15 of Cycle 1, Day 1 of Cycle 2 and subsequent cycles	

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects	2	1	1	2

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: subjects	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax): PF-05212384, Irinotecan, and Fluorouracil

End point title	Maximum Observed Plasma Concentration (Cmax): PF-05212384, Irinotecan, and Fluorouracil

End point description:

Maximum Plasma Concentration of PF-05212384, Irinotecan, and Fluorouracil

End point type	Secondary

End point timeframe:

PF-05212384: Cycle 1 Day 3. Irinotecan: Cycle 1 Day 1. Fluorouracil: Cycle 1 Day 1.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: nanogram (ng)/milliliter (mL)				
geometric mean (geometric coefficient of variation)				
PF-05212384 (n=3,4,2,5,3)	8245 (± 25)	6554 (± 66)	33470 (± 99999)	8222 (± 35)
Irinotecan (n=3,4,1,5,3)	1782 (± 4)	1323 (± 43)	1550 (± 99999)	1585 (± 17)
Fluorouracil (n=3,4,1,4,3)	18390 (± 85)	18950 (± 41)	44000 (± 99999)	26790 (± 18)

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: nanogram (ng)/milliliter (mL)				
geometric mean (geometric coefficient of variation)				
PF-05212384 (n=3,4,2,5,3)	10250 (± 11)			
Irinotecan (n=3,4,1,5,3)	1755 (± 6)			
Fluorouracil (n=3,4,1,4,3)	26920 (± 3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax): PF-05212384, Irinotecan, and Fluorouracil

End point title	Time to Reach Maximum Observed Plasma Concentration

	(Tmax): PF-05212384, Irinotecan, and Fluorouracil

End point description:

Time to Reach Maximum Observed Plasma Concentration of PF-05212384, Irinotecan, and Fluorouracil

End point type	Secondary

End point timeframe:

PF-05212384: Cycle 1 Day 3. Irinotecan: Cycle 1 Day 1. Fluorouracil: Cycle 1 Day 1.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: hour (hr)				
median (full range (min-max))				
PF-05212384 (n=3,4,2,5,3)	0.5 (0.45 to 0.5)	0.55 (0.45 to 0.617)	0.5 (0.5 to 0.5)	0.5 (0.383 to 0.5)
Irinotecan (n=3,4,1,5,3)	2.02 (1.98 to 2.02)	2.04 (2 to 2.15)	1.95 (1.95 to 1.95)	2.25 (1.98 to 2.5)
Fluorouracil (n=3,4,1,4,3)	0.083 (0.033 to 0.15)	0.167 (0.167 to 0.233)	0.083 (0.083 to 0.083)	0.125 (0.067 to 0.25)

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hour (hr)				
median (full range (min-max))				
PF-05212384 (n=3,4,2,5,3)	0.5 (0.483 to 1.03)			
Irinotecan (n=3,4,1,5,3)	2 (1.98 to 2.02)			
Fluorouracil (n=3,4,1,4,3)	0.15 (0.15 to 46.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast): PF-05212384, and Irinotecan

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast): PF-05212384, and Irinotecan

End point description:

Area Under the Curve From Time Zero to Last Quantifiable Concentration of PF-05212384 and Irinotecan

End point type	Secondary

End point timeframe:

PF-05212384: Cycle 1 Day 3. Irinotecan: Cycle 1 Day 1.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
PF-05212384 (n=3,4,1,5,3)	11460 (± 22)	9129 (± 33)	30700 (± 99999)	13570 (± 40)
Irinotecan (n=3,4,1,4,3)	12510 (± 8)	9164 (± 53)	8050 (± 99999)	10340 (± 15)

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
PF-05212384 (n=3,4,1,5,3)	14760 (± 34)			
Irinotecan (n=3,4,1,4,3)	11030 (± 28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Profile From Time 0 Extrapolated to Infinite Time (AUCinf): PF-05212384 and Irinotecan

End point title	Area Under the Plasma Concentration-Time Profile From Time 0 Extrapolated to Infinite Time (AUCinf): PF-05212384 and Irinotecan

End point description:

Area Under the Plasma Concentration-Time Profile From Time 0 Extrapolated to Infinite Time of PF-05212384 and Irinotecan

End point type	Secondary

End point timeframe:

PF-05212384: Cycle 1 Day 3. Irinotecan: Cycle 1 Day 1. Fluorouracil: Cycle 1 Day 1.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	1	5
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
PF-05212384	11820 (± 22)	9289 (± 32)	30900 (± 99999)	13830 (± 40)
Irinotecan	13120 (± 10)	9709 (± 54)	8350 (± 99999)	10900 (± 16)

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
PF-05212384	15270 (± 34)			
Irinotecan	11560 (± 29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-Life (t1/2): PF-05212384 and Irinotecan

End point title	Terminal Elimination Half-Life (t1/2): PF-05212384 and Irinotecan

End point description:

Terminal Elimination Half-Life of PF-05212384 and Irinotecan

End point type	Secondary

End point timeframe:

PF-05212384: Cycle 1 Day 3. Irinotecan: Cycle 1 Day 1.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	1	5
Units: hour				
arithmetic mean (standard deviation)				
PF-05212384	33.63 (± 1.3503)	27.9 (± 3.3695)	29.2 (± 99999)	29.18 (± 6.9909)
Irinotecan	5.127 (± 0.70692)	5.533 (± 1.1621)	4.97 (± 99999)	5.36 (± 0.40817)

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hour				
arithmetic mean (standard deviation)				
PF-05212384	36.97 (± 1.9035)			
Irinotecan	5.107 (± 0.40427)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Meeting Maximum Post-Baseline QTc Interval Values

End point title	Number of Subjects Meeting Maximum Post-Baseline QTc Interval Values

End point description:

Criteria for corrected QT interval using Fridericia's formula (QTcF) meeting potential clinical concern included: an absolute value >=450 - <480 msec, >=480-<500 msec, >500 msec; an absolute change 30 - <60, >=60 msec.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Day 1, and Cycle 2 Day 2

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	5
Units: subjects				
QTcF Interval <450 msec	3	4	3	3
QTcF Interval 450-480 msec	0	0	0	2
QTcF Interval >480-500 msec	0	0	0	0
QTcF Interval >500 msec	0	0	0	0
QTcF Interval increase =< 30 msec	2	3	3	4
QTcF Interval increase >30 to =<60 msec	1	1	0	1
QTcF Interval increase >60	0	0	0	0

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
QTcF Interval <450 msec	3			
QTcF Interval 450-480 msec	0			
QTcF Interval >480-500 msec	0			
QTcF Interval >500 msec	0			
QTcF Interval increase =< 30 msec	3			
QTcF Interval increase >30 to =<60 msec	0			
QTcF Interval increase >60	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Expression of Gene Sequences or Gene Amplications in Biopsied Tumor Tissue

End point title	Number of Subjects with Expression of Gene Sequences or Gene Amplications in Biopsied Tumor Tissue

End point description:

Biomarker evaluation were to be performed on fresh biopsies, as well as on archival biopsies collected during the study. Samples were to be analyzed for biomarkers indicative of pathway modulation or for genetic markers correlated to drug sensitivity.

End point type	Secondary

End point timeframe:

Baseline and Cycle 2 Day 17

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	0[9]	0[10]	0[11]
Units: subjects				

Notes:

[8] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

[9] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

[10] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

[11] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: subjects				

Notes:

[12] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Gene and/or Protein Expression Biomarkers Relating to the PI3K and/or mTOR Pathway Activation in Biopsied Tumor Tissue

End point title	Number of Subjects with Gene and/or Protein Expression Biomarkers Relating to the PI3K and/or mTOR Pathway Activation in Biopsied Tumor Tissue

End point description:

Biomarker evaluation were to be performed on fresh biopsies, as well as on archival biopsies collected during the study. Samples were to be analyzed for biomarkers indicative of pathway modulation or for genetic markers correlated to drug sensitivity.

End point type	Secondary

End point timeframe:

Baseline and Cycle 2 Day 17

End point values	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan +Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[13]	0[14]	0[15]	0[16]

Units: subjects				

Notes:

[13] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

[14] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

[15] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

[16] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[17]			
Units: subjects				

Notes:

[17] - Not summarized. Paired fresh tumor biopsies were only done in 1 subject.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Best Overall Response (Phase 2)

End point title	Number of Subjects With Best Overall Response (Phase 2)

End point description:

Best overall response is defined as the best response recorded from randomization (or first dose for patients in the Phase 1B) until disease progression, death, start of new anti-cancer treatment or end of study. The categories for best overall response include: complete response (CR) (complete disappearance of all target lesions with the exception of nodal disease and all target nodes must decrease to normal size (short axis <10 millimeters (mm)); partial response (PR) (at least a 30 percent (%) decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters); stable disease (SD) (not qualify for CR, PR or Progression); progressive disease (PD) (20% increase in the sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm); indeterminate (IND) (progression has not been documented).

End point type	Secondary

End point timeframe:

Day 1 up to Day 28

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	0[19]	0[20]	0[21]
Units: subjects				

Notes:

[18] - Study was terminated prior to the Phase 2 portion and no data were collected.

[19] - Study was terminated prior to the Phase 2 portion and no data were collected.

[20] - Study was terminated prior to the Phase 2 portion and no data were collected.

[21] - Study was terminated prior to the Phase 2 portion and no data were collected.

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[22]			
Units: subjects				

Notes:

[22] - Study was terminated prior to the Phase 2 portion and no data were collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (Phase 2)

End point title	Duration of Response (Phase 2)

End point description:

Duration of response is the time from first documentation of CR or PR to date of first documentation of objective progression or death.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[23]	0[24]	0[25]	0[26]
Units: weeks				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[23] - Study was terminated prior to the Phase 2 portion and no data were collected.

[24] - Study was terminated prior to the Phase 2 portion and no data were collected.

[25] - Study was terminated prior to the Phase 2 portion and no data were collected.

[26] - Study was terminated prior to the Phase 2 portion and no data were collected.

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[27]			
Units: weeks				
median (confidence interval 95%)	(to)			

Notes:

[27] - Study was terminated prior to the Phase 2 portion and no data were collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Phase 2)

End point title	Overall Survival (Phase 2)

End point description:

Overall survival is the time from randomization date to date of death due to any cause.

End point type	Secondary

End point timeframe:

Day 1 up to Day 28

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[28]	0[29]	0[30]	0[31]
Units: Weeks				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[28] - Study was terminated prior to the Phase 2 portion and no data were collected.

[29] - Study was terminated prior to the Phase 2 portion and no data were collected.

[30] - Study was terminated prior to the Phase 2 portion and no data were collected.

[31] - Study was terminated prior to the Phase 2 portion and no data were collected.

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[32]			
Units: Weeks				
median (confidence interval 95%)	(to)			

Notes:

[32] - Study was terminated prior to the Phase 2 portion and no data were collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Evidence of Pathway Signaling Related Genes and/or Proteins in Biopsied Tumor Tissue (Phase 2)

End point title	Number of Subjects with Evidence of Pathway Signaling Related Genes and/or Proteins in Biopsied Tumor Tissue (Phase 2)

End point description:

Biomarker evaluation were to be performed on these fresh biopsies, as well as on archival biopsies collected during the study. Samples were to be analyzed for biomarkers indicative of pathway modulation or for genetic markers correlated to drug sensitivity.

End point type	Secondary

End point timeframe:

Baseline and Cycle 2 Day 17

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[33]	0[34]	0[35]	0[36]
Units: subjects				

Notes:

[33] - Phase 2 only and no data were collected for Phase 2.

[34] - Phase 2 only and no data were collected for Phase 2.

[35] - Phase 2 only and no data were collected for Phase 2.

[36] - Phase 2 only and no data were collected for Phase 2.

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[37]			
Units: subjects				

Notes:

[37] - Phase 2 only and no data were collected for Phase 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Cancer Therapy-Colorectal (FACT-C) (Phase 2)

End point title	Change from Baseline in Functional Assessment of Cancer Therapy-Colorectal (FACT-C) (Phase 2)

End point description:

The FACT-C was to assess health-related quality of life and colorectal cancer (CRC)-related symptoms. It includes a total of 36 items, which are summarized into 6 subscales: physical well-being (7 items), functional well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), CRC subscale (9 items) which addresses a subset of CRC concerns such as diarrhea.

End point type	Secondary

End point timeframe:

Day 1 of each cycle

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[38]	0[39]	0[40]	0[41]
Units: units on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[38] - Study was terminated prior to the Phase 2 portion and no data were collected.

[39] - Study was terminated prior to the Phase 2 portion and no data were collected.

[40] - Study was terminated prior to the Phase 2 portion and no data were collected.

[41] - Study was terminated prior to the Phase 2 portion and no data were collected.

End point values	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4			
Subject group type	Reporting group			
Number of subjects analysed	0[42]			
Units: units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[42] - Study was terminated prior to the Phase 2 portion and no data were collected.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to end of treatment

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1

Reporting group description:

Participants received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 150 mg/m^2, leucovorin 320 mg/m^2, 5- fluorouracil (FU) 1920 mg/m^2, and IV bolus of 5-FU 320 mg/m^2 on Days 1 and 15 of each cycle.

Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A

Reporting group description:

Participants received intravenous (IV) infusion of PF-05212384 90 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B

Reporting group description:

Participants received intravenous (IV) infusion of PF-05212384 110 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3

Reporting group description:

Participants received intravenous (IV) infusion of PF-05212384 130 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Reporting group title	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4

Reporting group description:

Participants received intravenous (IV) infusion of PF-05212384 150 mg weekly and IV infusions of irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5- fluorouracil (FU) 2400 mg/m^2, and IV bolus of 5-FU 400 mg/m^2 on Days 1 and 15 of each cycle.

Serious adverse events	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	2 / 3 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Transient ischaemic attack			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Periorbital infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	3 / 3 (100.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Anal fistula			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Periorbital infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 1	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2A	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 2B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	4 / 4 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	2 / 3 (66.67%)
occurrences (all)	1	8	11
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2

Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	2 / 3 (66.67%)
occurrences (all)	0	2	2
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	2
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	4
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinus disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Psychiatric disorders			

Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Derailment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 3 (66.67%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood albumin decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	4 / 4 (100.00%)	1 / 3 (33.33%)
occurrences (all)	0	8	3
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	111	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wound dehiscence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	5	1
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	3 / 4 (75.00%)	3 / 3 (100.00%)
occurrences (all)	1	4	10
Dry mouth			

subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Impaired gastric emptying			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lip disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lip swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	2	4	4
Oral dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Paraesthesia oral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	3	3
Tongue coated			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	3	1
Rash generalised			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 4 (75.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Periorbital infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Pharyngitis streptococcal			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 3	PF-05212384+5-FU+Irinotecan+Leucovorin:Dose Level 4	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	3 / 3 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Flushing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Early satiety			

subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 5 (40.00%)	1 / 3 (33.33%)	
occurrences (all)	5	3	
Mucosal inflammation			
subjects affected / exposed	1 / 5 (20.00%)	1 / 3 (33.33%)	
occurrences (all)	1	3	
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hiccups			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Sinus disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Derailment			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood albumin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	3	
Platelet count decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	2 / 5 (40.00%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Wound dehiscence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Disturbance in attention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Head discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Headache			

subjects affected / exposed	1 / 5 (20.00%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Lethargy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 3 (33.33%)	
occurrences (all)	1	3	
Cheilitis			

subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)		
occurrences (all)	1	0		
Constipation				
subjects affected / exposed	1 / 5 (20.00%)	2 / 3 (66.67%)		
occurrences (all)	1	2		
Diarrhoea				
subjects affected / exposed	3 / 5 (60.00%)	3 / 3 (100.00%)		
occurrences (all)	3	5		
Dry mouth				
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Dyspepsia				
subjects affected / exposed	2 / 5 (40.00%)	0 / 3 (0.00%)		
occurrences (all)	2	0		
Dysphagia				
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)		
occurrences (all)	1	0		
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Haematochezia				
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)		
occurrences (all)	1	0		
Impaired gastric emptying				
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)		
occurrences (all)	1	0		
Lip disorder				
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Lip swelling				
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Nausea				
subjects affected / exposed	3 / 5 (60.00%)	3 / 3 (100.00%)		
occurrences (all)	3	5		
Oral dysaesthesia				

subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Oral pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Paraesthesia oral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Proctalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	3 / 5 (60.00%)	2 / 3 (66.67%)	
occurrences (all)	10	2	
Tongue coated			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	2 / 5 (40.00%)	2 / 3 (66.67%)	
occurrences (all)	2	4	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 3 (66.67%)	
occurrences (all)	1	2	
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Night sweats			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Rash generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Renal failure			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Periorbital infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	3 / 5 (60.00%)	1 / 3 (33.33%)	
occurrences (all)	4	2	
Dehydration			
subjects affected / exposed	2 / 5 (40.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Hyperglycaemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2013	To incorporate starting dose infromation for the Phase 1b and LIC 5-FU colus infusion and adjust the top dose for the 5-FU continuous infusion in the FOLFIRI regimen.
20 February 2014	This amendment incorporates all revisions to date, including amendments made at the request of country health authorities, instituional review boards/external review boards.

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.

As this study was terminated due to Pfizer portfolio prioritization prior to the Phase 2 portion, there are no efficacy evaluations for Phase 2.

Notes: