Clinical trial results:
A Phase II, Multicenter, Open-Label, Randomized Study Evaluating the Efficacy and Safety of FOLFIRI + MEHD7945A versus FOLFIRI + Cetuximab in Second Line in Patients with KRAS Wild-Type Metastatic Colorectal Cancer

Summary

EudraCT number	2011-005547-27
Trial protocol	DE GB BE ES IT
Global end of trial date	26 November 2014

Results information

Result version number	v1 (current)
This version publication date	26 March 2016
First version publication date	26 March 2016

Trial information

Trial identification

Sponsor protocol code	GO28074

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01652482
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse124, Basel, Switzerland, CH-4070
Public contact	F.Hoffmann-LaRocheAG, Roche Trial Information Hotline, +41 616878333, global.trial_information@roche.com
Scientific contact	F.Hoffmann-LaRocheAG, Roche Trial Information Hotline, +41 616878333, global.trial_information@roche.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	26 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of folinic acid-fluorouracil-Irinotecan (FOLFIRI) + MEHD7945A versus FOLFIRI + cetuximab in participants with KRAS wild-type metastatic colorectal cancer (mCRC) and in participants with KRAS wild - type mCRC whose tumors expressed low levels of Human Epidermal Growth Factor Receptor 3 (HER3).

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) and investigators were trained according to applicable Sponsor standard operating procedures (SOPs).

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	22 October 2012
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: 19
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	New Zealand: 22
Country: Number of subjects enrolled	Romania: 3
Worldwide total number of subjects	134
EEA total number of subjects	63

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)	74
From 65 to 84 years	59
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participant screening was conducted from Day -14 to Day -1.

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	FOLFIRI+ MEHD7945A

Arm description:

Participants received MEHD7945A 1100 milligrams (mg) intravenous (IV) infusion every two weeks (14-day cycle) until unacceptable toxicity, documented disease progression or death. Participants also received 5 fluorouracil (5-FU) 400 milligrams per square meter (mg/m^2) as an IV bolus and then 5-FU 2400 mg/m^2 as a continuous IV infusion, irinotecan 180 milligrams per square meter (mg/m^2) IV infusion concurrently (using a y connector) with leucovorin 400 mg/m^2 (racemic form) or 200 mg/m^2 (L-isomer form) IV infusion (FOLFIRI) on Day 1 of 14-day continuous cycles.

Arm type	Experimental
Investigational medicinal product name	MEHD7945A
Investigational medicinal product code	RO5541078
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg IV infusion every two weeks

Arm title	FOLFIRI + Cetuximab

Arm description:

All participants received cetuximab 400 mg/m^2 initial dose followed by 250 mg/m^2 IV infusion once a week until unacceptable toxicity, documented disease progression or death. Participants also received FOLFIRI on Day 1 of 14-day continuous cycles.

Arm type	Active comparator
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	Erbitux
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg/m^2 initial dose followed by 250 mg/m^2 IV infusion once a week

Number of subjects in period 1	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab
Started	68	66
Completed	0	0
Not completed	68	66
Consent withdrawn by subject	5	3
Randomized but not enrolled	-	1
Death	34	33
Study termination by sponsor	28	29
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	FOLFIRI+ MEHD7945A
Reporting group description:	
Participants received MEHD7945A 1100 milligrams (mg) intravenous (IV) infusion every two weeks (14-day cycle) until unacceptable toxicity, documented disease progression or death. Participants also received 5 fluorouracil (5-FU) 400 milligrams per square meter (mg/m^2) as an IV bolus and then 5-FU 2400 mg/m^2 as a continuous IV infusion, irinotecan 180 milligrams per square meter (mg/m^2) IV infusion concurrently (using a y connector) with leucovorin 400 mg/m^2 (racemic form) or 200 mg/m^2 (L-isomer form) IV infusion (FOLFIRI) on Day 1 of 14-day continuous cycles.	
Reporting group title	FOLFIRI + Cetuximab
Reporting group description:	
All participants received cetuximab 400 mg/m^2 initial dose followed by 250 mg/m^2 IV infusion once a week until unacceptable toxicity, documented disease progression or death. Participants also received FOLFIRI on Day 1 of 14-day continuous cycles.	

Reporting group values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab	Total
Number of subjects	68	66	134
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.9	61.8	
standard deviation	± 12.4	± 12.5	-
Gender categorical Units: Subjects			
Female	32	19	51
Male	36	46	82
Not recorded	0	1	1

End points

End points reporting groups

Reporting group title	FOLFIRI+ MEHD7945A

Reporting group description:

Participants received MEHD7945A 1100 milligrams (mg) intravenous (IV) infusion every two weeks (14-day cycle) until unacceptable toxicity, documented disease progression or death. Participants also received 5 fluorouracil (5-FU) 400 milligrams per square meter (mg/m^2) as an IV bolus and then 5-FU 2400 mg/m^2 as a continuous IV infusion, irinotecan 180 milligrams per square meter (mg/m^2) IV infusion concurrently (using a y connector) with leucovorin 400 mg/m^2 (racemic form) or 200 mg/m^2 (L-isomer form) IV infusion (FOLFIRI) on Day 1 of 14-day continuous cycles.

Reporting group title	FOLFIRI + Cetuximab

Reporting group description:

All participants received cetuximab 400 mg/m^2 initial dose followed by 250 mg/m^2 IV infusion once a week until unacceptable toxicity, documented disease progression or death. Participants also received FOLFIRI on Day 1 of 14-day continuous cycles.

Primary: Percentage of Participants With Disease Progression or Death

End point title	Percentage of Participants With Disease Progression or Death[1]

End point description:

Tumor assessments were performed according to modified Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). Progressive Disease (PD) was defined as at least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including Baseline. In addition, the sum must also have shown an absolute increase of 5 millimeters (mm). The appearance of one or more new lesions was also considered progression. Analysis of primary endpoints was performed on All randomized participants defined as all participants who were randomized. Participants were grouped according to the treatment to which they were randomized.

End point type	Primary

End point timeframe:

Baseline and every 8 weeks until disease progression, unacceptable toxicity or death until 29 September 2014 (up to approximately 23 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint. The statistical analysis for progression-free survival is reported in next end point.

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	66		
Units: percentage of participants				
number (not applicable)	79.4	75.8		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Disease Progression or Death in the HER3-Low Group

End point title	Percentage of Participants With Disease Progression or Death in

	the HER3-Low Group[2]

End point description:

HER3 is a protein encoded by the ERBB3 gene. HER3-low participants were identified based on the median ERBB3 expression. Tumor assessments were performed according to modified RECIST v1.1. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including Baseline. In addition, the sum must also have shown an absolute increase of 5 mm. The appearance of one or more new lesions was also considered progression. Analysis of primary endpoints was performed on All randomized participants defined as all participants who were randomized. Participants were grouped according to the treatment to which they were randomized within the HER3-low expressing group.

End point type	Primary

End point timeframe:

Baseline and every 8 weeks until disease progression, unacceptable toxicity or death until 29 September 2014 (up to approximately 23 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: No statistical analysis was planned for this endpoint.

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	27		
Units: percentage of participants				
number (not applicable)	77.78	85.19		

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Progression Free Survival (PFS)

End point title	Duration of Progression Free Survival (PFS)

End point description:

PFS was defined as the time from randomization to documented disease progression assessed by the investigator or death, whichever occurred first. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including Baseline. In addition the sum must also have shown an absolute increase of 5 mm. The appearance of one or more new lesions was also considered progression. Analysis of primary endpoints was performed on all randomized participants and on those with HER3-low tumors.

End point type	Primary

End point timeframe:

Baseline and every 8 weeks until disease progression, unacceptable toxicity or death until Study termination on 29 September 2014 (up to approximately 23 months)

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	66		
Units: months				
median (confidence interval 90%)	5.4 (3.8 to 7.5)	5.6 (5.3 to 7.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratification variables included time between last 1L oxaliplatin-containing chemotherapy and disease progression less than or equal to 6 months versus greater than 6 months (<= 6 mo vs > 6 mo) and prior bevacizumab therapy (yes vs no). Hazard ratios were estimated by Cox regression.

Comparison groups	FOLFIRI+ MEHD7945A v FOLFIRI + Cetuximab
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.198
Method	Logrank
Parameter estimate	Log hazard ratio
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.93
upper limit	1.82

Primary: Duration of PFS in HER3-Low Group

End point title	Duration of PFS in HER3-Low Group[3]

End point description:

HER3 is a protein encoded by the ERBB3 gene. HER3-low participants were identified based on the median ERBB3 expression. PFS was defined as the time from randomization to documented disease progression assessed by the investigator or death, whichever occurred first. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including Baseline. In addition the sum must also have shown an absolute increase of 5 mm. The appearance of one or more new lesions was also considered progression. Analysis of primary endpoints was performed on all randomized participants and on those with HER3-low tumors.

End point type	Primary

End point timeframe:

Baseline and every 8 weeks until disease progression, unacceptable toxicity or death until Study termination on 29 September 2014 (up to approximately 23 months)

Notes:

[3] - 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 analysis was planned for this endpoint.

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	27		
Units: months				
median (confidence interval 90%)	3.9 (3.7 to 7.5)	5.5 (3.9 to 5.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Objective Response (Complete Response [CR] or Partial Response [PR])

End point title	Percentage of Participants with Objective Response (Complete Response [CR] or Partial Response [PR])

End point description:

Objective response is defined as a CR or PR, objective responses had to be confirmed ≥ 4 weeks after the initial response. Tumor assessments were performed according to modified RECIST v1.1. CR: Disappearance of all target lesions, and any pathological lymph nodes (whether target or non-target) must have shown a reduction in the short axis to less than (<)10 mm. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Analysis of secondary outcomes was performed on all randomized participants.

End point type	Secondary

End point timeframe:

Baseline and every 8 weeks until Disease progression, Unacceptable Toxicity or Death until Study termination on 29 September 2014 (up to approximately 23 months)

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	66		
Units: percentage of partticipants				
number (confidence interval 90%)	16.2 (9.9 to 24.38)	31.8 (22.41 to 42.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response

End point title	Duration of Objective Response

End point description:

Duration of objective response was defined as the time from the first occurrence of a documented objective response (CR or PR) to documented disease progression or death, whichever occurred first. Analysis was performed on all randomized participants. Time to event was determined using Kaplan-Meier estimates. Confidence Interval (CI) for median was computed using the method of Brookmeyer and Crowley.

End point type	Secondary

End point timeframe:

Baseline and every 8 weeks until Disease progression, Unacceptable Toxicity or Death until Study termination on 29 September 2014 (up to approximately 23 months)

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	21		
Units: months				
median (confidence interval 90%)	7.1 (5.5 to 9.1)	9 (5.6 to 11)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Stratification variables include time between last 1L oxaliplatin-containing chemotherapy and disease progression (<= 6 months vs > 6 months and prior bevacizumab therapy (yes vs no). Hazard ratios were estimated by Cox regression.

Comparison groups	FOLFIRI+ MEHD7945A v FOLFIRI + Cetuximab
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2185
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8
upper limit	4.22

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died

End point description:

Overall survival was defined as the time from randomization to death by any cause.

End point type	Secondary

End point timeframe:

Baseline and every 8 weeks until Death (up to approximately 25 months)

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	66		
Units: percentage of participants				
number (not applicable)	50	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Survival

End point title	Duration of Overall Survival

End point description:

Overall survival was defined as the time from randomization to death by any cause. Time to event was estimated using Kaplan-Meier estimates. The number "99999" in data field signifies not estimated (NE) data, as the upper limit of 90% CI was not reached in the Kaplan-Meier analysis.

End point type	Secondary

End point timeframe:

Baseline and every 8 weeks until Death (up to approximately 25 months)

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	66		
Units: months				
median (confidence interval 90%)	14 (11 to 20.3)	12.4 (10.2 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Stratification variables include time between last 1L oxaliplatin-containing chemotherapy and disease progression (<= 6 months vs > 6 months and prior bevacizumab therapy (yes vs no). Hazard ratios were estimated by Cox regression.

Comparison groups	FOLFIRI + Cetuximab v FOLFIRI+ MEHD7945A
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9009
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.64
upper limit	1.46

Secondary: Minimum (Cmin) and Maximum (Cmax) Serum Concentrations of MEHD7945A

End point title	Minimum (Cmin) and Maximum (Cmax) Serum Concentrations of MEHD7945A[4]

End point description:

Cmax was defined as the maximum or "peak" concentration of MEHD7945A observed after its administration (30 minutes post dose); Cmin was the minimum or "trough" concentration of MEHD7945A (pre dose).

End point type	Secondary

End point timeframe:

Pre dose and 30 minutes post dose on Cycle 1 Day 1, Pre dose on Cycle 10 Day 1

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to be reported only in those participants who received MEHD7945A.

End point values	FOLFIRI+ MEHD7945A			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)				
Cycle 1 Cmin	39.466 (± 43.66)			
Cycle 1 Cmax	299.028 (± 66.319)			
Cycle 10 Cmin	75.965 (± 42.619)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with anti-MEHD7945A antibodies

End point title	Percentage of participants with anti-MEHD7945A antibodies

End point description:

Anti-therapeutic antibodies (ATAs) directed against MEHD7945A were analyzed in serum samples obtained at baseline, before dosing, and at multiple time points (Day 1 of Cycles 1, 4, 8, and at treatment completion) after dosing. Number (n) = number of evaluable participants for the specified category.

End point type	Secondary

End point timeframe:

Baseline; Post Baseline (assessed at Day 1 of Cycles 1, 4 and 8 and at study termination on 29 September 2014 [up to approximately 23 months])

End point values	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	17		
Units: percentage of participants				
number (not applicable)				
Baseline (n=66,4)	0	0		
Post-baseline treatment induced ATA (n=59,17)	0	0		
Post-baseline treatment enhanced ATA (n=59,17)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were recorded from the date of randomization until 45 days after study termination (up to approximately 25 months).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	FOLFIRI+ MEHD7945A

Reporting group description:

Participants received MEHD7945A 1100 mg IV infusion every two weeks (14-day cycle) until unacceptable toxicity, documented disease progression or death. Participants also received 5-FU 400 mg/m^2 as an IV bolus and then 5-FU 2400 mg/m^2 as a continuous IV infusion, irinotecan 180 mg/m^2 IV infusion concurrently (using a y connector) with leucovorin 400 mg/m^2 (racemic form) or 200 mg/m^2 (L-isomer form) IV infusion (FOLFIRI) on Day 1 of 14-day continuous cycles. AEs were reported for Safety Evaluable population which included all participants who were randomized and received any amount of study medication.

Reporting group title	FOLFIRI + Cetuximab

Reporting group description:

All participants received cetuximab 400 mg/m^2 initial dose followed by 250 mg/m^2 IV infusion once a week until unacceptable toxicity, documented disease progression or death. Participants also received FOLFIRI on Day 1 of 14-day continuous cycles. AEs were reported for Safety Evaluable population which included all participants who were randomized and received any amount of study medication.

Serious adverse events	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 67 (35.82%)	23 / 63 (36.51%)	
number of deaths (all causes)	34	33	
number of deaths resulting from adverse events			
Vascular disorders			
Vena cava thrombosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Device occlusion			

subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 67 (1.49%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 67 (1.49%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 67 (7.46%)	4 / 63 (6.35%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis in device			

subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 67 (1.49%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	4 / 67 (5.97%)	3 / 63 (4.76%)	
occurrences causally related to treatment / all	3 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriospasm coronary			

subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsions			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 67 (2.99%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Corneal perforation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 67 (1.49%)	4 / 63 (6.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 67 (8.96%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	7 / 7	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 67 (1.49%)	3 / 63 (4.76%)	
occurrences causally related to treatment / all	1 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal perforation			

subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric haematoma			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 67 (2.99%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 67 (0.00%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	3 / 67 (4.48%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Palmar- plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis acneiform			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Obstructive uropathy			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postrenal failure			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 67 (2.99%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site cellulitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 67 (0.00%)	3 / 63 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nail bed infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 67 (1.49%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 67 (1.49%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter infection			

subjects affected / exposed	0 / 67 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 67 (1.49%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 63 (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	FOLFIRI+ MEHD7945A	FOLFIRI + Cetuximab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 67 (100.00%)	63 / 63 (100.00%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	43 / 67 (64.18%)	37 / 63 (58.73%)	
occurrences (all)	64	88	
Mucosal inflammation			
subjects affected / exposed	26 / 67 (38.81%)	23 / 63 (36.51%)	
occurrences (all)	49	40	
Asthenia			
subjects affected / exposed	10 / 67 (14.93%)	9 / 63 (14.29%)	
occurrences (all)	18	18	
Pyrexia			

subjects affected / exposed	6 / 67 (8.96%)	11 / 63 (17.46%)	
occurrences (all)	8	15	
Oedema peripheral			
subjects affected / exposed	5 / 67 (7.46%)	6 / 63 (9.52%)	
occurrences (all)	5	7	
Chest pain			
subjects affected / exposed	0 / 67 (0.00%)	4 / 63 (6.35%)	
occurrences (all)	0	4	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	13 / 67 (19.40%)	8 / 63 (12.70%)	
occurrences (all)	16	10	
Dyspnoea			
subjects affected / exposed	8 / 67 (11.94%)	5 / 63 (7.94%)	
occurrences (all)	8	8	
Cough			
subjects affected / exposed	2 / 67 (2.99%)	12 / 63 (19.05%)	
occurrences (all)	2	13	
Dysphonia			
subjects affected / exposed	6 / 67 (8.96%)	2 / 63 (3.17%)	
occurrences (all)	6	2	
Oropharyngeal pain			
subjects affected / exposed	4 / 67 (5.97%)	3 / 63 (4.76%)	
occurrences (all)	4	3	
Pulmonary embolism			
subjects affected / exposed	3 / 67 (4.48%)	4 / 63 (6.35%)	
occurrences (all)	3	4	
Rhinorrhoea			
subjects affected / exposed	5 / 67 (7.46%)	1 / 63 (1.59%)	
occurrences (all)	5	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 67 (5.97%)	11 / 63 (17.46%)	
occurrences (all)	4	12	
Investigations			

Weight decreased			
subjects affected / exposed	8 / 67 (11.94%)	5 / 63 (7.94%)	
occurrences (all)	11	5	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 67 (1.49%)	4 / 63 (6.35%)	
occurrences (all)	1	4	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	11 / 67 (16.42%)	6 / 63 (9.52%)	
occurrences (all)	15	6	
Headache			
subjects affected / exposed	10 / 67 (14.93%)	6 / 63 (9.52%)	
occurrences (all)	10	6	
Dizziness			
subjects affected / exposed	4 / 67 (5.97%)	3 / 63 (4.76%)	
occurrences (all)	8	3	
Neuropathy peripheral			
subjects affected / exposed	3 / 67 (4.48%)	4 / 63 (6.35%)	
occurrences (all)	3	6	
Paraesthesia			
subjects affected / exposed	2 / 67 (2.99%)	4 / 63 (6.35%)	
occurrences (all)	2	6	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	17 / 67 (25.37%)	21 / 63 (33.33%)	
occurrences (all)	27	41	
Anaemia			
subjects affected / exposed	9 / 67 (13.43%)	11 / 63 (17.46%)	
occurrences (all)	14	14	
Leukopenia			
subjects affected / exposed	1 / 67 (1.49%)	5 / 63 (7.94%)	
occurrences (all)	1	9	
Thrombocytopenia			
subjects affected / exposed	1 / 67 (1.49%)	4 / 63 (6.35%)	
occurrences (all)	1	5	
Eye disorders			

Vision blurred			
subjects affected / exposed	5 / 67 (7.46%)	1 / 63 (1.59%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	60 / 67 (89.55%)	42 / 63 (66.67%)	
occurrences (all)	145	107	
Nausea			
subjects affected / exposed	33 / 67 (49.25%)	32 / 63 (50.79%)	
occurrences (all)	49	61	
Stomatitis			
subjects affected / exposed	21 / 67 (31.34%)	26 / 63 (41.27%)	
occurrences (all)	34	44	
Vomiting			
subjects affected / exposed	16 / 67 (23.88%)	11 / 63 (17.46%)	
occurrences (all)	23	27	
Abdominal pain			
subjects affected / exposed	12 / 67 (17.91%)	21 / 63 (33.33%)	
occurrences (all)	18	26	
Constipation			
subjects affected / exposed	6 / 67 (8.96%)	16 / 63 (25.40%)	
occurrences (all)	6	26	
Gastroesophageal reflux disease			
subjects affected / exposed	10 / 67 (14.93%)	6 / 63 (9.52%)	
occurrences (all)	11	7	
Mouth ulceration			
subjects affected / exposed	4 / 67 (5.97%)	4 / 63 (6.35%)	
occurrences (all)	8	8	
Oral pain			
subjects affected / exposed	7 / 67 (10.45%)	1 / 63 (1.59%)	
occurrences (all)	8	4	
Abdominal pain upper			
subjects affected / exposed	5 / 67 (7.46%)	6 / 63 (9.52%)	
occurrences (all)	5	6	
Dry mouth			

subjects affected / exposed	4 / 67 (5.97%)	4 / 63 (6.35%)	
occurrences (all)	6	4	
Haemorrhoids			
subjects affected / exposed	6 / 67 (8.96%)	4 / 63 (6.35%)	
occurrences (all)	6	4	
Rectal haemorrhage			
subjects affected / exposed	3 / 67 (4.48%)	5 / 63 (7.94%)	
occurrences (all)	3	7	
Cheilitis			
subjects affected / exposed	4 / 67 (5.97%)	1 / 63 (1.59%)	
occurrences (all)	4	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	26 / 67 (38.81%)	32 / 63 (50.79%)	
occurrences (all)	48	68	
Dermatitis acneiform			
subjects affected / exposed	24 / 67 (35.82%)	22 / 63 (34.92%)	
occurrences (all)	42	57	
Alopecia			
subjects affected / exposed	18 / 67 (26.87%)	22 / 63 (34.92%)	
occurrences (all)	19	24	
Dry skin			
subjects affected / exposed	17 / 67 (25.37%)	13 / 63 (20.63%)	
occurrences (all)	19	19	
Skin fissures			
subjects affected / exposed	10 / 67 (14.93%)	12 / 63 (19.05%)	
occurrences (all)	16	18	
Palmar- plantar erythrodysaesthesia syndrome			
subjects affected / exposed	12 / 67 (17.91%)	13 / 63 (20.63%)	
occurrences (all)	13	20	
Pruritus			
subjects affected / exposed	6 / 67 (8.96%)	7 / 63 (11.11%)	
occurrences (all)	9	7	
Rash maculo-papular			

subjects affected / exposed	6 / 67 (8.96%)	4 / 63 (6.35%)	
occurrences (all)	6	5	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 67 (1.49%)	4 / 63 (6.35%)	
occurrences (all)	1	5	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 67 (11.94%)	6 / 63 (9.52%)	
occurrences (all)	10	7	
Arthralgia			
subjects affected / exposed	6 / 67 (8.96%)	3 / 63 (4.76%)	
occurrences (all)	9	3	
Pain in extremity			
subjects affected / exposed	2 / 67 (2.99%)	6 / 63 (9.52%)	
occurrences (all)	2	8	
Muscle spasms			
subjects affected / exposed	4 / 67 (5.97%)	2 / 63 (3.17%)	
occurrences (all)	5	2	
Infections and infestations			
Paronychia			
subjects affected / exposed	21 / 67 (31.34%)	18 / 63 (28.57%)	
occurrences (all)	39	34	
Folliculitis			
subjects affected / exposed	1 / 67 (1.49%)	8 / 63 (12.70%)	
occurrences (all)	1	12	
Urinary tract infection			
subjects affected / exposed	7 / 67 (10.45%)	6 / 63 (9.52%)	
occurrences (all)	7	6	
Conjunctivitis			
subjects affected / exposed	5 / 67 (7.46%)	4 / 63 (6.35%)	
occurrences (all)	7	5	
Localised infection			
subjects affected / exposed	0 / 67 (0.00%)	4 / 63 (6.35%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			

Hypokalaemia			
subjects affected / exposed	25 / 67 (37.31%)	13 / 63 (20.63%)	
occurrences (all)	35	21	
Decreased appetite			
subjects affected / exposed	16 / 67 (23.88%)	14 / 63 (22.22%)	
occurrences (all)	23	23	
Hypomagnesaemia			
subjects affected / exposed	12 / 67 (17.91%)	23 / 63 (36.51%)	
occurrences (all)	12	23	
Dehydration			
subjects affected / exposed	9 / 67 (13.43%)	4 / 63 (6.35%)	
occurrences (all)	10	9	
Hypophosphataemia			
subjects affected / exposed	4 / 67 (5.97%)	4 / 63 (6.35%)	
occurrences (all)	7	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2012	The protocol was updated to include two interim safety analyses by the internal monitoring committee (IMC) instead of one interim analysis. The duration of safety monitoring (including reporting of AEs and SAEs) was extended from 30 days to 45 days. Changes were made to Inclusion and Exclusion criteria.
26 April 2013	Incidence of ATA to MEHD7945A was added as a safety outcome measure. Electrocardiogram (ECG) was added as a safety assessment. The follow-up period for reporting pregnancy was updated to 45 days. Clarification was added to the dosage modification of 1) MEHD7945A, 2) cetuximab and 3) folinic acid

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.

The study was terminated on 29 September 2014, following the primary analysis, which indicated that treatment with MEHD7945A FOLFIRI did not improve PFS compared with FOLFIRI cetuximab, by investigator assessment.

Notes: