ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 06/18/2014

ClinicalTrials.gov ID: NCT00439517

Study Identification

Unique Protocol ID:	EMR200025-001
Brief Title:	Study to Evaluate the Efficacy and Safety of FOLFOX-4 Plus Cetuximab Versus UFOX Plus Cetuximab. (FUTURE)
Official Title:	A Randomized, Open-label Phase II Study Evaluating the Efficacy and Safety of FOLFOX-4 Plus Cetuximab Versus UFOX Plus Cetuximab as First-line Therapy in Subjects With Metastatic Colorectal Cancer.
Secondary IDs:	

Study Status

Record Verification:	June 2014
Overall Status:	Completed
Study Start:	February 2007
Primary Completion:	June 2009 [Actual]
Study Completion:	May 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 18-036 ex 06/07 Board Name: Med. Universität Graz Board Affiliation: Ethikkommission Phone: +43 316 385 3928 Email: ethikkommission@meduni-graz.at
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	Germany: BfArM (Bundesinstitut für Arzneimittel und Medizinprodukte)

Study Description

Brief Summary:	This is an exploratory study to compare activity and safety in 400 patients with previously untreated metastatic carcinoma of the colon treated with UFOX (a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin, Folinic Acid) plus Cetuximab or FOLFOX-4 (a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid) plus Cetuximab)
Detailed Description:	

Conditions

Conditions:	Previously Untreated Metastatic Colorectal Cancer
Keywords:	Cancer Colorectal Metastatic Untreated

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 302 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 UFOX + Cetuximab	Drug: UFOX + Cetuximab · Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) · Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) · Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 · Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
Active Comparator: 2 FOLFOX4 + Cetuximab	Drug: FOLFOX4 + Cetuximab · Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) · Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) · 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 · Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria

- Signed written informed consent
- Inpatient or outpatient ≥ 18 years of age
- Diagnosis of histologically confirmed adenocarcinoma of the colon or rectum
- First occurrence of metastatic disease (not curatively resectable)
- Presence of at least one lesion measurable uni dimensionally by computerised tomography (CT) scan or magnetic resonance imaging (MRI). (Target lesion(s) must not lie within an irradiated area)
- Life expectancy of ≥ 3 months
- Karnofsky performance status of ≥ 60, at study entry
- White blood cell count (WBC) ≥ 3 x 10^9/L, with neutrophils ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L, and hemoglobin ≥ 9 g/dL

- Aspartate transaminase and alanine transaminase ≤ 2.5 x Upper Limit of Normal (ULN) (≤ 5 x ULN if liver metastasis are present)
- Normal serum creatinine (in case of elevated creatinine, labelled ethylenediaminetetraacetic acid clearance ≥ 65 mL/min is acceptable)
- Effective contraception for both male and female subjects if the risk of conception exists
- Tumor biopsy or archived sample available

Exclusion criteria:

- Brain metastasis and/or leptomeningeal disease (known or suspected)
- Previous chemotherapy for colorectal cancer except adjuvant treatment with progression of disease documented > 6 months after end of adjuvant treatment.
- Previous oxaliplatin-based chemotherapy
- Surgery (excluding diagnostic biopsy) or irradiation within 4 weeks prior to randomization
- Concurrent or previous chronic systemic immune therapy, targeted therapy, anti-vascular epithelial growth factor (VEGF) therapy, epidermal growth factor receptor (EGFR) pathway targeting therapy not indicated in the study protocol
- Concurrent hormonal therapy not indicated in the study protocol except for physiologic replacement or contraception
- Clinically relevant coronary artery disease, history of myocardial infarction in the last 12 months, or high risk of uncontrolled arrhythmia
- Peripheral neuropathy >grade 1
- Known hypersensitivity reaction to any of the components of the treatment.
- Any concurrent malignancy other than basal cell cancer of the skin, or pre-invasive cancer of the cervix. (Subjects with a previous malignancy but without evidence of disease for ≥ 5 years will be allowed to enter the study)
- Pregnancy (absence to be confirmed by ß-human chorionic gonadotrophin test) or lactation period
- Known drug abuse/alcohol abuse
- Legal incapacity or limited legal capacity
- Medical or psychological condition which in the opinion of the investigator would not permit the subject to complete the study or sign meaningful informed consent
- Participation in another clinical study within the 30 days before randomization
- Significant disease which, in the investigator's opinion, would exclude the subject from the study

Contacts/Locations

Study Officials: Jean-Yves Douillard, MD PhD
Study Principal Investigator
Centre R Gauducheau

Locations: Austria
Research Site
Graz, Austria

Research Site
Wien, Austria

Brazil
Research Site
Fortaleza, Brazil

Germany
Research Site
Heidelberg, Germany

Research Site
Kassel, Germany

Research Site
Hamburg, Germany

Research Site
Magdeburg, Germany

Research Site
Krefeld, Germany

Research Site
München, Germany

Research Site
Wiesbaden, Germany

Research Site
Dortmund, Germany

Research Site
Hannover, Germany

Research Site
Berlin, Germany

Research Site
Oldenburg, Germany

Research Site
Dresden, Germany

France
Research Site
Saint-Herblain, France

Research Site

Besancon Cedex, France

Research Site
Caen-Cedex 5, France

Research Site
Strasbourg, France

Research Site
Lille, France

Greece
Research Site
Thessaloniki, Greece

Research Site
Voutes, Greece

Research Site
Dragana, Greece

Hong Kong
Research Site
Sha Tin, Hong Kong

Italy
Research Site
Reggio Emilia, Italy

Research Site
Sassari, Italy

Research Site
Pavia, Italy

Research Site
Benevento, Italy

Research Site
Roma, Italy

Research Site
Forli, Italy

Israel
Research Site

Jerusalem, Israel

Research Site
Haifa, Israel

Mexico
Research Site
Mexico-City, Mexico

Poland
Research Site
Warsaw, Poland

Research Site
Lublin, Poland

Research Site
Opole, Poland

Research Site
Krakow, Poland

Argentina
Research Site
Buenos Aires, Argentina

Australia
Research Site
Wollongong, Australia

Research Site
Perth, Australia

Belgium
Research Site
Liège, Belgium

Brazil
Research Site
Belo Horizonte, Brazil

Hong Kong
Research Site
Hong Kong, Hong Kong

Italy

Research Site
Brescia, Italy

Thailand
Research Site
Bangkok, Thailand

Research Site
Pathumwan, Thailand

Belgium
Research Site
Leuven, Belgium

France
Research Site
La Roche sur Yon, France

Research Site
Marseille, France

Italy
Research Site
Rimini, Italy

Research Site
Cremona, Italy

Germany
Research Site
Frankfurt / Main, Germany

Brazil
Research site
Cep Sao Paulo-SP, Brazil

Italy
Research Site
Padova, Italy

Argentina
Research Site
Ciudad Autónoma Buenos Aires, Argentina

France
Research Site

Nice, France

Italy
Research Site
Potenza, Italy

References

Citations: [Study Results] Douillard JY, Zemelka T, Fountzilas G, Barone C, Schlichting M, Heighway J, Eggleton SP, Srimuninnimit V. FOLFOX4 with cetuximab vs. UFOX with cetuximab as first-line therapy in metastatic colorectal cancer: The randomized phase II FUTURE study. Clin Colorectal Cancer. 2014 Mar;13(1):14-26.e1. doi: 10.1016/j.clcc.2013.11.009. Epub 2013 Nov 16. PubMed 24370353

Links: URL: http://annonc.oxfordjournals.org/content/23/suppl_4.toc
Description Annals of Oncology, Volume 23 suppl 4 June 2012, Abstract to oral presentation O-0017

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First subject randomised 12 February 2007, last subject randomised 30 June 2008. Cut off date was 30th June 2009
Pre-Assignment Details	A total of 329 participants were screened and 302 participants were included in the Intent to Treat (ITT) Population. One patient included in the ITT population received no study medication and was not included in the Safety Population which comprised 301 participants (151 received UFOX plus cetuximab and 150 FOLFOX4 plus cetuximab).

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21

	Description
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Overall Study

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Started	152	150
Completed	150	150
Not Completed	2	0
Subject on treatment	1	0
Subject in survival follow-up	1	0

Baseline Characteristics

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Baseline Measures

	UFOX + Cetuximab	FOLFOX4 + Cetuximab	Total
Number of Participants	152	150	302
Age, Continuous [units: years] Mean (Standard Deviation)	60.1 (10.01)	61 (11.04)	60.5 (10.53)
Age, Customized [units: participants]			
<65 years	93	84	177
>=65 years	57	66	123
Missing	2	0	2
Gender, Male/Female [units: participants]			
Female	57	55	112
Male	95	95	190
Region of Enrollment [units: participants]			
Hong Kong	7	4	11
Greece	9	5	14
Thailand	7	9	16
Austria	13	9	22
Italy	28	33	61
France	6	8	14
Mexico	4	0	4
Argentina	5	6	11
Brazil	5	9	14
Poland	30	27	57
Belgium	5	7	12
Australia	6	5	11
Germany	27	28	55

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression-free Survival (PFS)
Measure Description	Duration from randomization until progression or death due to any cause. Only deaths within 12 weeks of last tumor assessment are considered. Patients without event are censored on the date of last tumor assessment. Response and progression were assessed by the Investigators using response evaluation criteria in solid tumors (RECIST) 1.0 criteria
Time Frame	Time from randomization to disease progression, death, or last tumor assessment reported between day of first patient randomised, Feb 2007, until cut off date, 30 Jun 2009
Safety Issue?	No

Analysis Population Description

Intention-to-treat (ITT) population i.e. all randomized subjects .

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	152	150
Progression-free Survival (PFS) [units: months] Median (95% Confidence Interval)	6.6 (5.6 to 7.2)	8.2 (7.5 to 9.2)

Statistical Analysis 1 for Progression-free Survival (PFS)

Statistical Analysis Overview	Comparison Groups	UFOX + Cetuximab, FOLFOX4 + Cetuximab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0048
	Comments	[Not specified]
	Method	Other [Stratified log rank]
	Comments	Kaplan-Meier method was used to estimate median PFS time. HR was calculated using Cox proportional hazards model stratified by randomization strata.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.677
	Confidence Interval	(2-Sided) 95% 0.515 to 0.889
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Best Overall Response (BOR)
Measure Description	BOR defined as percentage of subjects, whose BOR was either (confirmed) complete response (CR) or partial response (PR), relative to the number of subjects belonging to the study population of interest. CR defined as "Disappearance of all target lesions plus disappearance of all non-target lesions & without appearance of any new lesions; confirmed minimum 4 weeks later. PR defined as "At least 30% reduction in the SOLD of target lesions plus no significant change in non-target lesions to qualify for either CR or PD without appearance of new lesions; confirmed minimum 4 weeks later
Time Frame	Evaluations were performed every 8 weeks until disease progression, reported between day of first patient randomised, Feb 2007, until cut off date, 30 Jun 2009
Safety Issue?	No

Analysis Population Description

ITT population i.e. all randomized subjects.

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	152	150
Best Overall Response (BOR) [units: percentage of participants] Number (95% Confidence Interval)	37.5 (29.8 to 45.7)	51.3 (43.0 to 59.6)

Statistical Analysis 1 for Best Overall Response (BOR)

Statistical Analysis Overview	Comparison Groups	UFOX + Cetuximab, FOLFOX4 + Cetuximab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.016
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	Stratified odds ratio and Cochran-Mantel- Haenszel (CMH) statistics were calculated considering the randomization strata.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.756
	Confidence Interval	(2-Sided) 95% 1.110 to 2.777
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	Time from randomization to death. Patients without event are censored at the last date known to be alive or at the clinical cut-off date, whatever is earlier.
Time Frame	Time from randomization to death or last known to be alive, reported between day of first patient randomised, Feb 2007, until cut off date, 30 Jun 2009
Safety Issue?	No

Analysis Population Description

ITT population i.e. all randomized subjects.

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	152	150
Overall Survival (OS) [units: months] Median (95% Confidence Interval)	12.9 (11.5 to 15.8)	15.5 (12.6 to 18.1)

Statistical Analysis 1 for Overall Survival (OS)

Statistical Analysis Overview	Comparison Groups	UFOX + Cetuximab, FOLFOX4 + Cetuximab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3797
	Comments	[Not specified]
	Method	Other [Stratified log rank]
	Comments	Kaplan-Meier method was used to estimate median OS time. HR was calculated using Cox proportional hazards model stratified by randomization strata.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.855
	Confidence Interval	(2-Sided) 95% 0.603 to 1.213
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	Time from randomization to death. Patients without event are censored at the last date known to be alive or at the clinical cut-off date, whatever is earlier.
Time Frame	Time from randomization to death or last known to be alive, reported between day of first patient randomised, Feb 2007, until cut off date, 31 Aug 2011
Safety Issue?	No

Analysis Population Description

ITT population i.e. all randomized subjects.

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	152	150
Overall Survival (OS) [units: months] Median (95% Confidence Interval)	16.8 (13.9 to 18.5)	18.4 (15.3 to 20.9)

Statistical Analysis 1 for Overall Survival (OS)

Statistical Analysis Overview	Comparison Groups	UFOX + Cetuximab, FOLFOX4 + Cetuximab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8575
	Comments	[Not specified]

	Method	Other [Stratified log rank]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.977
	Confidence Interval	(2-Sided) 95% 0.755 to 1.263
	Estimation Comments	Kaplan-Meier method was used to estimate median OS time. HR was calculated using Cox proportional hazards model stratified by randomization strata.

5. Secondary Outcome Measure:

Measure Title	Quality of Life (QOL) Functional Assessment of Cancer Therapy-Colorectal (FACT-C)
Measure Description	All of the single-item measures of the FACT-C are assessed on ordinal response categories ranging from 0=”Not at all” to 4=”Very much”. For scoring purposes the response scores are reversed on negatively phrased questions. The principle for scoring the sub-scales is the same in all cases: subscale score = (Sum of items × Number of items in the subscale) / numbers of items answered. The lowest possible total score is 0 and the highest is 136. A high scale score represents a high QOL.
Time Frame	At baseline, at every first day of every third cycle during active - treatment, and at final tumor assessment , reported between day of first patient randomised, Feb 2007, until cut-off date, 30 Jun 2009. Cycles were 4 weeks long unless dosing delays
Safety Issue?	No

Analysis Population Description

Patients were considered evaluable for FACT-C provided they had at least one evaluable FACT-C questionnaire and provided that they were also included in the ITT Population

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21

	Description
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	137	132
Quality of Life (QOL) Functional Assessment of Cancer Therapy-Colorectal (FACT-C) [units: scores on a scale] Least Squares Mean (Standard Error)		
Baseline	98.22 (1.725)	96.45 (1.749)
Cycle 3	95.41 (1.735)	95.89 (1.806)
Cycle 6	94.75 (2.090)	94.70 (2.126)

6. Secondary Outcome Measure:

Measure Title	QOL EuroQuol-5D (EQ-5D) Health Outcome Questionnaire
Measure Description	The EQ-5D questionnaire is a measure of health status that provides a simple descriptive profile and a single index value. The optional part of the questionnaire was not applied. The EQ-5D defines health in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The 5 items are combined to generate health profiles. These profiles were converted to a continuous single index score using a one to one matching. The lowest possible score is -0.59 and the highest is 1.00, higher scores on the EQ-5D represent a better QOL.
Time Frame	at baseline, at every first day of every third cycle during active - treatment, and at final tumor assessment , reported between day of first patient randomised, Feb 2007, until cut-off date, 30 Jun 2009. All cycles were 4 weeks long unless dosing delays
Safety Issue?	No

Analysis Population Description

Patients were considered evaluable for EQ-5D provided they had at least one evaluable EQ-5D questionnaire and provided that they were also included in the ITT Population.

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	136	130
QOL EuroQuol-5D (EQ-5D) Health Outcome Questionnaire [units: scores on a scale] Least Squares Mean (Standard Error)		
Baseline	0.747 (0.021)	0.734 (0.021)
Cycle 3	0.782 (0.021)	0.758 (0.022)
Cycle 6	0.758 (0.026)	0.771 (0.026)

7. Secondary Outcome Measure:

Measure Title	QOL Therapy Preference Questionnaire (TPQ)
Measure Description	TPQ was used to investigate which features of chemotherapy treatment are the most relevant in ensuring patient satisfaction. The most essential characteristics of a cancer medication are shown at baseline and at cycle 3, along with percentage of subjects selecting that characteristic.

Time Frame	at baseline, at every first day of every third cycle during active - treatment, and at final tumor assessment , reported between day of first patient randomised, Feb 2007, until cut-off date, 30 Jun 2009. All cycles were 4 weeks long unless dosing delays
Safety Issue?	No

Analysis Population Description

Patients were considered evaluable for TPQ provided they had at least one evaluable TPQ questionnaire and they were also included in the ITT TPQ subset population.

The most essential characteristics of a cancer medication score are shown at baseline and cycle 3, no further cycles are available due to the low number of patients in later cycles

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	99	99
QOL Therapy Preference Questionnaire (TPQ) [units: percentage of participants]		
Baseline: Does not increase your risk of infection	18	16
Baseline: Does not interfere with daily activities	17	15
Baseline: Does not make you vomit	4	14
Baseline: Does not give you diarrhea	9	5

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Cycle 3: Does not increase your risk of infection	15	15
Cycle 3: Does not interfere with daily activities	10	11
Cycle 3: Does not make you vomit	4	10
Cycle 3: Does not give you diarrhea	15	4

8. Secondary Outcome Measure:

Measure Title	Treatment Impact on Social Daily Living and Health Care Resource Utilization
Measure Description	Non-protocol medical care visits and consultations
Time Frame	From randomisation until final visit, reported between day of first patient randomised, Feb 2007, until cut-off date, 30 Jun 2009
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	152	150
Treatment Impact on Social Daily Living and Health Care Resource Utilization [units: visits or consultations]		
Emergency room visit	34	26
Hospital oupatient clinic visit	40	35
Practice visit	71	159
Home visit	15	130
General Practitioner consultation	65	124
Specialist consultation	62	84
Nurse consultation	15	123
Other consultation	19	18

9. Secondary Outcome Measure:

Measure Title	Safety - Number of Patients Experiencing Any Adverse Event
Measure Description	Please refer to Adverse Events section for details of individual serious adverse events and other adverse events
Time Frame	Time from first dose up to 30 days after last dose of study treatment, reported between day of first patient randomised, Feb 2007, until cut off date, 30 Jun 2009
Safety Issue?	Yes

Analysis Population Description

Safety population

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Measured Values

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
Number of Participants Analyzed	151	150
Safety - Number of Patients Experiencing Any Adverse Event [units: participants]	151	149

Reported Adverse Events

Time Frame	Time from first dose up to 30 days after last dose of study treatment, reported between day of first patient randomised, Dec 2006, until cut off date, 30 Jun 2009
Additional Description	[Not specified]

Reporting Groups

	Description
UFOX + Cetuximab	UFOX is a combination regimen of UFT® (Tegafur plus Uracil), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85mg/m^2) on days 1 and 15 (every 2 weeks) • Oral UFT® (250mg/m^2 tegafur + 560 mg/m^2 uracil in 3 daily doses rounded to the nearest number of whole capsules) on days 1-21 • Oral Folinic Acid (90 mg in 3 daily divided doses) on days 1-21
FOLFOX4 + Cetuximab	FOLFOX4 is a combination regimen of 5 Fluorouracil (5-FU), Oxaliplatin and Folinic Acid. • Cetuximab infusion (400 mg/m^2 on day 1 of cycle 1 and 250 mg/m^2 at each subsequent day 1, as well as on days 8, 15 and 22) • Oxaliplatin infusion (85 mg/m^2) on days 1 and 15 (every 2 weeks) • 5-FU bolus + infusions (400 mg/m^2) on days 1, 2, 15 and 16 • Folinic Acid infusions (200 mg/m^2) on days 1, 2, 15 and 16

Serious Adverse Events

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Total	52/151 (34.44%)	48/150 (32%)
Blood and lymphatic system disorders		
Anaemia [A] †	1/151 (0.66%)	1/150 (0.67%)
Coagulopathy [A] †	1/151 (0.66%)	0/150 (0%)
Febrile neutropenia [A] †	0/151 (0%)	2/150 (1.33%)
Neutropenia [A] †	0/151 (0%)	2/150 (1.33%)
Splenic vein thrombosis [A] †	1/151 (0.66%)	0/150 (0%)
Thrombocytopenia [A] †	0/151 (0%)	1/150 (0.67%)
Cardiac disorders		
Cardiac failure [A] †	0/151 (0%)	1/150 (0.67%)
Myocardial infarction [A] †	1/151 (0.66%)	0/150 (0%)
Eye disorders		

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Ulcerative keratitis [A] †	0/151 (0%)	1/150 (0.67%)
Gastrointestinal disorders		
Abdominal pain [A] †	5/151 (3.31%)	4/150 (2.67%)
Anal fistula [A] †	1/151 (0.66%)	0/150 (0%)
Colitis [A] †	1/151 (0.66%)	0/150 (0%)
Diarrhoea [A] †	13/151 (8.61%)	4/150 (2.67%)
Faecaloma [A] †	0/151 (0%)	1/150 (0.67%)
Gastrointestinal obstruction [A] †	0/151 (0%)	1/150 (0.67%)
Ileus [A] †	5/151 (3.31%)	2/150 (1.33%)
Intestinal obstruction [A] †	5/151 (3.31%)	2/150 (1.33%)
Nausea [A] †	4/151 (2.65%)	0/150 (0%)
Proctalgia [A] †	1/151 (0.66%)	0/150 (0%)
Rectal haemorrhage [A] †	1/151 (0.66%)	0/150 (0%)
Stomatitis [A] †	0/151 (0%)	1/150 (0.67%)
Subileus [A] †	1/151 (0.66%)	0/150 (0%)
Vomiting [A] †	9/151 (5.96%)	3/150 (2%)
General disorders		
Asthenia [A] †	0/151 (0%)	1/150 (0.67%)
Chills [A] †	1/151 (0.66%)	0/150 (0%)
Fatigue [A] †	1/151 (0.66%)	2/150 (1.33%)
General physical health deterioration [A] †	0/151 (0%)	4/150 (2.67%)
Inflammation [A] †	1/151 (0.66%)	0/150 (0%)

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Pyrexia [A] †	3/151 (1.99%)	8/150 (5.33%)
Hepatobiliary disorders		
Biliary colic [A] †	1/151 (0.66%)	0/150 (0%)
Cholecystitis [A] †	0/151 (0%)	1/150 (0.67%)
Hepatic failure [A] †	1/151 (0.66%)	0/150 (0%)
Hepatorenal syndrome [A] †	1/151 (0.66%)	0/150 (0%)
Immune system disorders		
Drug hypersensitivity [A] †	0/151 (0%)	2/150 (1.33%)
Infections and infestations		
Anal abscess [A] †	1/151 (0.66%)	0/150 (0%)
Catheter related infection [A] †	0/151 (0%)	1/150 (0.67%)
Cellulitis [A] †	0/151 (0%)	1/150 (0.67%)
Central line infection [A] †	1/151 (0.66%)	5/150 (3.33%)
Clostridium difficile colitis [A] †	0/151 (0%)	1/150 (0.67%)
Hepatitis C [A] †	1/151 (0.66%)	0/150 (0%)
Pneumonia [A] †	1/151 (0.66%)	1/150 (0.67%)
Pyelonephritis [A] †	0/151 (0%)	1/150 (0.67%)
Pyelonephritis acute [A] †	1/151 (0.66%)	0/150 (0%)
Rectal abscess [A] †	1/151 (0.66%)	0/150 (0%)
Septic shock [A] †	1/151 (0.66%)	2/150 (1.33%)
Urinary tract infection [A] †	0/151 (0%)	2/150 (1.33%)
Urosepsis [A] †	0/151 (0%)	1/150 (0.67%)
Injury, poisoning and procedural complications		

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Accidental overdose [A] †	1/151 (0.66%)	0/150 (0%)
Overdose [A] †	1/151 (0.66%)	2/150 (1.33%)
Post procedural haemorrhage [A] †	1/151 (0.66%)	0/150 (0%)
Investigations		
Blood glucose abnormal [A] †	0/151 (0%)	1/150 (0.67%)
Metabolism and nutrition disorders		
Anorexia [A] †	1/151 (0.66%)	1/150 (0.67%)
Dehydration [A] †	2/151 (1.32%)	1/150 (0.67%)
Hyperglycaemia [A] †	1/151 (0.66%)	0/150 (0%)
Hypocalcaemia [A] †	0/151 (0%)	1/150 (0.67%)
Hypokalaemia [A] †	2/151 (1.32%)	0/150 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/151 (0.66%)	0/150 (0%)
Back pain [A] †	1/151 (0.66%)	0/150 (0%)
Pathological fracture [A] †	1/151 (0.66%)	0/150 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Malignant ascites [A] †	0/151 (0%)	1/150 (0.67%)
Metastases to central nervous system [A] †	1/151 (0.66%)	0/150 (0%)
Nervous system disorders		
Cerebral ischaemia [A] †	0/151 (0%)	1/150 (0.67%)
Coma hepatic [A] †	1/151 (0.66%)	0/150 (0%)
Grand mal convulsion [A] †	1/151 (0.66%)	0/150 (0%)
Headache [A] †	0/151 (0%)	1/150 (0.67%)

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Syncope [A] †	0/151 (0%)	2/150 (1.33%)
Psychiatric disorders		
Anxiety [A] †	0/151 (0%)	1/150 (0.67%)
Confusional state [A] †	1/151 (0.66%)	0/150 (0%)
Renal and urinary disorders		
Hydronephrosis [A] †	1/151 (0.66%)	0/150 (0%)
Renal failure acute [A] †	1/151 (0.66%)	0/150 (0%)
Ureteric perforation [A] †	0/151 (0%)	1/150 (0.67%)
Urethral disorder [A] †	1/151 (0.66%)	0/150 (0%)
Urinary bladder haemorrhage [A] †	0/151 (0%)	1/150 (0.67%)
Urinary retention [A] †	0/151 (0%)	1/150 (0.67%)
Reproductive system and breast disorders		
Vaginal fistula [A] †	0/151 (0%)	1/150 (0.67%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] †	1/151 (0.66%)	2/150 (1.33%)
Haemoptysis [A] †	0/151 (0%)	1/150 (0.67%)
Pleural effusion [A] †	0/151 (0%)	1/150 (0.67%)
Pneumonitis [A] †	0/151 (0%)	2/150 (1.33%)
Pulmonary artery thrombosis [A] †	0/151 (0%)	1/150 (0.67%)
Pulmonary embolism [A] †	1/151 (0.66%)	2/150 (1.33%)
Skin and subcutaneous tissue disorders		
Dermatitis acneiform [A] †	1/151 (0.66%)	0/150 (0%)
Vascular disorders		

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Arterial thrombosis [A] †	0/151 (0%)	1/150 (0.67%)
Circulatory collapse [A] †	0/151 (0%)	1/150 (0.67%)
Femoral artery embolism [A] †	1/151 (0.66%)	0/150 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (12.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Total	151/151 (100%)	146/150 (97.33%)
Blood and lymphatic system disorders		
Anaemia [A] †	15/151 (9.93%)	26/150 (17.33%)
Leukopenia [A] †	5/151 (3.31%)	28/150 (18.67%)
Neutropenia [A] †	10/151 (6.62%)	65/150 (43.33%)
Thrombocytopenia [A] †	33/151 (21.85%)	37/150 (24.67%)
Eye disorders		
Conjunctivitis [A] †	14/151 (9.27%)	14/150 (9.33%)
Gastrointestinal disorders		
Abdominal pain [A] †	34/151 (22.52%)	25/150 (16.67%)
Abdominal pain upper [A] †	10/151 (6.62%)	8/150 (5.33%)
Constipation [A] †	29/151 (19.21%)	30/150 (20%)
Diarrhoea [A] †	79/151 (52.32%)	72/150 (48%)
Dyspepsia [A] †	10/151 (6.62%)	8/150 (5.33%)
Flatulence [A] †	9/151 (5.96%)	1/150 (0.67%)

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Nausea [A] †	67/151 (44.37%)	55/150 (36.67%)
Stomatitis [A] †	15/151 (9.93%)	36/150 (24%)
Vomiting [A] †	40/151 (26.49%)	32/150 (21.33%)
General disorders		
Asthenia [A] †	25/151 (16.56%)	27/150 (18%)
Chills [A] †	5/151 (3.31%)	9/150 (6%)
Fatigue [A] †	38/151 (25.17%)	38/150 (25.33%)
Mucosal inflammation [A] †	15/151 (9.93%)	34/150 (22.67%)
Oedema peripheral [A] †	11/151 (7.28%)	11/150 (7.33%)
Pyrexia [A] †	30/151 (19.87%)	36/150 (24%)
Hepatobiliary disorders		
Hyperbilirubinaemia [A] †	12/151 (7.95%)	6/150 (4%)
Immune system disorders		
Drug hypersensitivity [A] †	12/151 (7.95%)	10/150 (6.67%)
Hypersensitivity [A] †	3/151 (1.99%)	8/150 (5.33%)
Infections and infestations		
Folliculitis [A] †	8/151 (5.3%)	14/150 (9.33%)
Nasopharyngitis [A] †	6/151 (3.97%)	11/150 (7.33%)
Paronychia [A] †	26/151 (17.22%)	33/150 (22%)
Pharyngitis [A] †	8/151 (5.3%)	7/150 (4.67%)
Investigations		
Alanine aminotransferase increased [A] †	9/151 (5.96%)	8/150 (5.33%)
Aspartate aminotransferase increased [A] †	10/151 (6.62%)	5/150 (3.33%)

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Platelet count decreased [A] †	9/151 (5.96%)	6/150 (4%)
Weight decreased [A] †	12/151 (7.95%)	16/150 (10.67%)
Metabolism and nutrition disorders		
Anorexia [A] †	40/151 (26.49%)	36/150 (24%)
Hypokalaemia [A] †	17/151 (11.26%)	15/150 (10%)
Hypomagnesaemia [A] †	15/151 (9.93%)	14/150 (9.33%)
Musculoskeletal and connective tissue disorders		
Back pain [A] †	10/151 (6.62%)	10/150 (6.67%)
Pain in extremity [A] †	5/151 (3.31%)	8/150 (5.33%)
Nervous system disorders		
Dysaesthesia [A] †	11/151 (7.28%)	5/150 (3.33%)
Dysgeusia [A] †	13/151 (8.61%)	20/150 (13.33%)
Headache [A] †	6/151 (3.97%)	10/150 (6.67%)
Neuropathy peripheral [A] †	17/151 (11.26%)	22/150 (14.67%)
Paraesthesia [A] †	38/151 (25.17%)	43/150 (28.67%)
Peripheral sensory neuropathy [A] †	29/151 (19.21%)	27/150 (18%)
Polyneuropathy [A] †	6/151 (3.97%)	17/150 (11.33%)
Psychiatric disorders		
Insomnia [A] †	9/151 (5.96%)	5/150 (3.33%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	8/151 (5.3%)	7/150 (4.67%)
Dyspnoea [A] †	5/151 (3.31%)	8/150 (5.33%)
Epistaxis [A] †	9/151 (5.96%)	13/150 (8.67%)

	UFOX + Cetuximab	FOLFOX4 + Cetuximab
	Affected/At Risk (%)	Affected/At Risk (%)
Skin and subcutaneous tissue disorders		
Acne [A] †	20/151 (13.25%)	14/150 (9.33%)
Alopecia [A] †	6/151 (3.97%)	13/150 (8.67%)
Dermatitis [A] †	5/151 (3.31%)	9/150 (6%)
Dermatitis acneiform [A] †	40/151 (26.49%)	45/150 (30%)
Dry skin [A] †	27/151 (17.88%)	29/150 (19.33%)
Erythema [A] †	10/151 (6.62%)	12/150 (8%)
Nail disorder [A] †	7/151 (4.64%)	11/150 (7.33%)
Palmar-plantar erythrodysaesthesia syndrome [A] †	10/151 (6.62%)	13/150 (8.67%)
Pruritus [A] †	8/151 (5.3%)	15/150 (10%)
Rash [A] †	63/151 (41.72%)	47/150 (31.33%)
Skin fissures [A] †	13/151 (8.61%)	22/150 (14.67%)
Vascular disorders		
Hypertension [A] †	8/151 (5.3%)	11/150 (7.33%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (12.0)

Limitations and Caveats

Dosing of UFT/ folinic acid in the experimental arm were not directly recorded, so dosing data is not fully available in the UFOX plus cetuximab arm (36/151). Comparative conclusions on drug exposure might be impacted by a bias due to missing data.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

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