Clinical trial results:
FIGHT: A Phase 2 Randomized, Double-Blind, Controlled Study Evaluating FPA144 and Modified FOLFOX6 in Patients with Previously Untreated Advanced Gastric and Gastroesophageal Cancer: Phase 2 Preceded by Dose-Finding in Phase 1

Summary

EudraCT number	2017-003507-22
Trial protocol	HU GB DE PT FR ES RO PL IT
Global end of trial date	13 May 2022

Results information

Result version number	v1 (current)
This version publication date	31 December 2022
First version publication date	31 December 2022

Trial information

Trial identification

Sponsor protocol code	FPA144-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03694522
WHO universal trial number (UTN)	-
Other trial identifiers	ClinicalTrials.gov (Phase 1): NCT03343301

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	13 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the Phase 1 portion of this study was to determine the recommended dose of bemarituzumab (FPA144), a targeted antibody, in combination with 5-fluorouracil, leucovorin and oxaliplatin (modified FOLFOX6) to use in the Phase 2 portion of the trial.
The main objective of the Phase 2 part of the study was to evaluate the efficacy of bemarituzumab in combination with modified FOLFOX6 compared to placebo in combination with modified FOLFOX6 in participants with advanced gastrointestinal cancer.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonization (ICH) Good Clinical Practice (GCP) and applicable national or regional regulations/guidelines.
The study protocol and all amendments, the informed consent form (ICF), and any accompanying materials provided to the subjects were reviewed and approved by an Institutional Review Board (IRB) or Independent Ethics Committee (IEC) at each study center.
The investigator or his/her designee informed the subject of all aspects pertaining to the subject's participation in the study before any screening procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	China: 27
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 54

Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Turkey: 15
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	167
EEA total number of subjects	38

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)	117
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study FPA144-004 was a Phase 1/2 study. Phase 1 was a safety run-in to determine the recommended dose of bemarituzumab to be administered in combination with a fixed dose of modified FOLFOX6 (mFOLFOX6) chemotherapy regimen in the Phase 2 part of the study.

Pre-assignment

Screening details:

In Phase 1, dose cohorts began at bemarituzumab 6 mg/kg per dose, with enrollment into subsequent dose cohorts depending on safety and tolerability.
In Phase 2 participants were randomized equally, stratified based on geographic region, prior treatment status, and administration of a single dose of mFOLFOX6 prior to enrollment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

The Phase 1 safety run-in was an open-label dose escalation study.
The Phase 2 part was a randomized, controlled, double-blind study design.

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6

Arm description:

Participants received 6 mg/kg bemarituzumab administered every 2 weeks (Q2W) and modified FOLFOX6 (mFOLFOX6) chemotherapy administered Q2W until unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Bemarituzumab
Investigational medicinal product code	FPA144
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over approximately 30 minutes.

Investigational medicinal product name	Modified FOLFOX6
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Modified FOLFOX6 regimen consists of the following:
- Oxaliplatin 85 mg/m² IV infusion over 120 minutes;
- Leucovorin 400 mg/m² IV infusion over 120 minutes, or 200 mg/m² levo-leucovorin if leucovorin is unavailable;
- 5-fluorouracil (5-FU) 400 mg/m² bolus over approximately 5 minutes then 5-FU 2400 mg/m² as a continuous IV infusion over approximately 48 hours.

Arm title	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6

Arm description:

Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy

administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Bemarituzumab
Investigational medicinal product code	FPA144
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over approximately 30 minutes.

Investigational medicinal product name	Modified FOLFOX6
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Modified FOLFOX6 regimen consists of the following:
- Oxaliplatin 85 mg/m² IV infusion over 120 minutes;
- Leucovorin 400 mg/m² IV infusion over 120 minutes, or 200 mg/m² levo-leucovorin if leucovorin is unavailable;
- 5-fluorouracil (5-FU) 400 mg/m² bolus over approximately 5 minutes then 5-FU 2400 mg/m² as a continuous IV infusion over approximately 48 hours.

Arm title	Phase 2: Bemarituzumab + mFOLFOX6

Arm description:

Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Bemarituzumab
Investigational medicinal product code	FPA144
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over approximately 30 minutes.

Investigational medicinal product name	Modified FOLFOX6
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Modified FOLFOX6 regimen consists of the following:
- Oxaliplatin 85 mg/m² IV infusion over 120 minutes;
- Leucovorin 400 mg/m² IV infusion over 120 minutes, or 200 mg/m² levo-leucovorin if leucovorin is unavailable;
- 5-fluorouracil (5-FU) 400 mg/m² bolus over approximately 5 minutes then 5-FU 2400 mg/m² as a continuous IV infusion over approximately 48 hours.

Arm title	Phase 2: Placebo + mFOLFOX6

Arm description:

Participants received placebo for bemarituzumab administered Q2W with a single additional placebo dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.

Arm type	Active comparator

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over approximately 30 minutes.

Investigational medicinal product name	Modified FOLFOX6
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Modified FOLFOX6 regimen consists of the following:
- Oxaliplatin 85 mg/m² IV infusion over 120 minutes;
- Leucovorin 400 mg/m² IV infusion over 120 minutes, or 200 mg/m² levo-leucovorin if leucovorin is unavailable;
- 5-fluorouracil (5-FU) 400 mg/m² bolus over approximately 5 minutes then 5-FU 2400 mg/m² as a continuous IV infusion over approximately 48 hours.

Number of subjects in period 1	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6	Phase 2: Bemarituzumab + mFOLFOX6
Started	3	9	77
Received Any Study Treatment	3	9	76
Completed	0	0	15
Not completed	3	9	62
Consent withdrawn by subject	1	1	8
Death	-	2	53
Other	-	6	1
Lost to follow-up	-	-	-
Missing	2	-	-

Number of subjects in period 1	Phase 2: Placebo + mFOLFOX6
Started	78
Received Any Study Treatment	77
Completed	12
Not completed	66
Consent withdrawn by subject	10
Death	54
Other	1
Lost to follow-up	1
Missing	-

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6
Reporting group description:	
Participants received 6 mg/kg bemarituzumab administered every 2 weeks (Q2W) and modified FOLFOX6 (mFOLFOX6) chemotherapy administered Q2W until unacceptable toxicity, disease progression, or death.	
Reporting group title	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6
Reporting group description:	
Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.	
Reporting group title	Phase 2: Bemarituzumab + mFOLFOX6
Reporting group description:	
Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.	
Reporting group title	Phase 2: Placebo + mFOLFOX6
Reporting group description:	
Participants received placebo for bemarituzumab administered Q2W with a single additional placebo dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.	

Reporting group values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6	Phase 2: Bemarituzumab + mFOLFOX6
Number of subjects	3	9	77
Age categorical Units: Subjects			
< 65 years	1	5	58
>= 65 years	2	4	19
Age continuous Units: years			
arithmetic mean	64.7	62.3	58.0
standard deviation	± 21.46	± 16.45	± 11.11
Gender categorical Units: Subjects			
Female	2	0	25
Male	1	9	52
Ethnicity Units: Subjects			
Hispanic or Latino	2	2	2
Not Hispanic or Latino	1	7	74
Missing	0	0	1
Race Units: Subjects			
Asian	0	1	45
Black or African American	1	0	0
American Indian or Alaska Native	0	0	0
White	2	7	30
Other	0	1	2

Geographic Region			
Geographic region was a stratification factor in Phase 2. European Union (EU) includes Italy, Turkey, Spain, Portugal, Hungary, Germany, France, Romania, Poland, and the United Kingdom. Rest of Asia includes Japan, Taiwan, and South Korea. Phase 1 was only conducted in the United States.			
Units: Subjects			
United States / European Union	3	9	32
China	0	0	14
Rest of Asia	0	0	31
Prior Treatment Status			
Prior treatment status based on history of prior chemotherapy administered for neo-adjuvant or adjuvant therapy, was a stratification factor in Phase 2.			
Units: Subjects			
Prior adjuvant/ neoadjuvant therapy	0	0	14
No prior adjuvant/ neoadjuvant therapy	0	0	63
Not Reported	3	9	0
Administration of a Single Dose of mFOLFOX6 Prior to Enrollment			
In Phase 2 participants were stratified based on whether they have received a single dose of mFOLFOX6 chemotherapy for advanced stage disease prior to enrollment. Confirmation of positive fibroblast growth factor receptor 2 (FGFR2) overexpression status was required for enrolment in Phase 2. The results of the centralised FGFR2 testing took approximately 2 weeks; therefore, patients were permitted to receive a single dose of mFOLFOX6 during this prescreening period at the discretion of the investigator.			
Units: Subjects			
Yes	0	0	35
No	0	0	42
Not applicable	3	9	0
Phase 1: Clinical Diagnosis of Cancer			
Patients enrolling in Phase 1 of the study must have had histologically or cytologically confirmed gastrointestinal (GI) malignancy for which mFOLFOX6 was considered an appropriate treatment (eg, gastric cancer, colorectal carcinoma, pancreatic adenocarcinoma).			
Units: Subjects			
Colorectal Cancer	3	5	0
Gastric Cancer / Esophageal Cancer	0	3	0
Pancreatic Cancer	0	1	0
Not applicable	0	0	77
Phase 2: Clinical Diagnosis of Cancer			
Patients enrolling in Phase 2 of the study must have had histologically documented gastric or gastroesophageal junction (GEJ) adenocarcinoma (not amenable to curative therapy).			
Units: Subjects			
Gastric Adenocarcinoma	0	0	66
Gastroesophageal Junction (GEJ) Adenocarcinoma	0	0	11
Not applicable	3	9	0
Eastern Cooperative Oncology Group (ECOG) Performance Status			
A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self-care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead.			
Units: Subjects			

0 (Fully active)	0	6	25
1 (Restricted activity but ambulatory)	3	3	52

Reporting group values	Phase 2: Placebo + mFOLFOX6	Total	
Number of subjects	78	167	
Age categorical			
Units: Subjects			
< 65 years	53	117	
>= 65 years	25	50	
Age continuous			
Units: years			
arithmetic mean	59.1		
standard deviation	± 12.04	-	
Gender categorical			
Units: Subjects			
Female	19	46	
Male	59	121	
Ethnicity			
Units: Subjects			
Hispanic or Latino	3	9	
Not Hispanic or Latino	75	157	
Missing	0	1	
Race			
Units: Subjects			
Asian	44	90	
Black or African American	1	2	
American Indian or Alaska Native	1	1	
White	31	70	
Other	1	4	
Geographic Region			
Geographic region was a stratification factor in Phase 2. European Union (EU) includes Italy, Turkey, Spain, Portugal, Hungary, Germany, France, Romania, Poland, and the United Kingdom. Rest of Asia includes Japan, Taiwan, and South Korea. Phase 1 was only conducted in the United States.			
Units: Subjects			
United States / European Union	34	78	
China	13	27	
Rest of Asia	31	62	
Prior Treatment Status			
Prior treatment status based on history of prior chemotherapy administered for neo-adjuvant or adjuvant therapy, was a stratification factor in Phase 2.			
Units: Subjects			
Prior adjuvant/ neoadjuvant therapy	13	27	
No prior adjuvant/ neoadjuvant therapy	65	128	
Not Reported	0	12	
Administration of a Single Dose of mFOLFOX6 Prior to Enrollment			
In Phase 2 participants were stratified based on whether they have received a single dose of mFOLFOX6 chemotherapy for advanced stage disease prior to enrollment. Confirmation of positive fibroblast growth factor receptor 2 (FGFR2) overexpression status was required			

for enrolment in Phase 2. The results of the centralised FGFR2 testing took approximately 2 weeks; therefore, patients were permitted to receive a single dose of mFOLFOX6 during this prescreening period at the discretion of the investigator.			
Units: Subjects			
Yes	36	71	
No	42	84	
Not applicable	0	12	
Phase 1: Clinical Diagnosis of Cancer			
Patients enrolling in Phase 1 of the study must have had histologically or cytologically confirmed gastrointestinal (GI) malignancy for which mFOLFOX6 was considered an appropriate treatment (eg, gastric cancer, colorectal carcinoma, pancreatic adenocarcinoma).			
Units: Subjects			
Colorectal Cancer	0	8	
Gastric Cancer / Esophageal Cancer	0	3	
Pancreatic Cancer	0	1	
Not applicable	78	155	
Phase 2: Clinical Diagnosis of Cancer			
Patients enrolling in Phase 2 of the study must have had histologically documented gastric or gastroesophageal junction (GEJ) adenocarcinoma (not amenable to curative therapy).			
Units: Subjects			
Gastric Adenocarcinoma	71	137	
Gastroesophageal Junction (GEJ) Adenocarcinoma	7	18	
Not applicable	0	12	
Eastern Cooperative Oncology Group (ECOG) Performance Status			
A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self-care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead.			
Units: Subjects			
0 (Fully active)	28	59	
1 (Restricted activity but ambulatory)	50	108	

End points

End points reporting groups

Reporting group title	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6
Reporting group description:	
Participants received 6 mg/kg bemarituzumab administered every 2 weeks (Q2W) and modified FOLFOX6 (mFOLFOX6) chemotherapy administered Q2W until unacceptable toxicity, disease progression, or death.	
Reporting group title	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6
Reporting group description:	
Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.	
Reporting group title	Phase 2: Bemarituzumab + mFOLFOX6
Reporting group description:	
Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.	
Reporting group title	Phase 2: Placebo + mFOLFOX6
Reporting group description:	
Participants received placebo for bemarituzumab administered Q2W with a single additional placebo dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.	

Primary: Phase 1: Number of Participants With Treatment-related Adverse Events ≥ Grade 2

End point title	Phase 1: Number of Participants With Treatment-related Adverse Events ≥ Grade 2[1][2]
End point description:	
A treatment-related adverse event (TRAE) is defined as an adverse event (AE) with an onset date on or after the date of first dose of study treatment, or an event present before treatment that worsened after treatment, and with an onset date prior to 28 days after the last date of dose, for which the investigator assessed as related to investigational product The investigator classified the severity of each AE using the National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE), version 5.0 on a scale from mild (Grade 1), moderate (Grade 2), severe (Grade 3), life-threatening (Grade 4), or death due to the AE (Grade 5).	
End point type	Primary
End point timeframe:	
From first dose of study drug up to 28 days after last dose; Actual median (min, max) duration of treatment emergent period was 19.3 (12.3, 22.3) weeks in the bemarituzumab 6 mg/kg group and 19.4 (4.0, 35.4) weeks in the bemarituzumab 15 mg/kg group.	

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: Statistical analyses were not conducted in Phase 1.

[2] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[3]	9[4]		
Units: participants	1	4		

Notes:

[3] - Safety analysis set (participants who received any portion of at least 1 dose of study treatment)

[4] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs)

End point title	Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs)[5][6]

End point description:

DLTs were defined as any of the following events considered by the investigator to be related to study drug:
-Absolute neutrophil count (ANC) < 0.5 × 10^9/L > 5 days duration or febrile neutropenia.
-Platelets < 25 × 10^9/L or < 50 × 10^9/L with bleeding requiring medical intervention or for > 3 days.
-Grade 4 anemia.
-Any Grade 2-3 ophthalmologic AE not resolving within 7 days.
-Any Grade 4 ophthalmologic AE.
-Any Grade 4 laboratory value.
-Any Grade 3 laboratory values that are not of clinical significance according to investigator and Sponsor agreement if they do not resolve within 72 hours.
-Aspartate aminotransferase/alanine aminotransferase (AST/ALT) ≥ 3 × upper limit of normal (ULN) and concurrent total bilirubin ≥ 2 × ULN not related to liver involvement with cancer.
-Any non-hematological AE ≥ Grade 3 (except nausea, vomiting, and diarrhea).
-Grade 3 nausea, vomiting or diarrhea not resolving with supportive care in 72 hours.
-Grade 4 nausea, vomiting or diarrhea.

End point type	Primary

End point timeframe:

28 days

Notes:

[5] - 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: Statistical analyses were not conducted in Phase 1.

[6] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[7]	8[8]		
Units: participants	0	0		

Notes:

[7] - DLT-evaluable analysis set (participants who completed 2 cycles of treatment or experienced a DLT)
[8] - DLT-evaluable analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Progression-Free Survival (PFS)

End point title	Phase 2: Progression-Free Survival (PFS)[9]

End point description:

PFS was defined as time from randomization until the date of radiographic disease progression based on investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 or death from any cause, whichever came first. PFS was analyzed using Kaplan-Meier methods. Participants with no progression or death, or who started new anticancer therapy before documented progression or death without documented progression, or who had ≥ 2 consecutive missing tumor assessments before documented progression or death without documented progression were censored on the date of last adequate tumor assessment. Participants with no baseline tumor assessment, were censored at the date of randomization.
The primary efficacy analysis was pre-specified to be conducted after at least 84 PFS events were observed.

End point type	Primary

End point timeframe:

From randomization until the primary analysis data cut-off date of 23 September 2020; median time on follow-up was 10.9 months.

Notes:

[9] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 2: Bemarituzumab + mFOLFOX6	Phase 2: Placebo + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77[10]	78[11]		
Units: months				
median (confidence interval 95%)	9.5 (7.3 to 12.9)	7.4 (5.8 to 8.4)		

Notes:

[10] - Intent-to-treat population (all participants randomized in Phase 2)

[11] - Intent-to-treat population

Statistical analyses

Statistical analysis title	Primary Analysis

Statistical analysis description:

A non-parametric stratified log-rank test was used to compare the treatment groups with the stratification factors of geographical region and administration of a single dose of mFOLFOX6. Hazard ratio and 95% CIs were calculated using the Cox proportional hazards model, adjusted for randomization stratification factors.

Comparison groups	Phase 2: Bemarituzumab + mFOLFOX6 v Phase 2: Placebo + mFOLFOX6
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0727 [12]
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.04

Notes:

[12] - Stratified log-rank test adjusted for randomization stratification factors of geographic region and administration of mFOLFOX6 single dose prior to randomization.

Secondary: Phase 1: Number of Participants With Treatment-emergent Adverse Events

End point title	Phase 1: Number of Participants With Treatment-emergent Adverse Events[13]

End point description:

Treatment-emergent adverse events are defined as AEs that started or worsened between the start of study drug and 28 days after permanent discontinuation of study drug.
A serious AE is defined as any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability or incapacity, or was a congenital anomaly or birth defect.
The investigator assessed the causality/relationship between the study treatment and each AE, and assessed the severity of each AE according to the NCI-CTCAE, version 5.0.
Ocular events associated with symptomatic corneal involvement and symptomatic and asymptomatic retinal involvement were events of special interest (TE-AESI) in this study. Cornea and retina AEs were defined by Standardized Medical Dictionary for Regulatory Activities Queries (SMQs) of corneal disorders and retinal disorders (broad).

End point type	Secondary

End point timeframe:

From first dose of study drug up to 28 days after last dose; Actual median (min, max) duration of the treatment emergent period was 19.3 (12.3, 22.3) weeks in the bemarituzumab 6 mg/kg group and 19.4 (4.0, 35.4) weeks in the bemarituzumab 15 mg/kg group.

Notes:

[13] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[14]	9[15]		
Units: participants				
Any treatment-emergent adverse event (TEAE)	3	9		
TEAE with Grade ≥ 3	1	6		
TEAE related to any study drug	3	9		
TEAE related to bemarituzumab (BEMA)	2	5		
TEAE related to any agent of mFOLFOX6	3	9		
TEAE with Grade ≥ 3 related to any study drug	1	4		
Serious adverse event (SAE)	0	4		
SAE related to any study drug	0	1		
SAE related to bemarituzumab	0	0		
SAE related to any agent of mFOLFOX6	0	1		
TEAE leading to discontinuation (DC) of BEMA	0	4		
TEAE leading to DC of any agent of mFOLFOX6	0	4		

TEAE leading to dose reduction of bemarituzumab	1	0		
TEAE leading to dose reduction of mFOLFOX6	1	5		
TE-AESI: corneal/retina disorders (C/R)	0	4		
TE-AESI: C/R disorders related to bemarituzumab	0	4		
TE-AESI: C/R disorders leading to DC of BEMA	0	2		

Notes:

[14] - Safety analysis set

[15] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximum Observed Serum Concentration (Cmax) of Bemarituzumab

End point title	Phase 1: Maximum Observed Serum Concentration (Cmax) of Bemarituzumab[16]

End point description:

Bemarituzumab serum concentration was measured by a validated enzyme linked immunosorbent assay (ELISA). The lower limit of quantitation (LLOQ) of the assay was 0.125 µg/mL.
The pharmacokinetic (PK)-evaluable analysis set included all participants who had sufficient PK data for the reliable calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Cycle 1 day 1 at predose, 0.25, 4, 48, and 168 hours after end of infusion, and for participants in Cohort 2 day 8 at 0.25 and 4 hours end of infusion; Cycle 2 day 1 at predose, 0.25 and 48 hours after end of infusion.

Notes:

[16] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[17]	8[18]		
Units: µg/mL				
arithmetic mean (standard deviation)				
Cycle 1	119 (± 8.52)	329 (± 60.3)		
Cycle 2	123 (± 13.8)	377 (± 82.8)		

Notes:

[17] - PK-evaluable analysis set

[18] - PK-evaluable analysis set; N=7 for Cycle 2

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Observed Serum Concentration of Bemarituzumab at the End of the Dose Interval (Ctrough)

End point title	Phase 1: Observed Serum Concentration of Bemarituzumab at the End of the Dose Interval (Ctrough)[19]

End point description:

Bemarituzumab serum concentration was measured by a validated enzyme linked immunosorbent assay (ELISA). The lower limit of quantitation (LLOQ) of the assay was 0.125 µg/mL.

End point type	Secondary

End point timeframe:

Cycle 1 day 14 predose for cohort 1 and day 8 predose for cohort 2; Cycle 2 day 14 predose

Notes:

[19] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[20]	8[21]		
Units: µg/mL				
arithmetic mean (standard deviation)				
Cycle 1	16.5 (± 8.80)	118 (± 25.1)		
Cycle 2	25.6 (± 10.6)	131 (± 55.3)		

Notes:

[20] - PK-evaluable analysis set

[21] - PK-evaluable analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Observed Concentration-time Curve From the Time of Dosing to Day 14 (AUC0-14)

End point title	Phase 1: Area Under the Observed Concentration-time Curve From the Time of Dosing to Day 14 (AUC0-14)[22]

End point description:

Bemarituzumab serum concentration was measured by a validated enzyme linked immunosorbent assay (ELISA). The lower limit of quantitation (LLOQ) of the assay was 0.125 µg/mL.
Area under the observed concentration-time curve from the time of dosing to Day 14 (0-336h) calculated by log-linear trapezoidal approximation.

End point type	Secondary

End point timeframe:

Cycle 1 day 1 at predose, 0.25, 4, 48, and 168 hours after end of infusion, and for participants in Cohort 2 day 8 at 0.25 and 4 hours after the end of infusion.

Notes:

[22] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[23]	7[24]		
Units: µg*day/mL				
arithmetic mean (standard deviation)	556 (± 232)	2350 (± 394)		

Notes:

[23] - PK-evaluable analysis set

[24] - PK-evaluable analysis set with available AUC data

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Terminal Half-life (t1/2) of Bemarituzumab

End point title	Phase 1: Terminal Half-life (t1/2) of Bemarituzumab[25]

End point description:

Bemarituzumab serum concentration was measured by a validated enzyme linked immunosorbent assay (ELISA). The lower limit of quantitation (LLOQ) of the assay was 0.125 µg/mL.

End point type	Secondary

End point timeframe:

Cycle 1 day 1 at predose, 0.25, 4, 48, and 168 hours after end of infusion, and for participants in Cohort 2 day 8 at 0.25 and 4 hours after end of infusion.

Notes:

[25] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[26]	3[27]		
Units: days				
arithmetic mean (standard deviation)	8.35 (± 3.36)	4.23 (± 0.447)		

Notes:

[26] - PK-evaluable analysis set

[27] - PK-evaluable analysis set with available half-life data

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 : Number of Participants With Treatment Induced Anti-bemarituzumab Antibodies

End point title	Phase 1 : Number of Participants With Treatment Induced Anti-bemarituzumab Antibodies[28]

End point description:

Postbaseline treatment induced antidrug antibody (ADA) positive is defined as participants who were:
• ADA negative at baseline and ADA positive at any postbaseline timepoint, or
• ADA positive at baseline and ADA positive with titer of at least 4-fold of the baseline titer at one or more postbaseline timepoint.

The ADA-evaluable analysis set includes all enrolled participants who received at least 1 dose of bemarituzumab and had at least 1 ADA sample drawn at any timepoint with available ADA data.

End point type	Secondary

End point timeframe:

Samples were collected for ADA analysis predose on day 1 of Cycles 1, 2, 3, 7, and 10 and at 28 days following the last dose.

Notes:

[28] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1: Bemarituzumab 15 mg/kg + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[29]	9[30]		
Units: participants	0	0		

Notes:

[29] - ADA-evaluable analysis set

[30] - ADA-evaluable analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS)[31]

End point description:

OS is defined as time from randomization until death from any cause. Participants who were lost to follow-up or did not have a date of death were censored at the last date that they were known to be alive. Participants with confirmed death or alive status after the data cutoff date were censored at the data cutoff date. Median OS was estimated using a Kaplan-Meier analysis.
"99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 23 September 2020; median time on follow-up was 10.9 months.

Notes:

[31] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 2: Bemarituzumab + mFOLFOX6	Phase 2: Placebo + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77[32]	78[33]		
Units: months				
median (confidence interval 95%)	99999 (13.8 to 99999)	12.9 (9.1 to 15.0)		

Notes:

[32] - Intent-to-treat population

[33] - Intent-to-treat population

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Phase 2: Bemarituzumab + mFOLFOX6 v Phase 2: Placebo + mFOLFOX6
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0268 [34]
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.95

Notes:

[34] - Stratified log-rank test adjusted for randomization stratification factors, including geographic region and administration of mFOLFOX6 single dose prior to randomization.

Secondary: Phase 2: Overall Response Rate (ORR)

End point title	Phase 2: Overall Response Rate (ORR)[35]

End point description:

Tumor response assessment was performed by the investigator per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 guidelines. ORR is defined as the percentage of participants who achieved a best overall response (BOR) of either complete response (CR) or partial response (PR) based on investigator assessment of tumor lesions per RECIST v1.1.
CR was defined as the disappearance of all lesions except lymph node short axis < 10 mm; PR was defined as a ≥ 30% reduction in sum of diameters in target lesions.

End point type	Secondary

End point timeframe:

Tumor assessments were performed every 8 weeks until 12 months and then every 12 weeks thereafter until disease progression or additional anticancer therapy was initiated; the median duration of follow-up time was 10.9 months.

Notes:

[35] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 2: Bemarituzumab + mFOLFOX6	Phase 2: Placebo + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77[36]	78[37]		
Units: percentage of participants				
number (confidence interval 95%)	46.8 (35.3 to 58.5)	33.3 (23.1 to 44.9)		

Notes:

[36] - Intent-to-treat population

[37] - Intent-to-treat population

Statistical analyses

Statistical analysis title	Analysis of ORR
Comparison groups	Phase 2: Bemarituzumab + mFOLFOX6 v Phase 2: Placebo + mFOLFOX6
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.106 [38]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference
Point estimate	13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	29

Notes:

[38] - P-value was calculated based on stratum-adjusted Cochran-Mantel-Haenszel (CMH) proportions

Secondary: Phase 2: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Phase 2: Number of Participants With Treatment-emergent Adverse Events (TEAEs)[39]

End point description:

TEAEs are defined as adverse events (AEs) that started or worsened from the start of study drug to 28 days after permanent discontinuation of study drug.
A serious AE is defined as any untoward medical occurrence that:
• Resulted in death;
• Was life-threatening;
• Required inpatient hospitalization or prolongation of existing hospitalization;
• Resulted in persistent or significant disability or incapacity;
• Was a congenital anomaly or birth defect.
The investigator assessed the causality/relationship between study treatment and each AE, and assessed the severity of each AE according to the NCI-CTCAE, version 5.0 on a scale from mild (Grade 1), moderate (Grade 2), severe (Grade 3), life-threatening (Grade 4), or death due to the AE (Grade 5). Cornea and retina AEs were defined by Standardized Medical Dictionary for Regulatory Activities Queries (SMQs) of corneal disorders and retinal disorders (broad).

End point type	Secondary

End point timeframe:

From first dose of study drug to 28 days after last dose of study drug. Actual median (min, max) duration of treatment emergent period was 29 (4.1, 157) weeks in the bemarituzumab + mFOLFOX6 group and 28 (4.3, 133) weeks in the placebo + mFOLFOX6 group.

Notes:

[39] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 2: Bemarituzumab + mFOLFOX6	Phase 2: Placebo + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[40]	77[41]		
Units: participants				
Any treatment-emergent adverse event (TEAE)	76	76		
TEAE with Grade ≥ 3	63	58		
TEAE related to any study drug	72	73		

TEAE with Grade ≥ 3 related to any study drug	57	48		
Serious adverse event (SAE)	26	28		
SAE related to any study drug	11	15		
TEAE leading to discontinuation of BEMA/placebo	31	4		
TEAE leading to DC of any agent of mFOLFOX6	35	29		
TEAE leading to dose reduction of BEMA/placebo	9	7		
TEAE leading to dose reduction of mFOLFOX6	48	44		
TEAE leading to dose delay of BEMA/placebo	51	41		
TEAE leading to dose delay of mFOLFOX6	54	44		
TE-AESI: Corneal disorders	51	8		
TE-AESI: Corneal disorders with Grade ≥ 3	21	0		
TE-AESI: Corneal disorders related to BEMA/placebo	46	7		
TE-AESI: Corneal disorders leading to DC of BEMA	24	0		
TE-AESI: Retinal disorders	18	7		
TE-AESI: Retinal disorders with Grade ≥ 3	1	0		
TE-AESI: Retinal disorders related to BEMA/placebo	12	5		
TE-AESI: Retinol disorders leading to DC of BEMA	2	0		
TEAE leading to death (Grade 5)	5	4		

Notes:

[40] - Safety analysis set

[41] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Post-hoc: Phase 2: Overall Survival - Updated Analysis

End point title	Phase 2: Overall Survival - Updated Analysis[42]

End point description:

OS is defined as time from randomization until death from any cause. Participants who were lost to follow-up or did not have a date of death were censored at the last date that they were known to be alive. Median OS was estimated using a Kaplan-Meier analysis.
"99999" indicates values that could not be estimated due to the low number of events.

End point type	Post-hoc

End point timeframe:

From randomization until 28 February 2021; median time on follow-up was 12.5 months.

Notes:

[42] - 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: Phase 1 and Phase 2 results are reported separately.

End point values	Phase 2: Bemarituzumab + mFOLFOX6	Phase 2: Placebo + mFOLFOX6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77[43]	78[44]		
Units: months				
median (confidence interval 95%)	19.2 (13.6 to 99999)	13.5 (9.3 to 15.9)		

Notes:

[43] - Intent-to-treat population

[44] - Intent-to-treat population

Statistical analyses

Statistical analysis title	Post-hoc Analysis of Overall Survival

Statistical analysis description:

Hazard ratio and 95% CIs were calculated using the Cox proportional hazards model, adjusted for randomization stratification factors, including geographic region and administration of mFOLFOX6 single dose prior to randomization.

Comparison groups	Phase 2: Bemarituzumab + mFOLFOX6 v Phase 2: Placebo + mFOLFOX6
Number of subjects included in analysis	155
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.94

Adverse events information

Timeframe for reporting adverse events:

Deaths: Up to end of study; median (range) time on study was 21 (4-50) weeks in Phase 1, 59 (1-176) weeks in Phase 2.
AEs: From first dose to 28 days after last dose; median (range) duration was 19 (4-35) weeks in Phase 1, 29 (4-157) weeks in Phase 2.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6

Reporting group description:

Participants received 6 mg/kg bemarituzumab administered Q2W and mFOLFOX6 chemotherapy administered Q2W until unacceptable toxicity, disease progression, or death.

Reporting group title	Phase 1:Bemarituzumab 15 mg/kg + mFOLFOX6

Reporting group description:

Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W.
Treatment continued until unacceptable toxicity, disease progression, or death.

Reporting group title	Phase 2: Placebo + mFOLFOX6

Reporting group description:

Participants received placebo for bemarituzumab administered Q2W with a single additional placebo dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.

Reporting group title	Phase 2: Bemarituzumab + mFOLFOX6

Reporting group description:

Participants received 15 mg/kg bemarituzumab administered Q2W with a single additional bemarituzumab 7.5 mg/kg dose on cycle 1 day 8. Participants also received mFOLFOX6 chemotherapy administered Q2W. Treatment continued until unacceptable toxicity, disease progression, or death.

Serious adverse events	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1:Bemarituzumab 15 mg/kg + mFOLFOX6	Phase 2: Placebo + mFOLFOX6
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	4 / 9 (44.44%)	28 / 77 (36.36%)
number of deaths (all causes)	0	2	55
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tumour haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Hypovolaemic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Incarcerated hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Drug hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Product issues			
Device issue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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

Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Cholecystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
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			
Appendicitis perforated			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Biliary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Lung abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
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 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2: Bemarituzumab + mFOLFOX6		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 76 (34.21%)		
number of deaths (all causes)	53		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Incarcerated hernia			

subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug hypersensitivity				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	2 / 76 (2.63%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			

Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device issue			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
White blood cell count increased			

subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Procedural complication			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombotic microangiopathy			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Diarrhoea			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric perforation			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mechanical ileus			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal perforation				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Oesophageal varices haemorrhage				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 76 (2.63%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholangitis				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaundice cholestatic				

subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary tract infection			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lung abscess			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Pneumonia aspiration			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	1 / 2		
Septic shock			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			

subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1: Bemarituzumab 6 mg/kg + mFOLFOX6	Phase 1:Bemarituzumab 15 mg/kg + mFOLFOX6	Phase 2: Placebo + mFOLFOX6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	9 / 9 (100.00%)	75 / 77 (97.40%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	5 / 77 (6.49%)
occurrences (all)	0	0	12
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	16 / 77 (20.78%)
occurrences (all)	0	0	25
Chills			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	2 / 77 (2.60%)
occurrences (all)	0	2	2
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	8 / 9 (88.89%)	21 / 77 (27.27%)
occurrences (all)	1	13	57

Feeling cold			
subjects affected / exposed	0 / 3 (0.00%)	3 / 9 (33.33%)	1 / 77 (1.30%)
occurrences (all)	0	4	1
Infusion site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	3 / 9 (33.33%)	4 / 77 (5.19%)
occurrences (all)	1	4	4
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	4
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	12 / 77 (15.58%)
occurrences (all)	0	0	17
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	8 / 77 (10.39%)
occurrences (all)	0	0	8
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	3 / 77 (3.90%)
occurrences (all)	1	1	5
Nasal congestion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Nasal ulcer			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			

subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	5 / 77 (6.49%)
occurrences (all)	0	1	7
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	5 / 77 (6.49%)
occurrences (all)	1	1	6
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	11 / 77 (14.29%)
occurrences (all)	0	0	37
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	15 / 77 (19.48%)
occurrences (all)	0	0	45
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	5 / 77 (6.49%)
occurrences (all)	0	0	6
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	18
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	7
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 9 (33.33%)	2 / 77 (2.60%)
occurrences (all)	0	4	12
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	33 / 77 (42.86%)
occurrences (all)	0	1	116
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	21 / 77 (27.27%)
occurrences (all)	0	3	72
Weight decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	10 / 77 (12.99%)
occurrences (all)	0	1	15
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	5
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	12 / 77 (15.58%)
occurrences (all)	0	0	51
Injury, poisoning and procedural complications			
Corneal abrasion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	2 / 77 (2.60%)
occurrences (all)	0	1	3
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	7 / 77 (9.09%)
occurrences (all)	0	0	21
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	4
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	6 / 77 (7.79%)
occurrences (all)	0	1	10
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	1	0	6
Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			

subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	11 / 77 (14.29%)
occurrences (all)	0	3	17
Neurotoxicity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	5 / 77 (6.49%)
occurrences (all)	0	0	8
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	10 / 77 (12.99%)
occurrences (all)	0	2	22
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	15 / 77 (19.48%)
occurrences (all)	0	0	27
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Tremor			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 9 (33.33%)	28 / 77 (36.36%)
occurrences (all)	0	3	92
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	9 / 77 (11.69%)
occurrences (all)	0	1	60
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 9 (33.33%)	13 / 77 (16.88%)
occurrences (all)	0	3	38
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 9 (33.33%)	4 / 77 (5.19%)
occurrences (all)	2	4	7
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Blepharospasm			

subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Conjunctivochalasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Corneal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Corneal epithelium defect			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	5 / 77 (6.49%)
occurrences (all)	0	3	5
Eye pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	3 / 77 (3.90%)
occurrences (all)	1	0	5
Eye pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	2	1	0
Limbal stem cell deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Myopia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Photophobia			

subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Pinguecula			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Punctate keratitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	2 / 77 (2.60%)
occurrences (all)	0	5	2
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	1 / 77 (1.30%)
occurrences (all)	0	3	1
Vitreous floaters			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	2 / 77 (2.60%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	6 / 77 (7.79%)
occurrences (all)	1	0	8
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	3 / 9 (33.33%)	20 / 77 (25.97%)
occurrences (all)	3	3	28
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	5 / 77 (6.49%)
occurrences (all)	0	0	8
Anorectal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	3 / 77 (3.90%)
occurrences (all)	0	1	3

Constipation			
subjects affected / exposed	1 / 3 (33.33%)	2 / 9 (22.22%)	24 / 77 (31.17%)
occurrences (all)	1	2	30
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	4 / 9 (44.44%)	23 / 77 (29.87%)
occurrences (all)	3	5	30
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	1 / 77 (1.30%)
occurrences (all)	0	2	1
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	9 / 77 (11.69%)
occurrences (all)	0	0	11
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	6
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Loose tooth			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	3 / 3 (100.00%)	4 / 9 (44.44%)	41 / 77 (53.25%)
occurrences (all)	4	4	95
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	1 / 77 (1.30%)
occurrences (all)	0	2	1
Stomatitis			
subjects affected / exposed	2 / 3 (66.67%)	3 / 9 (33.33%)	10 / 77 (12.99%)
occurrences (all)	2	3	19
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	4 / 9 (44.44%)	23 / 77 (29.87%)
occurrences (all)	1	5	41
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	6 / 77 (7.79%)
occurrences (all)	0	0	6
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	2 / 77 (2.60%)
occurrences (all)	0	1	2
Nail discolouration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Onychalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Onycholysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Onychomadesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences (all)	1	1	1
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	2	0

Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	8 / 77 (10.39%)
occurrences (all)	0	0	11
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	2
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	3 / 9 (33.33%)	1 / 77 (1.30%)
occurrences (all)	0	3	1
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	3 / 77 (3.90%)
occurrences (all)	0	1	5
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	3 / 77 (3.90%)
occurrences (all)	0	1	3
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	2 / 77 (2.60%)
occurrences (all)	0	1	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 9 (22.22%)	5 / 77 (6.49%)
occurrences (all)	0	2	7
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	3 / 77 (3.90%)
occurrences (all)	0	1	3
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	4 / 77 (5.19%)
occurrences (all)	0	0	5
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	5 / 77 (6.49%)
occurrences (all)	0	0	6
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	2 / 77 (2.60%)
occurrences (all)	0	2	2

Dermatophytosis of nail			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Stoma site infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	3 / 77 (3.90%)
occurrences (all)	1	0	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	4 / 9 (44.44%)	28 / 77 (36.36%)
occurrences (all)	2	4	53
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	3 / 77 (3.90%)
occurrences (all)	0	2	4
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	10 / 77 (12.99%)
occurrences (all)	0	0	14
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	7 / 77 (9.09%)
occurrences (all)	0	1	8
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Hyponatraemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	4 / 77 (5.19%)
occurrences (all)	0	1	4
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	1 / 77 (1.30%)
occurrences (all)	0	1	1

Non-serious adverse events	Phase 2: Bemarituzumab + mFOLFOX6		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 76 (100.00%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	20 / 76 (26.32%)		
occurrences (all)	65		
Chills			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	16 / 76 (21.05%)		
occurrences (all)	31		
Feeling cold			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Infusion site pain			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	8 / 76 (10.53%)		
occurrences (all)	35		
Oedema peripheral			

subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	10 / 76 (13.16%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	8 / 76 (10.53%)		
occurrences (all)	11		
Dyspnoea			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	17 / 76 (22.37%)		
occurrences (all)	24		
Nasal congestion			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Nasal ulcer			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	3		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	23 / 76 (30.26%)		
occurrences (all)	52		
Aspartate aminotransferase increased			
subjects affected / exposed	24 / 76 (31.58%)		
occurrences (all)	56		
Blood alkaline phosphatase increased			
subjects affected / exposed	7 / 76 (9.21%)		
occurrences (all)	13		
Blood bilirubin increased			
subjects affected / exposed	7 / 76 (9.21%)		
occurrences (all)	17		
Blood creatinine increased			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Lymphocyte count decreased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	31 / 76 (40.79%)		
occurrences (all)	129		
Platelet count decreased			
subjects affected / exposed	14 / 76 (18.42%)		
occurrences (all)	37		
Weight decreased			
subjects affected / exposed	16 / 76 (21.05%)		
occurrences (all)	22		
Weight increased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	16 / 76 (21.05%)		
occurrences (all)	103		
Injury, poisoning and procedural complications			

Corneal abrasion			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	6 / 76 (7.89%)		
occurrences (all)	16		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 76 (7.89%)		
occurrences (all)	9		
Dysgeusia			
subjects affected / exposed	5 / 76 (6.58%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	7 / 76 (9.21%)		
occurrences (all)	8		
Neuralgia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	13 / 76 (17.11%)		
occurrences (all)	23		
Neurotoxicity			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	5		
Paraesthesia			
subjects affected / exposed	13 / 76 (17.11%)		
occurrences (all)	24		
Peripheral sensory neuropathy			

subjects affected / exposed	15 / 76 (19.74%)		
occurrences (all)	28		
Taste disorder			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	3		
Tremor			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	25 / 76 (32.89%)		
occurrences (all)	80		
Leukopenia			
subjects affected / exposed	8 / 76 (10.53%)		
occurrences (all)	35		
Neutropenia			
subjects affected / exposed	15 / 76 (19.74%)		
occurrences (all)	63		
Thrombocytopenia			
subjects affected / exposed	11 / 76 (14.47%)		
occurrences (all)	36		
Eye disorders			
Blepharitis			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	4		
Blepharospasm			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Cataract			
subjects affected / exposed	7 / 76 (9.21%)		
occurrences (all)	9		
Conjunctivochalasis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Corneal disorder			

subjects affected / exposed	4 / 76 (5.26%)			
occurrences (all)	11			
Corneal epithelium defect				
subjects affected / exposed	7 / 76 (9.21%)			
occurrences (all)	13			
Dry eye				
subjects affected / exposed	21 / 76 (27.63%)			
occurrences (all)	32			
Eye pain				
subjects affected / exposed	3 / 76 (3.95%)			
occurrences (all)	3			
Eye pruritus				
subjects affected / exposed	1 / 76 (1.32%)			
occurrences (all)	1			
Keratitis				
subjects affected / exposed	11 / 76 (14.47%)			
occurrences (all)	22			
Lacrimation increased				
subjects affected / exposed	3 / 76 (3.95%)			
occurrences (all)	7			
Limbal stem cell deficiency				
subjects affected / exposed	6 / 76 (7.89%)			
occurrences (all)	7			
Myopia				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences (all)	0			
Photophobia				
subjects affected / exposed	2 / 76 (2.63%)			
occurrences (all)	2			
Pinguecula				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences (all)	0			
Punctate keratitis				
subjects affected / exposed	10 / 76 (13.16%)			
occurrences (all)	23			
Ulcerative keratitis				

subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	4		
Vision blurred			
subjects affected / exposed	13 / 76 (17.11%)		
occurrences (all)	16		
Vitreous floaters			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	3		
Abdominal distension			
subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	4		
Abdominal pain			
subjects affected / exposed	17 / 76 (22.37%)		
occurrences (all)	31		
Abdominal pain upper			
subjects affected / exposed	6 / 76 (7.89%)		
occurrences (all)	7		
Anorectal discomfort			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Ascites			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	23 / 76 (30.26%)		
occurrences (all)	37		
Diarrhoea			
subjects affected / exposed	31 / 76 (40.79%)		
occurrences (all)	58		
Dry mouth			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	4		

Dyspepsia			
subjects affected / exposed	7 / 76 (9.21%)		
occurrences (all)	11		
Dysphagia			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Loose tooth			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	37 / 76 (48.68%)		
occurrences (all)	92		
Oral pain			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Stomatitis			
subjects affected / exposed	26 / 76 (34.21%)		
occurrences (all)	68		
Vomiting			
subjects affected / exposed	23 / 76 (30.26%)		
occurrences (all)	51		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 76 (6.58%)		
occurrences (all)	5		
Dermatitis acneiform			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Nail discolouration			

subjects affected / exposed	1 / 76 (1.32%)			
occurrences (all)	1			
Nail disorder				
subjects affected / exposed	6 / 76 (7.89%)			
occurrences (all)	6			
Night sweats				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences (all)	0			
Onychalgia				
subjects affected / exposed	3 / 76 (3.95%)			
occurrences (all)	4			
Onychoclasis				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences (all)	0			
Onycholysis				
subjects affected / exposed	5 / 76 (6.58%)			
occurrences (all)	10			
Onychomadesis				
subjects affected / exposed	5 / 76 (6.58%)			
occurrences (all)	5			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	6 / 76 (7.89%)			
occurrences (all)	13			
Photosensitivity reaction				
subjects affected / exposed	0 / 76 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	8 / 76 (10.53%)			
occurrences (all)	14			
Rash				
subjects affected / exposed	4 / 76 (5.26%)			
occurrences (all)	9			
Rash maculo-papular				
subjects affected / exposed	2 / 76 (2.63%)			
occurrences (all)	2			

Urticaria			
subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	8		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	3		
Muscular weakness			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	5 / 76 (6.58%)		
occurrences (all)	6		
Dermatophytosis of nail			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Oesophageal candidiasis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Onychomycosis			
subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	4		

Rhinitis subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Stoma site infection subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	23 / 76 (30.26%) 38		
Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 3		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 10		
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 14		
Hypomagnesaemia subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 7		
Hyponatraemia subjects affected / exposed occurrences (all)	5 / 76 (6.58%) 9		
Hypophosphataemia subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2018	Major changes included: - Updated phase 3 objectives and endpoints to reflect OS instead of PFS; - Updated method of radiological assessment to investigator assessed instead of blinded independent central review; - Updated statistical methods to support revised endpoint of OS, increase in phase 3 sample size; - Revised adverse event reporting period for ophthalmologic exams; - Updated clinical experience of bemarituzumab based on recent data, clarified the timing for serious adverse event reporting; - Defined adverse events of special interest; - Updated timing of tumor scans.
19 November 2018	Major changes included: - Removed language involving informed consent requirements in protocol synopsis; - Clarified distinction between prescreening and screening period; - Added phase 3 recommended dose; - Added exception for anemia to exclusion criteria; - Revised window for baseline radiographic imaging to be within 28 days (± 3 days); - Clarified when and how bemarituzumab dose recalculations should be performed; - Removed rounding convention for oxaliplatin and 5-FU; - Addressed explicit dose levels for dose reduction; - Added PI ability to unblind treatment code in case of emergency.
05 June 2020	Major changes included: - Changed study design to phase 2; - Changed primary endpoint to PFS; - Changed secondary endpoint to OS; - Changed PK/ADA to exploratory endpoints; - Removed circulating tumor DNA (ctDNA) analysis at end of treatment (EOT).
10 March 2021	Major changes included: - Updated long term follow up (LTFU) survival duration (phase 2) to 24 months; - The planned duration for study completion approximately 43 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36244398

http://www.ncbi.nlm.nih.gov/pubmed/32965540