Clinical trial results:
A Phase 2a Randomized, Open-Label Study to Assess the Safety, Tolerability, and Efficacy of BAX69 in Combination with 5 FU/Leucovorin or Panitumumab versus Standard of Care in Subjects with Metastatic Colorectal Cancer

Summary

EudraCT number	2015-000896-28
Trial protocol	GB DE ES
Global end of trial date	15 February 2017

Results information

Result version number	v1 (current)
This version publication date	03 March 2018
First version publication date	03 March 2018

Trial information

Trial identification

Sponsor protocol code	391401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02448810
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, MA,, United States, 02421
Public contact	Study Physician, Shire, 1 866-842-5335, ClinicalTransparency@shire.com
Scientific contact	Study Physician, Shire, 1 866-842-5335, ClinicalTransparency@shire.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	15 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to determine the recommended Phase 2 dose (RP2D) of imalumab in combination with 5 Fluorouracil (5 FU)/Leucovorin (LV) or panitumumab (Part 1) and to compare progression free survival (PFS) between imalumab in combination with 5 FU/LV for subjects with mutated kirsten rat sarcoma viral oncogene homolog, mutated neuroblastoma rat sarcoma viral oncogene homolog (KRAS mut and/or NRAS mut tumors) or in combination with panitumumab for subjects with wild type kirsten rat sarcoma viral oncogene homolog, wild type neuroblastoma rat sarcoma viral oncogene homolog (KRAS wt and NRAS wt tumors), versus standard of care ([SoC] investigator choice), as third or fourth treatment line (Part 2).

Protection of trial subjects:

This study was conducted in accordance with current applicable regulations, International Council for Harmonisation (ICH) of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	United States: 44
Worldwide total number of subjects	85
EEA total number of subjects	41

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)	53
From 65 to 84 years	31
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 21 centers in the United States, the United Kingdom and Spain between 15 June 2015 (first subject first visit) and 15 February 2017 (last subject last visit).

Pre-assignment

Screening details:

A total of 115 subjects were screened (17 and 98 for part 1 and part 2). Of them, 5 subjects failed screening and 12 received treatment in part 1 and 17 failed screening and 8 signed informed consent but were not enrolled due to over screening, thus 73 subjects were enrolled, of which 67 subjects received treatment in part 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV

Arm description:

Subjects with mutated tumors (mutated kirsten rat sarcoma viral oncogene homolog, mutated neuroblastoma rat sarcoma viral oncogene homolog [KRAS mut, NRAS mut]) received 7.5 milligram per kilogram (mg/kg) dose of imalumab every week (QW) in combination with 5-Fluorouracil/Leucovorin ([FU/LV] LV 400 milligram per square meter [mg/m^2] intravenous [IV] infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) for every two weeks (Q2W) IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	5 Fluorouracil (FU)/Leucovorin (LV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 7.5 mg/kg or 10 mg/kg of imalumab IV infusion QW as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm title	Part 1: Imalumab 7.5 mg/kg + Panitumumab

Arm description:

Subjects with wild-type tumors (wild type Kirsten rat sarcoma viral oncogene homolog, wild neuroblastoma rat sarcoma viral oncogene homolog [KRAS wt, NRAS wt]) received 7.5 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 7.5 mg/kg or 10 mg/kg of imalumab IV infusion QW as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

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

Dosage and administration details:

Subjects received 6 mg/kg of panitumumab IV infusion Q2W as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm title	Part 1: Imalumab 10 mg/kg + 5-FU/LV

Arm description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	5 Fluorouracil (FU)/Leucovorin (LV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 7.5 mg/kg or 10 mg/kg of imalumab IV infusion QW as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm title	Part 1: Imalumab 10 mg/kg + Panitumumab

Arm description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	Experimental

Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 7.5 mg/kg or 10 mg/kg of imalumab IV infusion QW as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

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

Dosage and administration details:

Subjects received 6 mg/kg of panitumumab IV infusion Q2W as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm title	Part 2: Imalumab 10 mg/kg + 5-FU/LV

Arm description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab as a recommended phase 2 dose (RP2D) QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 7.5 mg/kg or 10 mg/kg of imalumab IV infusion QW as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Investigational medicinal product name	5 Fluorouracil (FU)/Leucovorin (LV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm title	Part 2: Standard of Care Mutant

Arm description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received standard of care (SoC) as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Part 2: Imalumab 10 mg/kg + Panitumumab

Arm description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab as a RP2D

QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

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

Dosage and administration details:

Subjects received 6 mg/kg of panitumumab IV infusion Q2W as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 7.5 mg/kg or 10 mg/kg of imalumab IV infusion QW as part of a 4-week /28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm title	Part 2: Standard of Care Wild Type

Arm description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received SoC as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV
Started	3	3	3
Treated	3	3	3
Completed	0	0	0
Not completed	3	3	3
Adverse event, serious fatal	1	-	1
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	1
Other (study terminated by sponsor)	-	-	-
Other (Progressive disease)	2	2	-
Other (unspecified)	-	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Part 1: Imalumab 10 mg/kg + Panitumumab	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant

Started	3	31	16
Treated	3	29	13
Completed	0	0	0
Not completed	3	31	16
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	3	5
Adverse event, non-fatal	-	-	-
Other (study terminated by sponsor)	-	4	2
Other (Progressive disease)	3	23	9
Other (unspecified)	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Started	18	8
Treated	18	7
Completed	0	0
Not completed	18	8
Adverse event, serious fatal	-	-
Consent withdrawn by subject	-	2
Adverse event, non-fatal	-	-
Other (study terminated by sponsor)	2	1
Other (Progressive disease)	14	5
Other (unspecified)	2	-
Lost to follow-up	-	-

Baseline characteristics

Reporting groups

Reporting group title	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV

Reporting group description:

Subjects with mutated tumors (mutated kirsten rat sarcoma viral oncogene homolog, mutated neuroblastoma rat sarcoma viral oncogene homolog [KRAS mut, NRAS mut]) received 7.5 milligram per kilogram (mg/kg) dose of imalumab every week (QW) in combination with 5-Fluorouracil/Leucovorin ([FU/LV] LV 400 milligram per square meter [mg/m^2] intravenous [IV] infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) for every two weeks (Q2W) IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 7.5 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (wild type Kirsten rat sarcoma viral oncogene homolog, wild neuroblastoma rat sarcoma viral oncogene homolog [KRAS wt, NRAS wt]) received 7.5 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 10 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 10 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Imalumab 10 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab as a recommended phase 2 dose (RP2D) QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Standard of Care Mutant

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received standard of care (SoC) as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Imalumab 10 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab as a RP2D QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Standard of Care Wild Type

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received SoC as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV
Number of subjects	3	3	3
Age categorical Units: Subjects			
Adults (18-64 years)	1	0	3
From 65-84 years	2	3	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	1	0	0
Male	2	3	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	3	2	3
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	2	3	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Part 1: Imalumab 10 mg/kg + Panitumumab	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant
Number of subjects	3	31	16
Age categorical Units: Subjects			
Adults (18-64 years)	2	19	12
From 65-84 years	1	11	4
85 years and over	0	1	0
Gender categorical Units: Subjects			
Female	1	13	5
Male	2	18	11
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	5	2
Not Hispanic or Latino	2	26	14
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	2

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	4	0
White	2	26	14
More than one race	0	0	0
Unknown or Not Reported	1	0	0

Reporting group values	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type	Total
Number of subjects	18	8	85
Age categorical Units: Subjects			
Adults (18-64 years)	12	4	53
From 65-84 years	6	4	31
85 years and over	0	0	1
Gender categorical Units: Subjects			
Female	7	6	33
Male	11	2	52
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	0	12
Not Hispanic or Latino	15	8	73
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	7
White	18	6	74
More than one race	0	0	0
Unknown or Not Reported	0	0	1

End points

End points reporting groups

Reporting group title	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV

Reporting group description:

Subjects with mutated tumors (mutated kirsten rat sarcoma viral oncogene homolog, mutated neuroblastoma rat sarcoma viral oncogene homolog [KRAS mut, NRAS mut]) received 7.5 milligram per kilogram (mg/kg) dose of imalumab every week (QW) in combination with 5-Fluorouracil/Leucovorin ([FU/LV] LV 400 milligram per square meter [mg/m^2] intravenous [IV] infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) for every two weeks (Q2W) IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 7.5 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (wild type Kirsten rat sarcoma viral oncogene homolog, wild neuroblastoma rat sarcoma viral oncogene homolog [KRAS wt, NRAS wt]) received 7.5 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 10 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 10 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Imalumab 10 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab as a recommended phase 2 dose (RP2D) QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Standard of Care Mutant

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received standard of care (SoC) as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Imalumab 10 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab as a RP2D QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Standard of Care Wild Type

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received SoC as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

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

End point title	Part 2: Progression-Free Survival (PFS)[1]

End point description:

PFS was defined as time between treatment initiation and tumor progression or death from any cause, with censoring of subjects who were lost to follow-up or withdrew consent. Full analysis set (FAS) included all subjects who received at least 1 administration of study drug, and who had 1 postbaseline tumor response assessment based on RECIST v1.1, or died within 18 weeks of the start of treatment. '99999' indicates data for upper limit was not available.

End point type	Primary

End point timeframe:

From start of the study up to safety follow-up visit occurred (30 [-/+7]) days after the last dose of study treatment or until disease progression

Notes:

[1] - 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: Subjects included in Part 1 arms were excluded for this analysis since they did not contribute to the progression-free survival evaluation.

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	12	18	7
Units: weeks				
median (confidence interval 95%)				
weeks	11.1 (8.4 to 16.1)	8.3 (7.4 to 23.3)	9.3 (8.1 to 24.9)	7.3 (3.7 to 99999)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Hazard Ratio and 70% confidence interval (CI) are based on a Cox proportional hazards model with a covariate for treatment (imalumab vs SoC).

Comparison groups	Part 2: Imalumab 10 mg/kg + 5-FU/LV v Part 2: Standard of Care Mutant
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.246 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	Other: 70 %
sides	2-sided
lower limit	0.5
upper limit	1.1

Notes:

[2] - P-value is based on a one-sided log-rank test.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Hazard Ratio and 70% CI are based on a Cox proportional hazards model with a covariate for treatment (imalumab vs SoC).

Comparison groups	Part 2: Standard of Care Wild Type v Part 2: Imalumab 10 mg/kg + Panitumumab
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.354 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	Other: 70 %
sides	2-sided
lower limit	0.5
upper limit	1.4

Notes:

[3] - P-value is based on a one-sided log-rank test.

Primary: Part 1: Number of Subjects With Occurrence of Dose Limiting Toxicity (DLT)

End point title	Part 1: Number of Subjects With Occurrence of Dose Limiting Toxicity (DLT)[4][5]

End point description:

DLT was defined as any drug-related TEAE (graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] v4.03) that occurs during the first 28 days after treatment start and that meets any of the following criteria: i) >= Grade 3 non-hematologic toxicity (excluding: mucositis/stomatitis of Grade 3; diarrhea of <3 days duration; nausea and vomiting <3 days duration; fatigue of <7 days duration; alopecia; single laboratory value out of the normal range that has no clinical significance and that resolves to <= Grade 2 with adequate measures within 7 days ii) Any Grade 4 hematologic toxicity (excluding: grade 4 neutropenia lasting for <= 5 days; isolated grade 4 lymphocytopenia iii) Grade 3 febrile neutropenia iv) Grade 3 thrombocytopenia associated with bleeding v) Any life-threatening complication or abnormality not covered in NCI CTCAEv4.03. SAS included all subjects who received at least 1 administration of study drug.

End point type	Primary

End point timeframe:

From start of study treatment up to 28 days

Notes:

[4] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[5] - 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: Subjects from Part 2 arms were excluded from this analysis since they did not contribute to the dose-limiting toxicity evaluation.

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: subjects				
Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Occurrence of Binding and/or Neutralizing Anti-imalumab Antibodies

End point title	Number of Subjects With Occurrence of Binding and/or Neutralizing Anti-imalumab Antibodies

End point description:

Number of subjects with occurrence of binding and/or neutralizing anti-imalumab antibodies were reported. Safety analysis set (SAS) included all subjects who received at least 1 administration of study drug. Here BA refers to binding antibody and NA refers to neutralizing antibody.

End point type	Secondary

End point timeframe:

From start of study drug administration up to end of treatment (EOT) (approximately 21 Months)

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: subjects				
Baseline (BA) (n=3, 3, 3, 1, 27, 12,18, 6)	0	0	0	0
End of Study (BA) (n=2, 1, 3, 1, 19, 2, 12, 2)	0	0	0	1
Baseline (NA) (n=3, 3, 3, 1, 27, 12,18, 6)	0	0	0	0
End of Study (NA) (n=2, 1, 3, 1, 19, 2, 12, 2)	0	0	0	0

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	13	18	7
Units: subjects				

Baseline (BA) (n=3, 3, 3, 1, 27, 12,18, 6)	0	0	1	0
End of Study (BA) (n=2, 1, 3, 1, 19, 2, 12, 2)	0	0	0	0
Baseline (NA) (n=3, 3, 3, 1, 27, 12,18, 6)	0	0	0	0
End of Study (NA) (n=2, 1, 3, 1, 19, 2, 12, 2)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Incidence and Severity of Infusion Reactions After Imalumab Administration

End point title	Number of Subjects With Incidence and Severity of Infusion Reactions After Imalumab Administration

End point description:

Infusion reaction was defined as any relevant sign or symptom occurring during or after imalumab infusion and considered by the investigator as an infusion reaction. SAS included all subjects who received at least 1 administration of study drug.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOT (approximately 21 Months)

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: subjects				
Subjects	0	0	0	0

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	13	18	7
Units: subjects				
Subjects	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs) and Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Serious Adverse Events (SAEs) and Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was any AE that results in any of the following outcomes: death, a life-threatening event, inpatient hospitalization or prolongation of an existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly/birth defect, other medically important events based upon appropriate medical judgement. TEAEs were defined as any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments. SAS included all subjects who received at least 1 administration of study drug.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOT (approximately 21 Months)

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: number of subjects				
SAEs	1	1	1	2
TEAEs	3	3	3	3

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	13	18	7
Units: number of subjects				
SAEs	15	8	7	2
TEAEs	28	13	17	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Response Evaluation According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point title	Number of Subjects With Response Evaluation According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

End point description:

Number of subjects with response evaluation according to RECIST v1.1 was evaluated according to complete response (CR): disappearance of all target and non-target lesions and no new lesions; partial response (PR): >= 30 percent (%) decrease in the sum of diameters of target lesions (compared to baseline) and no new lesions; stable disease (SD): neither sufficient shrinkage to qualify as a response nor sufficient growth to qualify as progression; progressive disease (PD): >= 20% increase in the sum of diameters of target lesions and an absolute increase in sum of diameters of >=5 millimeter (mm) (compared to the previous minimum sum) or progression of a new lesion. FAS included all subjects who received at least 1 administration of study drug, and who had 1 postbaseline tumor response.

End point type	Secondary

End point timeframe:

Day 28 of Cycle 2 followed by every 2 Cycles of 28 day Cycles: Day 56, Day 112, Day 168 and Day 224

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: subjects				
Best Overall Response: Complete Response (CR)	0	0	0	0
Best Overall Response: Partial Response (PR)	0	2	0	0
Best Overall Response: Stable Disease (SD)	1	1	2	1
Best Overall Response: Progressive Disease (PD)	2	0	1	2
Best Overall Response: Not Evaluable (NE)	0	0	0	0

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	12	18	7
Units: subjects				
Best Overall Response: Complete Response (CR)	0	0	0	0
Best Overall Response: Partial Response (PR)	0	0	3	1
Best Overall Response: Stable Disease (SD)	14	4	6	2
Best Overall Response: Progressive Disease (PD)	15	7	8	4
Best Overall Response: Not Evaluable (NE)	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from randomization until death due to any cause. FAS included all subjects who received at least 1 administration of study drug, and who had 1 postbaseline tumor response. Here '99999' indicates upper limit of 95% CI was not available and '88888' indicates median and 95% CI were not available due to insufficient number of events at the end of the study.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOT (approximately 21 Months)

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	2
Units: weeks				
median (confidence interval 95%)				
weeks	24.9 (7.4 to 40.4)	42.7 (15.4 to 77.4)	42.7 (16.9 to 42.7)	24.9 (9.4 to 42.1)

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	10	8	3
Units: weeks				
median (confidence interval 95%)				
weeks	31.9 (26.3 to 58.0)	27.2 (9.3 to 46.7)	31.4 (19.9 to 99999)	88888 (88888 to 88888)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Plasma Imalumab Concentrations in Combination With 5-Fluourouracil/Leucovorin (FU/LV) or Panitumumab

End point title	Number of Subjects With Plasma Imalumab Concentrations in Combination With 5-Fluourouracil/Leucovorin (FU/LV) or Panitumumab

End point description:

Imalumab plasma pharmacokinetic (PK) was characterized using a population PK modeling approach. Due to early termination and discontinuation of the imalumab clinical development program, no population PK analysis was performed, as the results of this analysis will not be needed for further

studies.

End point type	Secondary

End point timeframe:

Day 1 predose and postdose; Day 2 post first dose; Day 4 post first dose; Days 8, 15 and 22 predose and postdose

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[6]	0[7]	0[8]	0[9]
Units: Subjects				

Notes:

[6] - No PK analysis was performed.

[7] - No PK analysis was performed.

[8] - No PK analysis was performed.

[9] - No PK analysis was performed.

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[10]	0[11]	0[12]	0[13]
Units: Subjects				

Notes:

[10] - No PK analysis was performed.

[11] - No PK analysis was performed.

[12] - No PK analysis was performed.

[13] - No PK analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline for Quality of Life (QoL) Measure - European Organization for Research and Treatment of Cancer Quality of life Questionnaire Core 30 (EORTC QLQ-C30)

End point title	Change From Baseline for Quality of Life (QoL) Measure - European Organization for Research and Treatment of Cancer Quality of life Questionnaire Core 30 (EORTC QLQ-C30)

End point description:

EORTC QLQ-C30 was used to measure QOL and assess symptoms and side effects of treatment and the impact on everyday life. The QLQ-C30 was composed of 5 multi-item functional scales (FS) (physical [PFS], role [RFS], social [SFS], emotional [EFS] and cognitive functioning [CFS]), a global health status (GHS)/QoL scale, and 9 symptom scales (SS) (fatigue [FSS], nausea/vomiting [NVSS], pain [PSS], financial impact/difficulties [FDSS], appetite loss [ALSS], diarrhea [Dia SS], constipation [CSS], sleep disturbance/insomnia [ISS] and dyspnea [Dys SS]). Most items were answered on a 4-point scale (i.e., 1=Not at all,2=A Little,3=Quite a bit,4=Very Much) except items contributing to GHS/QOL which have a 7-point scale:1=very poor to 7=excellent. For GHS/FS scores-higher score:better QOL; SS scores-lower score:better QoL. SAS included all subjects who received at least 1 administration of study drug. '99999' and '88888': Mean/SD not calculated as number of subjects analyzed were less or 0.

End point type	Secondary

End point timeframe:
Baseline, 21 Months (EOT) up to follow-up

End point values	Part 1: Imalumab 7.5 mg/kg + 5 FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + Panitumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score on a scale				
arithmetic mean (standard deviation)				
GHS (Baseline) (n=3, 3, 3, 3, 29, 13, 17, 7)	33.33 (± 16.665)	66.7 (± 8.335)	75 (± 8.330)	66.67 (± 16.665)
GHS (CFB) (n=2, 0, 3, 1, 19, 8, 12, 5)	8.33 (± 35.355)	99999 (± 99999)	-5.56 (± 4.812)	-16.67 (± 88888)
PFS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	63.33 (± 26.031)	75.56 (± 19.249)	88.89 (± 7.696)	80 (± 6.670)
PFS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	0 (± 0)	99999 (± 99999)	-2.22 (± 7.699)	-20 (± 88888)
RFS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	50 (± 50)	88.89 (± 19.243)	72.22 (± 9.619)	77.78 (± 19.243)
RFS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	-25 (± 35.355)	99999 (± 99999)	-16.67 (± 16.670)	0 (± 88888)
EFS (Baseline) (n=3, 3, 3, 3, 28, 13, 17, 7)	79.67 (± 26.274)	97.22 (± 4.809)	91.67 (± 8.335)	83.33 (± 16.665)
EFS (CFB) (n=2, 0, 3, 1, 18, 8, 12, 5)	-7 (± 13.675)	99999 (± 99999)	-5.56 (± 17.346)	-41.66 (± 88888)
CFS (Baseline) (n=3, 3, 3, 3, 28, 13, 17, 7)	83.33 (± 16.665)	88.89 (± 19.243)	100 (± 0)	83.33 (± 16.665)
CFS (CFB) (n=2, 0, 3, 1, 18, 8, 12, 5)	0 (± 0)	99999 (± 99999)	0 (± 0)	-33.33 (± 88888)
SFS (Baseline) (n=3, 3, 3, 3, 28, 13, 17, 7)	77.78 (± 25.458)	66.67 (± 0)	77.78 (± 9.619)	77.78 (± 9.619)
SFS (CFB) (n=2, 0, 3, 1, 18, 8, 12, 5)	-8.34 (± 11.787)	99999 (± 99999)	-22.22 (± 9.630)	-33.34 (± 88888)
FSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	29.67 (± 28.015)	29.66 (± 6.351)	22.33 (± 0)	26 (± 6.351)
FSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	44.50 (± 15.797)	99999 (± 99999)	29.45 (± 23.089)	44.34 (± 88888)
NVSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	11.11 (± 19.243)	0 (± 0)	5.56 (± 9.624)	16.67 (± 16.665)
NVSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	25 (± 11.780)	99999 (± 99999)	5.55 (± 9.619)	-16.66 (± 88888)
PSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	38.89 (± 38.486)	27.78 (± 9.619)	16.67 (± 16.665)	38.89 (± 19.243)
PSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	41.66 (± 35.355)	99999 (± 99999)	11.11 (± 19.243)	0 (± 88888)
Dys SS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	11.11 (± 19.243)	11.11 (± 19.243)	0 (± 0)	22.22 (± 19.243)
Dys SS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	33.34 (± 47.143)	99999 (± 99999)	11.11 (± 19.243)	33.33 (± 88888)
ISS (Baseline) (n=3, 3, 3, 3, 27, 13, 18, 7)	44.45 (± 38.492)	0 (± 0)	33.33 (± 0)	22.22 (± 19.243)
ISS (CFB) (n=2, 0, 3, 1, 17, 8, 13, 5)	-0.01 (± 47.143)	99999 (± 99999)	33.34 (± 33.335)	0 (± 88888)
ALSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	11.11 (± 19.243)	22.22 (± 38.492)	11.11 (± 19.243)	22.22 (± 19.243)

ALSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	66.67 (± 0)	99999 (± 99999)	33.33 (± 33.335)	66.67 (± 88888)
CSS (Baseline) (n=3, 3, 3, 3, 29, 13, 18, 7)	11.11 (± 19.243)	22.22 (± 19.243)	0 (± 0)	22.22 (± 19.243)
CSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	0 (± 0)	99999 (± 99999)	22.22 (± 38.492)	0 (± 88888)
Dia SS (Baseline) (n=3, 3, 3, 3, 29, 13, 17, 7)	0 (± 0)	0 (± 0)	22.22 (± 19.243)	11.11 (± 19.243)
Dia SS (CFB) (n=2, 0, 3, 1, 19, 8, 12, 5)	33.33 (± 0)	99999 (± 99999)	11.11 (± 19.243)	-33.33 (± 88888)
FDS (Baseline) (n=3, 3, 3, 3, 29, 13, 17, 7)	11.11 (± 19.243)	11.11 (± 19.243)	44.44 (± 50.918)	44.44 (± 19.249)
FDS (CFB) (n=2, 0, 3, 1, 19, 8, 12, 5)	16.67 (± 23.568)	99999 (± 99999)	-11.11 (± 19.243)	0 (± 88888)

End point values	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	13	18	7
Units: score on a scale				
arithmetic mean (standard deviation)				
GHS (Baseline) (n=3, 3, 3, 3, 29, 13, 17, 7)	68.10 (± 18.510)	62.18 (± 25.371)	66.18 (± 22.529)	59.52 (± 19.501)
GHS (CFB) (n=2, 0, 3, 1, 19, 8, 12, 5)	-13.16 (± 23.293)	-13.54 (± 21.333)	-10.42 (± 17.810)	-11.67 (± 9.502)
PFS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	78.45 (± 18.670)	81.15 (± 15.537)	78.89 (± 20.612)	70 (± 17.950)
PFS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	-5 (± 17.198)	-21.04 (± 23.489)	-4.10 (± 10.379)	-14.67 (± 15.918)
RFS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	74.41 (± 24.630)	73.08 (± 30.076)	76.85 (± 19.078)	66.67 (± 25.459)
RFS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	-12.04 (± 24.122)	-16.67 (± 43.642)	-11.54 (± 29.957)	-10 (± 14.910)
EFS (Baseline) (n=3, 3, 3, 3, 28, 13, 17, 7)	78.87 (± 18.494)	73.08 (± 25.720)	77.45 (± 19.490)	66.66 (± 18.003)
EFS (CFB) (n=2, 0, 3, 1, 18, 8, 12, 5)	-3.24 (± 15.163)	-1.04 (± 16.925)	-2.78 (± 16.792)	-11.66 (± 20.916)
CFS (Baseline) (n=3, 3, 3, 3, 28, 13, 17, 7)	88.10 (± 18.063)	89.74 (± 14.496)	93.14 (± 10.306)	83.33 (± 23.571)
CFS (CFB) (n=2, 0, 3, 1, 18, 8, 12, 5)	-1.85 (± 15.003)	-27.08 (± 30.779)	-8.33 (± 15.075)	-6.67 (± 9.128)
SFS (Baseline) (n=3, 3, 3, 3, 28, 13, 17, 7)	88.69 (± 15.080)	80.77 (± 24.387)	73.53 (± 29.498)	66.67 (± 27.215)
SFS (CFB) (n=2, 0, 3, 1, 18, 8, 12, 5)	-13.89 (± 25.726)	-25 (± 15.430)	0 (± 38.924)	-10 (± 19.004)
FSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	33.74 (± 20.645)	38.46 (± 28.580)	29.63 (± 19.041)	41.24 (± 21.943)
FSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	9.28 (± 19.828)	23.63 (± 19.197)	3.44 (± 21.919)	13.33 (± 18.209)
NVSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	13.10 (± 22.843)	6.41 (± 10.841)	7.41 (± 11.746)	4.76 (± 8.134)
NVSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	2.78 (± 24.421)	14.58 (± 20.773)	5.13 (± 30.720)	10 (± 14.906)
PSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	31.55 (± 27.719)	23.08 (± 30.074)	22.22 (± 17.149)	35.71 (± 29.546)

PSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	5.55 (± 21.390)	12.50 (± 21.362)	6.41 (± 19.882)	13.33 (± 18.258)
Dys SS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	11.90 (± 20.716)	20.51 (± 25.599)	14.81 (± 26.127)	9.52 (± 16.263)
Dys SS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	5.56 (± 20.612)	16.67 (± 30.861)	17.95 (± 17.296)	6.67 (± 27.886)
ISS (Baseline) (n=3, 3, 3, 3, 27, 13, 18, 7)	23.46 (± 28.964)	20.51 (± 25.599)	22.22 (± 25.566)	47.62 (± 42.415)
ISS (CFB) (n=2, 0, 3, 1, 17, 8, 13, 5)	7.84 (± 34.421)	12.50 (± 30.537)	7.69 (± 14.616)	-6.67 (± 27.886)
ALSS (Baseline) (n=3, 3, 3, 3, 28, 13, 18, 7)	25 (± 33.488)	33.33 (± 38.490)	12.96 (± 20.256)	14.28 (± 17.816)
ALSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	9.26 (± 29.826)	4.17 (± 27.820)	7.69 (± 24.165)	20 (± 29.816)
CSS (Baseline) (n=3, 3, 3, 3, 29, 13, 18, 7)	17.24 (± 26.157)	25.64 (± 30.895)	22.22 (± 28.005)	19.05 (± 26.227)
CSS (CFB) (n=2, 0, 3, 1, 18, 8, 13, 5)	7.41 (± 33.442)	16.67 (± 43.645)	2.56 (± 34.591)	6.67 (± 27.886)
Dia SS (Baseline) (n=3, 3, 3, 3, 29, 13, 17, 7)	10.34 (± 18.046)	20.51 (± 34.798)	17.65 (± 26.660)	23.81 (± 25.198)
Dia SS (CFB) (n=2, 0, 3, 1, 19, 8, 12, 5)	8.77 (± 33.040)	8.33 (± 38.834)	-11.11 (± 16.411)	0 (± 23.568)
FDS (Baseline) (n=3, 3, 3, 3, 29, 13, 17, 7)	18.39 (± 30.324)	25.64 (± 33.758)	19.61 (± 23.743)	28.57 (± 23.003)
FDS (CFB) (n=2, 0, 3, 1, 19, 8, 12, 5)	-1.75 (± 25.996)	-12.50 (± 24.801)	-5.56 (± 12.976)	20 (± 18.259)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to 30 (+/-7) days after the last dose of study treatment (approximately 21 months)

Adverse event reporting additional description:

The MHRA identified data integrity issues and deficiencies for AEs/SAEs for non-Shire IMPs. As per Sponsor assessment, there was no impact of initial non-assessment of absence of causality for SAEs associated with non-Shire IMPs (i.e.,apart from BAX069) on patient safety, integrity of safety conclusion or on post-marketing safety profile.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Part 1: Imalumab 7.5 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 7.5 mg/kg dose of imalumab QW in combination with 5- FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) for Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 10 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 7.5 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 7.5 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 1: Imalumab 10 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Imalumab 10 mg/kg + 5-FU/LV

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received 10 mg/kg dose of imalumab as a recommended phase 2 dose (RP2D) QW in combination with 5-FU/LV (LV 400 mg/m^2 IV infusion over 2 hours, followed by 5 FU 2400 mg/m^2 IV infusion over 46 hours) Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Standard of Care Mutant

Reporting group description:

Subjects with mutated tumors (KRAS mut, NRAS mut) received standard of care (SoC) as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Imalumab 10 mg/kg + Panitumumab

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received 10 mg/kg dose of imalumab as a RP2D QW in combination with panitumumab 6 mg/kg Q2W IV infusion as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Reporting group title	Part 2: Standard of Care Wild Type

Reporting group description:

Subjects with wild-type tumors (KRAS wt, NRAS wt) received SoC as chosen by the investigator and was administered in accordance to product label as a part of 4-week/28-day treatment cycle and continued until disease progression, unacceptable toxicity, death, or subject withdrawal of consent, whichever occurred first.

Serious adverse events	Part 1: Imalumab 7.5 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer metastatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Rectal haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallbladder pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Perineal abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1: Imalumab 10 mg/kg + Panitumumab	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	15 / 29 (51.72%)	8 / 13 (61.54%)
number of deaths (all causes)	0	10	7
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 2
Rectal cancer metastatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Injury, poisoning and procedural			

complications			
Femoral neck fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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			
Atrial fibrillation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	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%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
General disorders and administration site conditions			
Disease progression			

subjects affected / exposed	0 / 3 (0.00%)	8 / 29 (27.59%)	3 / 13 (23.08%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 8	0 / 3
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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
Large intestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallbladder pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
Hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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			
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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

Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (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
Infections and infestations			
Perineal abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 18 (38.89%)	2 / 7 (28.57%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 18 (11.11%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Rectal cancer metastatic			

subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
General physical health deterioration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intestinal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Gallbladder pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary embolism			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Perineal abscess			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: Imalumab 7.5 mg/kg + 5-FU/LV	Part 1: Imalumab 10 mg/kg + 5-FU/LV	Part 1: Imalumab 7.5 mg/kg + Panitumumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Hypothermia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Temperature intolerance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Prostatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Scrotal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sexual dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Upper-Airway cough syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood albumin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laceration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Parosmia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Coagulopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Episcleritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal rigidity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Oral dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry skin			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nail discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-Plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Skin fissures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trichorrhexis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bone pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lymph gland infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1: Imalumab 10 mg/kg + Panitumumab	Part 2: Imalumab 10 mg/kg + 5-FU/LV	Part 2: Standard of Care Mutant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	28 / 29 (96.55%)	12 / 13 (92.31%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	6
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	6 / 29 (20.69%)	3 / 13 (23.08%)
occurrences (all)	0	13	5
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	16 / 29 (55.17%)	4 / 13 (30.77%)
occurrences (all)	0	28	11
Hypothermia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	9 / 29 (31.03%)	1 / 13 (7.69%)
occurrences (all)	0	18	2
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	3 / 29 (10.34%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Temperature intolerance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Prostatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Scrotal disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Sexual dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	2 / 29 (6.90%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	4 / 29 (13.79%)	1 / 13 (7.69%)
occurrences (all)	0	5	1
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Upper-Airway cough syndrome			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	2
Depression			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	1 / 13 (7.69%)
occurrences (all)	0	3	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	2 / 13 (15.38%)
occurrences (all)	0	2	8
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	2 / 13 (15.38%)
occurrences (all)	0	2	6
Blood albumin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	2 / 13 (15.38%)
occurrences (all)	0	4	2
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Neutrophil count decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	16
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	13
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	6
Parosmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 29 (17.24%)	3 / 13 (23.08%)
occurrences (all)	0	11	3
Coagulopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	4
Thrombocytopenia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Episcleritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	7 / 29 (24.14%)	4 / 13 (30.77%)
occurrences (all)	0	8	4
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Abdominal rigidity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	9 / 29 (31.03%)	4 / 13 (30.77%)
occurrences (all)	0	9	4
Diarrhoea			

subjects affected / exposed	0 / 3 (0.00%)	8 / 29 (27.59%)	5 / 13 (38.46%)
occurrences (all)	0	10	11
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 29 (10.34%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	9 / 29 (31.03%)	5 / 13 (38.46%)
occurrences (all)	0	13	7
Oral dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	4 / 29 (13.79%)	1 / 13 (7.69%)
occurrences (all)	0	8	1
Tongue ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	8 / 29 (27.59%)	2 / 13 (15.38%)
occurrences (all)	0	9	3
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Nail discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nail discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Palmar-Plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	4
Pruritus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Trichorrhexis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	4 / 29 (13.79%)	3 / 13 (23.08%)
occurrences (all)	1	6	3
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 29 (10.34%)	0 / 13 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal stiffness			

subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 29 (6.90%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Lymph gland infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 29 (3.45%)	0 / 13 (0.00%)
occurrences (all)	1	1	0

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	6 / 29 (20.69%)	5 / 13 (38.46%)
occurrences (all)	0	10	6
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 29 (3.45%)	2 / 13 (15.38%)
occurrences (all)	0	1	3
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 29 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 29 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Non-serious adverse events	Part 2: Imalumab 10 mg/kg + Panitumumab	Part 2: Standard of Care Wild Type	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	7 / 7 (100.00%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Chest pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Early satiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	5 / 18 (27.78%)	5 / 7 (71.43%)	
occurrences (all)	6	8	
Hypothermia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Inflammation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Localised oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Mucosal inflammation			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pyrexia			

subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Temperature intolerance			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Pelvic pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Prostatitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Scrotal disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Sexual dysfunction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 18 (16.67%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Dyspnoea			
subjects affected / exposed	3 / 18 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Epistaxis			

subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Nasal congestion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Upper-Airway cough syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Blood albumin increased			

subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Laceration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Scratch			

subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Venomous sting			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Migraine			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Neuralgia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Parosmia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			

subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Coagulopathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Episcleritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			

subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)	3 / 7 (42.86%)	
occurrences (all)	1	4	
Abdominal pain upper			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Abdominal rigidity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	3 / 18 (16.67%)	1 / 7 (14.29%)	
occurrences (all)	7	1	
Diarrhoea			
subjects affected / exposed	5 / 18 (27.78%)	1 / 7 (14.29%)	
occurrences (all)	6	2	
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	4 / 18 (22.22%)	1 / 7 (14.29%)	
occurrences (all)	9	2	
Oral dysaesthesia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Proctalgia			

subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Rectal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Tongue ulceration			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 18 (11.11%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Blister			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dermatitis acneiform			
subjects affected / exposed	8 / 18 (44.44%)	2 / 7 (28.57%)	
occurrences (all)	22	4	
Dermatitis contact			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	6 / 18 (33.33%)	1 / 7 (14.29%)	
occurrences (all)	6	1	
Nail discolouration			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	

Nail discomfort				
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)		
occurrences (all)	0	2		
Nail disorder				
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)		
occurrences (all)	1	0		
Night sweats				
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)		
occurrences (all)	2	0		
Palmar-Plantar erythrodysaesthesia syndrome				
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)		
occurrences (all)	0	1		
Pruritus				
subjects affected / exposed	4 / 18 (22.22%)	1 / 7 (14.29%)		
occurrences (all)	5	3		
Rash				
subjects affected / exposed	9 / 18 (50.00%)	0 / 7 (0.00%)		
occurrences (all)	18	0		
Rash erythematous				
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)		
occurrences (all)	1	0		
Rash generalised				
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)		
occurrences (all)	1	0		
Rash maculo-papular				
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)		
occurrences (all)	1	1		
Rash papular				
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)		
occurrences (all)	0	0		
Skin fissures				
subjects affected / exposed	3 / 18 (16.67%)	1 / 7 (14.29%)		
occurrences (all)	9	1		
Skin ulcer				

subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Trichorrhexis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Micturition urgency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	3	2	
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Bone pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Flank pain			

subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Joint swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Genital herpes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Localised infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Lymph gland infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	4 / 18 (22.22%)	0 / 7 (0.00%)	
occurrences (all)	6	0	
Rash pustular			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 18 (11.11%)	2 / 7 (28.57%)	
occurrences (all)	2	3	
Dehydration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	2 / 18 (11.11%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Hypomagnesaemia			

subjects affected / exposed	3 / 18 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Iron deficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2015	Phase 1 safety data was updated; DLT definition was corrected specifically for the out of range laboratory values, to read as an exclusion to the DLT definition; Administration Description of Change was corrected in SoC Drugs for 5 FU, LV, Panitumumab, and SoC; Exclusion criteria were updated.
13 July 2015	Treatment descriptions involving BAX69 were clarified to indicate that BAX69 should be administered 1 hour before either 5 FU/LV or panitumumab; Updated screening and baseline assessments.
09 May 2016	"BAX69" was changed to "imalumab", where appropriate; "Patients" was changed to "subjects" where appropriate; Exploratory objectives were added to clinical study protocol, to be consistent with the exploratory outcome measures; Duration of Screening was extended from 3 weeks (21 days) to 4 weeks (28 days); Exclusion criteria was added; Included rationale for the inclusion of subjects in this study with ECOG PS 0 to 2 and potential treatment with panitumumab; Provided reference for dose modifications that were implemented in response to a dermatologic reaction (NCI CTCAE Grade 3 or higher, or considered intolerable) in subjects treated with panitumumab; Changed definition of FAS.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

On 2016 DEC 16, the Data Safety Monitoring Board (DSMB) reviewed the periodic safety data, and in addition also reviewed available efficacy data from the first 33 PFS events and non-clinical information and recommended to terminate Study 391401.

Notes: