Clinical trial results:
A Double-Blind, Placebo-Controlled Pivotal Phase III Study Evaluating Xilonix in Symptomatic Colorectal Cancer Patients Refractory to Standard Therapy

Summary

EudraCT number	2014-000550-12
Trial protocol	HU GB PL DE CZ BG
Global end of trial date	03 November 2015

Results information

Result version number	v2 (current)
This version publication date	31 March 2022
First version publication date	18 April 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	2014-PT026

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02138422
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, United States, NJ 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	03 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of the study was to evaluate objective response rate (ORR), a composite measure assessing change in Lean Body Mass (LBM), fatigue, pain, and appetite from baseline to week 8.

Protection of trial subjects:

The study was performed in accordance with the current version of the declaration of Helsinki (64th world medical association [WMA] General Assembly, Fortaleza, Brazil, October 2013). Safety assessment included Adverse events, hematology, and chemistry labs.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2014
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	Bulgaria: 14
Country: Number of subjects enrolled	Czechia: 32
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Georgia: 19
Country: Number of subjects enrolled	Hungary: 28
Country: Number of subjects enrolled	Poland: 164
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	United Kingdom: 17
Worldwide total number of subjects	309
EEA total number of subjects	250

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)	172
From 65 to 84 years	137
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 458 subjects were screened and 333 were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Controlled Period (CP) plus BSC

Arm description:

Subjects received matching Placebo via intravenous (IV) injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles). Best supportive care (BSC) is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received IV injection of matching Placebo.

Arm title	Bermekimab (Xilonix) plus BSC

Arm description:

Subjects received an intravenous (IV) injection of Bermekimab 7.5 milligrams per kilograms (mg/kg) once every 2 weeks (Cycle 1) for a total of 4 infusions (four cycles). BSC is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.

Arm type	Experimental
Investigational medicinal product name	Bermekimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received IV injection of Bermekimab 7.5 mg/kg.

Number of subjects in period 1	Placebo Controlled Period (CP) plus BSC	Bermekimab (Xilonix) plus BSC
Started	102	207
Completed	83	167
Not completed	19	40
Adverse event, serious fatal	5	9
Physician decision	3	6
Consent withdrawn by subject	1	5
Adverse event, non-fatal	3	3
Other	3	10
Lost to follow-up	-	3

Period 2

Period 2 title	Open Label Extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to Bermekimab (after CP)

Arm description:

Subjects who received Placebo at Week 0, 2, 4, and 6 in CP received Bermekimab 7.5 mg/kg IV injection at Week 8 and every two weeks onwards.

Arm type	Experimental
Investigational medicinal product name	Bermekimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Bermekimab 7.5 mg/kg IV injection.

Arm title	Bermekimab (after CP)

Arm description:

Subjects who received Bermekimab in CP were randomized to the control arm received IV placebo at 7.5 mg/kg via IV injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles).

Arm type	Experimental
Investigational medicinal product name	Bermekimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Bermekimab 7.5 mg/kg IV injection.

Number of subjects in period 2[1]	Placebo to Bermekimab (after CP)	Bermekimab (after CP)
Started	62	138
Completed	1	2
Not completed	61	136
Adverse event, serious fatal	9	22
Physician decision	14	31
Consent withdrawn by subject	17	34
Adverse event, non-fatal	2	10
Other	16	32
Protocol terminated	2	-
Lost to follow-up	-	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects who completed treatment period and opted to continue treatment entered in to the open label extension phase.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Controlled Period (CP) plus BSC
Reporting group description:	
Subjects received matching Placebo via intravenous (IV) injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles). Best supportive care (BSC) is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.	
Reporting group title	Bermekimab (Xilonix) plus BSC
Reporting group description:	
Subjects received an intravenous (IV) injection of Bermekimab 7.5 milligrams per kilograms (mg/kg) once every 2 weeks (Cycle 1) for a total of 4 infusions (four cycles). BSC is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.	

Reporting group values	Placebo Controlled Period (CP) plus BSC	Bermekimab (Xilonix) plus BSC	Total
Number of subjects	102	207	309
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	60	112	172
From 65 to 84 years	42	95	137
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	62.6	63.3	
standard deviation	± 9.21	± 10.08	-
Title for Gender Units: subjects			
Female	43	79	122
Male	59	128	187

End points

End points reporting groups

Reporting group title	Placebo Controlled Period (CP) plus BSC
Reporting group description:	
Subjects received matching Placebo via intravenous (IV) injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles). Best supportive care (BSC) is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.	
Reporting group title	Bermekimab (Xilonix) plus BSC
Reporting group description:	
Subjects received an intravenous (IV) injection of Bermekimab 7.5 milligrams per kilograms (mg/kg) once every 2 weeks (Cycle 1) for a total of 4 infusions (four cycles). BSC is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.	
Reporting group title	Placebo to Bermekimab (after CP)
Reporting group description:	
Subjects who received Placebo at Week 0, 2, 4, and 6 in CP received Bermekimab 7.5 mg/kg IV injection at Week 8 and every two weeks onwards.	
Reporting group title	Bermekimab (after CP)
Reporting group description:	
Subjects who received Bermekimab in CP were randomized to the control arm received IV placebo at 7.5 mg/kg via IV injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles).	

Primary: Objective Response Rate (ORR) for mITT population

End point title	Objective Response Rate (ORR) for mITT population
End point description:	
Objective response was defined as improvement or stabilization (greater than or equal to [>=] 0 kilograms [kg] change) of Lean Body Mass (LBM) as assessed by Dual-energy X-ray Absorptiometry (DEXA) scan; and improvement or no worsening (>=0 score point change) on any two of the three symptom scale measures (fatigue, pain, appetite) of European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire (EORTC QLQ-C30). Modified intent-to-treat (mITT) population was defined as all randomized subjects who received at least one infusion of the study drug.	
End point type	Primary
End point timeframe:	
Up to 8 weeks	

End point values	Placebo Controlled Period (CP) plus BSC	Bermekimab (Xilonix) plus BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	207		
Units: Subjects				
number (not applicable)	19	33		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo Controlled Period (CP) plus BSC v Bermekimab (Xilonix) plus BSC
Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.004
Method	Pearson Chi-Square test
Parameter estimate	Unadjusted Odds Ratio
Point estimate	2.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	3.78

Primary: ORR for per Protocol Population

End point title	ORR for per Protocol Population

End point description:

Objective response was defined as improvement or stabilization (>= 0 kg change) of LBM as assessed by DEXA scan; and improvement or no worsening (>=0 score point change) on any two of the three symptom scale measures (fatigue, pain, appetite) of EORTC QLQ-C30. Per protocol population set excluded the 24 subjects who were randomized but not dosed and the 17 placebo subjects from mITT population who showed significant level of MABp1 concentration at PK assessment.

End point type	Primary

End point timeframe:

Up to 8 weeks

End point values	Placebo Controlled Period (CP) plus BSC	Bermekimab (Xilonix) plus BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	207		
Units: Subjects				
number (not applicable)	19	68		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo Controlled Period (CP) plus BSC v Bermekimab (Xilonix) plus BSC

Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.037
Method	Pearson Chi-Square test
Parameter estimate	Unadjusted Odds Ratio
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	3.06

Secondary: Change from Baseline in Interleukin-6 (IL-6) up to 8 Weeks

End point title	Change from Baseline in Interleukin-6 (IL-6) up to 8 Weeks

End point description:

Change in IL-6 up to 8 weeks was analyzed. mITT population was defined as all randomized subjects who received at least one infusion of the study drug.

End point type	Secondary

End point timeframe:

Baseline up to 8 weeks

End point values	Placebo Controlled Period (CP) plus BSC	Bermekimab (Xilonix) plus BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	207		
Units: picograms per milliliter (pg/mL)				
arithmetic mean (standard deviation)	9.9 (± 2.7)	1.6 (± 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Platelet Count up to 8 Weeks

End point title	Change from Baseline in Platelet Count up to 8 Weeks

End point description:

Change in platelet count up to 8 weeks was reported. mITT population was defined as all randomized subjects who received at least one infusion of the study drug.

End point type	Secondary

End point timeframe:

Baseline up to 8 Weeks

End point values	Placebo Controlled Period (CP) plus BSC	Bermekimab (Xilonix) plus BSC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	207		
Units: 1000 per cubic millimeter (mm^-3)				
arithmetic mean (standard deviation)	39.53 (± 7.56)	13.45 (± 5.33)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 8 weeks

Adverse event reporting additional description:

Safety analysis set included enrolled subjects receiving at least one dose of the study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo (CP) plus BSC

Reporting group description:

Subjects received matching Placebo via intravenous (IV) injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles). Best supportive care (BSC) is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.

Reporting group title	Bermekimab plus BSC

Reporting group description:

Subjects received an intravenous (IV) injection of Bermekimab 7.5 milligrams per kilograms (mg/kg) once every 2 weeks (Cycle 1) for a total of 4 infusions (four cycles). BSC is defined as those measures intended to provide palliation of symptoms and improve quality of life. This included, but is not limited to, psychological support, dietary advice, exercise advice, antibiotics, anti-emetics, and analgesia.

Reporting group title	Placebo to Bermekimab (after CP)

Reporting group description:

Subjects who received Placebo at Week 0, 2, 4, and 6 in CP received Bermekimab 7.5 mg/kg IV injection at Week 8 and every two weeks onwards.

Reporting group title	Bermekimab (after CP)

Reporting group description:

Subjects who received Bermekimab in CP were randomized to the control arm received IV placebo at 7.5 mg/kg via IV injection once every 2 weeks (one cycle) for a total of 4 infusions (four cycles).

Serious adverse events	Placebo (CP) plus BSC	Bermekimab plus BSC	Placebo to Bermekimab (after CP)
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 102 (26.47%)	45 / 207 (21.74%)	15 / 62 (24.19%)
number of deaths (all causes)	14	23	11
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal Cancer			
subjects affected / exposed	0 / 102 (0.00%)	4 / 207 (1.93%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant Neoplasm Progression			

subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Metastases to Central Nervous System			
subjects affected / exposed	2 / 102 (1.96%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to Liver			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Metastasis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Metastatic Neoplasm			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 102 (0.00%)	2 / 207 (0.97%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Surgical and medical procedures			
Chemotherapy			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 207 (0.48%)	2 / 62 (3.23%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Disease Progression			
subjects affected / exposed	4 / 102 (3.92%)	7 / 207 (3.38%)	5 / 62 (8.06%)
occurrences causally related to treatment / all	0 / 4	0 / 8	0 / 5
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 1
Fatigue			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General Physical Health Deterioration			
subjects affected / exposed	2 / 102 (1.96%)	3 / 207 (1.45%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-Organ Failure			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Obstruction			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Pain			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 102 (0.98%)	2 / 207 (0.97%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Pneumonitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			
subjects affected / exposed	1 / 102 (0.98%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Platelet Count Decreased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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			
Cervical Vertebral Fracture			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Hip Fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Incisional Hernia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Stoma Site Haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Congenital, familial and genetic disorders			
Hydrocele			

subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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			
Cardiopulmonary Failure			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Coronary Artery Disease			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Myocardial Infarction			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Headache			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lateral Medullary Syndrome			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Spinal Cord Compression			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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	4 / 102 (3.92%)	3 / 207 (1.45%)	2 / 62 (3.23%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Anal Haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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 Obstruction			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal Stenosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	2 / 102 (1.96%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction Gastric			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Subileus			

subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Vomiting			
subjects affected / exposed	1 / 102 (0.98%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic Failure			
subjects affected / exposed	3 / 102 (2.94%)	2 / 207 (0.97%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage Urinary Tract			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Hydronephrosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Impairment			

subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Retention			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular Weakness			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal Pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Spinal Pain			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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			
Abdominal Abscess			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Bronchitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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

Bronchopneumonia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Cystitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Gastroenteritis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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
Peritonitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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
Pyonephrosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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 Tract Infection			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	0 / 102 (0.00%)	1 / 207 (0.48%)	0 / 62 (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 / 102 (0.00%)	2 / 207 (0.97%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 207 (0.00%)	0 / 62 (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	Bermekimab (after CP)		
Total subjects affected by serious adverse events			
subjects affected / exposed	50 / 138 (36.23%)		
number of deaths (all causes)	31		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal Cancer			
subjects affected / exposed	7 / 138 (5.07%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Malignant Neoplasm Progression			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to Central Nervous System			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to Liver			

subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastasis				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic Neoplasm				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep Vein Thrombosis				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Chemotherapy				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	2 / 138 (1.45%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			

Disease Progression				
subjects affected / exposed	12 / 138 (8.70%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 2			
Fatigue				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General Physical Health Deterioration				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Multi-Organ Failure				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Obstruction				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal				

disorders			
Dyspnoea			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural Effusion			
subjects affected / exposed	2 / 138 (1.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary Embolism			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory Failure			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet Count Decreased			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Cervical Vertebral Fracture			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip Fracture			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Incisional Hernia			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar Vertebral Fracture			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stoma Site Haemorrhage			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiopulmonary Failure			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary Artery Disease			

subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial Infarction			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lateral Medullary Syndrome			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Cord Compression			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 138 (2.17%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			

Vertigo				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal Pain				
subjects affected / exposed	5 / 138 (3.62%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Anal Haemorrhage				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Haemorrhage				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Obstruction				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileal Stenosis				

subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstruction Gastric				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis Acute				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal Haemorrhage				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small Intestinal Obstruction				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 138 (1.45%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic Failure				

subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	2 / 138 (1.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage Urinary Tract			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Failure			
subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal Impairment			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Retention			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			

Hypopituitarism				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Muscular Weakness				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal Pain				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal Pain				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal Abscess				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 138 (1.45%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Gastroenteritis				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyonephrosis				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				
subjects affected / exposed	1 / 138 (0.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper Respiratory Tract Infection				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 138 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				

subjects affected / exposed	1 / 138 (0.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo (CP) plus BSC	Bermekimab plus BSC	Placebo to Bermekimab (after CP)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 102 (52.94%)	122 / 207 (58.94%)	39 / 62 (62.90%)
Investigations			
Weight Decreased			
subjects affected / exposed	7 / 102 (6.86%)	20 / 207 (9.66%)	7 / 62 (11.29%)
occurrences (all)	8	21	8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 102 (5.88%)	16 / 207 (7.73%)	5 / 62 (8.06%)
occurrences (all)	6	27	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 102 (10.78%)	24 / 207 (11.59%)	8 / 62 (12.90%)
occurrences (all)	15	29	8
Asthenia			
subjects affected / exposed	9 / 102 (8.82%)	18 / 207 (8.70%)	11 / 62 (17.74%)
occurrences (all)	9	21	15
Oedema Peripheral			
subjects affected / exposed	8 / 102 (7.84%)	21 / 207 (10.14%)	3 / 62 (4.84%)
occurrences (all)	8	26	3
Pyrexia			
subjects affected / exposed	5 / 102 (4.90%)	9 / 207 (4.35%)	2 / 62 (3.23%)
occurrences (all)	5	9	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	7 / 102 (6.86%)	19 / 207 (9.18%)	4 / 62 (6.45%)
occurrences (all)	7	22	4
Ascites			

subjects affected / exposed	8 / 102 (7.84%)	11 / 207 (5.31%)	3 / 62 (4.84%)
occurrences (all)	8	13	3
Diarrhoea			
subjects affected / exposed	2 / 102 (1.96%)	9 / 207 (4.35%)	3 / 62 (4.84%)
occurrences (all)	4	10	4
Vomiting			
subjects affected / exposed	5 / 102 (4.90%)	13 / 207 (6.28%)	2 / 62 (3.23%)
occurrences (all)	5	18	2
Nausea			
subjects affected / exposed	12 / 102 (11.76%)	18 / 207 (8.70%)	2 / 62 (3.23%)
occurrences (all)	12	26	2
Abdominal Pain			
subjects affected / exposed	14 / 102 (13.73%)	32 / 207 (15.46%)	6 / 62 (9.68%)
occurrences (all)	16	32	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 102 (2.94%)	4 / 207 (1.93%)	1 / 62 (1.61%)
occurrences (all)	4	4	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 102 (3.92%)	3 / 207 (1.45%)	4 / 62 (6.45%)
occurrences (all)	4	5	4
Pain in Extremity			
subjects affected / exposed	2 / 102 (1.96%)	8 / 207 (3.86%)	4 / 62 (6.45%)
occurrences (all)	2	8	4
Infections and infestations			
Urinary Tract Infection			
subjects affected / exposed	3 / 102 (2.94%)	9 / 207 (4.35%)	2 / 62 (3.23%)
occurrences (all)	4	10	2
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	9 / 102 (8.82%)	17 / 207 (8.21%)	4 / 62 (6.45%)
occurrences (all)	9	17	4

Non-serious adverse events	Bermekimab (after CP)		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	87 / 138 (63.04%)		
Investigations			
Weight Decreased			
subjects affected / exposed	16 / 138 (11.59%)		
occurrences (all)	21		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 138 (7.97%)		
occurrences (all)	21		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	20 / 138 (14.49%)		
occurrences (all)	23		
Asthenia			
subjects affected / exposed	17 / 138 (12.32%)		
occurrences (all)	27		
Oedema Peripheral			
subjects affected / exposed	9 / 138 (6.52%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	12 / 138 (8.70%)		
occurrences (all)	14		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	11 / 138 (7.97%)		
occurrences (all)	11		
Ascites			
subjects affected / exposed	9 / 138 (6.52%)		
occurrences (all)	10		
Diarrhoea			
subjects affected / exposed	7 / 138 (5.07%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	5 / 138 (3.62%)		
occurrences (all)	7		
Nausea			

subjects affected / exposed occurrences (all) Abdominal Pain subjects affected / exposed occurrences (all)	8 / 138 (5.80%) 10 22 / 138 (15.94%) 28		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 8 / 138 (5.80%) 9		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in Extremity subjects affected / exposed occurrences (all)	 1 / 138 (0.72%) 1 4 / 138 (2.90%) 4		
Infections and infestations Urinary Tract Infection subjects affected / exposed occurrences (all)	 8 / 138 (5.80%) 8		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	 15 / 138 (10.87%) 17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported