Clinical trial results:
A Phase II, Multicenter, Open Label Study of Bintrafusp Alfa (M7824) Monotherapy in Participants With HMGA2-expressing Triple Negative Breast Cancer

Summary

EudraCT number	2019-004833-18
Trial protocol	IT FR
Global end of trial date	20 December 2021

Results information

Result version number	v1 (current)
This version publication date	05 July 2023
First version publication date	05 July 2023

Trial information

Trial identification

Sponsor protocol code	MS200647_0020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04489940
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Healthcare KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Center, Merck Healthcare KGaA, Darmstadt Germany, an affiliate of Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center,, Merck Healthcare KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.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	08 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate bintrafusp alfa monotherapy in subjects with triple negative breast cancer (TNBC) who express high levels of HMGA2 as determined by a centralized reverse transcriptase-polymerase chain reaction (RT-PCR) test.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	11
EEA total number of subjects	5

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)	7
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 15 subjects were screened, of which 11 subjects received bintrafusp alfa monotherapy.

Period 1

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

Arms

Arm title	Bintrafusp alfa

Arm description:

Subjects received an intravenous infusion of 1200 milligrams (mg) bintrafusp alfa once every 2 weeks until confirmed disease progression, unacceptable toxicity, study withdrawal or death.

Arm type	Experimental
Investigational medicinal product name	Bintrafusp alfa
Investigational medicinal product code	M7824
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received an intravenous infusion of 1200 milligrams (mg) bintrafusp alfa once every 2 weeks until confirmed disease progression, unacceptable toxicity, study withdrawal or death.

Number of subjects in period 1	Bintrafusp alfa
Started	11
Completed	1
Not completed	10
Adverse event, serious fatal	5
Consent withdrawn by subject	2
Other	2
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Bintrafusp alfa
Reporting group description:	
Subjects received an intravenous infusion of 1200 milligrams (mg) bintrafusp alfa once every 2 weeks until confirmed disease progression, unacceptable toxicity, study withdrawal or death.	

Reporting group values	Bintrafusp alfa	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	4	4	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	59		
standard deviation	± 11.3	-	
Sex: Female, Male Units: Subjects			
Female	11	11	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	9	9	
Unknown or Not Reported	2	2	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	9	9	
More than one race	0	0	
Unknown or Not Reported	2	2	

End points

End points reporting groups

Reporting group title	Bintrafusp alfa

Reporting group description:

Subjects received an intravenous infusion of 1200 milligrams (mg) bintrafusp alfa once every 2 weeks until confirmed disease progression, unacceptable toxicity, study withdrawal or death.

Primary: Objective Response Rate (ORR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by an Independent Review Committee (IRC)

End point title	Objective Response Rate (ORR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by an Independent Review Committee (IRC)[1]

End point description:

The ORR was defined as the percentage of subjects with a confirmed objective response of Complete Response (CR) or Partial Response (PR) according to RECIST v1.1 as assessed by IRC. CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30 percent (%) reduction from baseline in sum of longest diameter (SLD) of all lesions.

End point type	Primary

End point timeframe:

Time from first study intervention up to 321 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical and comparison analysis were performed in single arm for this endpoint.

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Percentage of subjects				

Notes:

[2] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) According to RECIST Version 1.1

End point title	Duration of Response (DOR) According to RECIST Version 1.1

End point description:

DOR was defined for subjects with a confirmed objective response as the time from first documentation of a confirmed objective response (CR or PR) according to RECIST 1.1 to the date of first documentation of objective PD or death due to any cause, whichever occurs first. CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30 percent (%) reduction from baseline in sum of longest diameter (SLD) of all lesions. PD: At least a 20 percent (%) increase in the SLD, taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. DOR was determined according to RECIST v1.1 and assessed by IRC.

End point type	Secondary

End point timeframe:

From first documented objective response to PD or death due to any cause, assessed up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Percentage of subjects				

Notes:

[3] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Durable Response Rate (DRR) of at Least 6 Months Assessed by an Independent Review Committee (IRC)

End point title	Durable Response Rate (DRR) of at Least 6 Months Assessed by an Independent Review Committee (IRC)

End point description:

DRR was defined as the number of subjects having a DOR of at least 6 months, out of the total number of subjects.

End point type	Secondary

End point timeframe:

Time from first study intervention up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Percentage of subjects				

Notes:

[4] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Investigator

End point title	Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Investigator

End point description:

PFS was defined as the time from first study intervention until the first documentation of PD or death due to any cause in the absence of documented PD, whichever occurred first. PD: At least a 20% increase in the SLD, taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. The tumor response was determined according to RECIST version 1.1 and assessed by the investigator.

End point type	Secondary

End point timeframe:

Time from first study intervention up to the first documentation of PD or death, assessed up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Percentage of subjects				
median (confidence interval 95%)	(to)			

Notes:

[5] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Durable Response Rate (DRR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Investigator

End point title	Durable Response Rate (DRR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Investigator

End point description:

DRR was defined as the number of subjects having a DOR of at least 6 months, out of the total number of subjects.

End point type	Secondary

End point timeframe:

Time from first study intervention up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Percentage of subjects				

Notes:

[6] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by the Investigator

End point title	Objective Response Rate (ORR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by the Investigator

End point description:

The ORR was defined as the percentage of subjects with a confirmed objective response of Complete Response (CR) or Partial Response (PR) according to RECIST v1.1 as assessed by investigator. CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30 percent (%) reduction

from baseline in sum of longest diameter (SLD) of all lesions.

End point type	Secondary

End point timeframe:

Time from first study intervention up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Percentage of subjects				

Notes:

[7] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from first day of study treatment to death due to any cause. Subjects without documented death at the time of analysis are censored at the date of the last follow-up. OS was summarized by Kaplan-Meier (KM) methods.

End point type	Secondary

End point timeframe:

Time from the first dose of study drug until occurrence of death due to any cause, assessed up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[8] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) According to RECIST Version 1.1 Assessed by the IRC

End point title	Progression-Free Survival (PFS) According to RECIST Version 1.1 Assessed by the IRC

End point description:

PFS was defined as the time from first study intervention until the first documentation of PD or death due to any cause in the absence of documented PD, whichever occurred first. PD: At least a 20%

increase in the SLD, taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. The tumor response was determined according to RECIST version 1.1 and assessed by the IRC.

End point type	Secondary

End point timeframe:

Time from first study intervention up to until the first documentation of PD or death, assessed up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[9] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by the Investigator

End point title	Duration of Response (DOR) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by the Investigator

End point description:

DOR was defined for subjects with a confirmed objective response as the time from first documentation of a confirmed objective response (CR or PR) according to RECIST 1.1 to the date of first documentation of objective PD or death due to any cause, whichever occurs first. CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30% reduction from baseline in sum of longest diameter (SLD) of all lesions. PD: At least a 20% increase in the SLD, taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. DOR was determined according to RECIST v1.1 and assessed by investigator.

End point type	Secondary

End point timeframe:

From first documented objective response to PD or death due to any cause, assessed up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: Percentage of subjects				

Notes:

[10] - As per changes in planned analysis, the endpoints related to efficacy were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-Drug Antibody (ADA) of Bintrafusp Alfa

End point title	Number of Subjects With Positive Anti-Drug Antibody (ADA) of Bintrafusp Alfa

End point description:

The detection of antibodies to bintrafusp alfa was performed using a validated ADA assay method with tiered testing of screening, confirmatory and titration.

End point type	Secondary

End point timeframe:

Pre-dose, End of Infusion from Day 1 to 321

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: subjects				

Notes:

[11] - As per changes in planned analysis, the endpoints related to immunogenicity were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Trough Concentration Levels (Ctrough) of Bintrafusp Alfa

End point title	Serum Trough Concentration Levels (Ctrough) of Bintrafusp Alfa

End point description:

Ctrough was the serum concentration observed immediately before next dosing.

End point type	Secondary

End point timeframe:

Pre-dose, End of Infusion from Day 1 to 321

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: microgram per milliliter (mcg/mL)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[12] - As per changes in planned analysis, the endpoints related to pharmacokinetics were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Immediate Observed Serum Concentration at End of Infusion (Ceoi) of Bintrafusp Alfa

End point title	Immediate Observed Serum Concentration at End of Infusion (Ceoi) of Bintrafusp Alfa

End point description:

Ceoi was the serum concentration observed immediately at the end of infusion. This was taken directly from the observed bintrafusp alfa concentration-time data.

End point type	Secondary

End point timeframe:

Pre-dose, End of Infusion from Day 1 to 321

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[13]			
Units: microgram per milliliter (mcg/mL)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[13] - As per changes in planned analysis the endpoints related to pharmacokinetics were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Treatment-Related AEs, and Adverse Events of Special Interest (AESIs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Treatment-Related AEs, and Adverse Events of Special Interest (AESIs)

End point description:

An AE was defined as any untoward medical occurrence in a subject administered a pharmaceutical product and which did not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether considered related to the medicinal product or protocol-specified procedure. Serious AE was defined AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial/prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAE was defined as events with onset date or worsening during the on-treatment period. TEAEs included serious TEAEs and non-serious TEAEs. The AESIs considered in this study are infusion-related reactions including immediate hypersensitivity, immune-related adverse events, skin adverse events, bleeding events and anemia.

End point type	Secondary

End point timeframe:

Time from first study intervention up to 321 days

End point values	Bintrafusp alfa			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Count of subjects				
Participants with TEAEs	10			
Participants with Treatment-Related TEAEs	5			

Participants with AESIs	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time from first study intervention up to 321 days.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Bintrafusp alfa

Reporting group description:

Participants received an intravenous infusion of 1200 milligrams (mg) bintrafusp alfa once every 2 weeks until confirmed disease progression, unacceptable toxicity, study withdrawal or death.

Serious adverse events	Bintrafusp alfa		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	1		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 5		
General physical health deterioration			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 11 (9.09%)		
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	Bintrafusp alfa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)		
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Throat irritation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Investigations			
Amylase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Alanine aminotransferase increased			

subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Blood creatine phosphokinase increase			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood phosphorus increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood thyroid stimulating hormone dec			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Thyroxine free increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

Gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Gingival bleeding subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Nausea subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Stomatitis subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Vomiting subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3		
Constipation subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Hepatobiliary disorders Hepatic function abnormal subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Pruritus subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Dry skin subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		

Arthralgia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Infections and infestations Vaginal infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Oral candidiasis subjects affected / exposed occurrences (all) Diverticulitis subjects affected / exposed occurrences (all) Respiratory tract infection viral subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyponatraemia subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2021	Updates in the Risk Classification.

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.

Based on sponsors decision for early termination of the study due to lack of probability to achieve interim data allowing expansion of this study.
Hence, analysis for efficacy, or biomarker were not performed.

Notes: