Clinical trial results:
A PHASE 2, OPEN-LABEL, SINGLE-ARM TRIAL OF TRASTUZUMAB DERUXTECAN (DS-8201A) IN HER2-POSITIVE, UNRESECTABLE OR METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION (GEJ) ADENOCARCINOMA SUBJECTS WHO HAVE PROGRESSED ON OR AFTER A TRASTUZUMAB-CONTAINING REGIMEN

Summary

EudraCT number	2019-001512-34
Trial protocol	ES BE IT
Global end of trial date	

Results information

Result version number	v2
This version publication date	24 February 2023
First version publication date	01 March 2022
Version creation reason	• New data added to full data set New data added as per addendum.

Trial information

Trial identification

Sponsor protocol code	DS8201-A-U205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04014075
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo Inc.
Sponsor organisation address	211 Mt. Airy Rd., Basking Ridge, United States, 07920
Public contact	Global Clinical Director, Daiichi Sankyo Inc., +1 908-992-6400, CTRinfo@dsi.com
Scientific contact	Global Clinical Director, Daiichi Sankyo Inc., +1 908-992-6400, CTRinfo@dsi.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	Interim
Date of interim/final analysis	09 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 April 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of Trastuzumab Deruxtecan (DS-8201a) based on objective response rate (ORR) by independent central review based on Response Evaluation Criteria in Solid Tumors (RECIST), version (v)1.1

Protection of trial subjects:

The study protocol, amendments, the informed consent form(s) (ICF[s]), and information sheets were approved by the appropriate and applicable Independent Ethics Committees (IECs) or Institutional Review Boards (IRBs). The study was conducted in compliance with the protocol, the ethical principles that have their origin in the Declaration of Helsinki, the International Council for Harmonisation (ICH) consolidated Guideline E6 for Good Clinical Practice (GCP) (CPMP/ICH/135/95), and applicable regulatory requirement(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 November 2019
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	European Union: 45
Country: Number of subjects enrolled	United States: 34
Worldwide total number of subjects	79
EEA total number of subjects	0

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)	46
From 65 to 84 years	33

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 79 participants who met all inclusion criteria and no exclusion criteria were enrolled and treated at clinic centers in United States, Spain, Italy, United Kingdom, and Belgium. Primary results reported is from baseline up to data cut-off date of 08 Nov 2021.

Pre-assignment

Screening details:

A total of 89 participants were screened and 10 participants failed screening. The results presented are based on primary analysis up to 23 months. Data collection is still on-going and additional results will be provided after study completion.

Period 1

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

Blinding implementation details:

This was an open-label study.

Arms

Arm title	Trastuzumab Deruxtecan

Arm description:

Participants who have centrally confirmed HER2-positive gastric or gastro-esophageal junction cancer received an intravenous (IV) infusion 6.4 mg/kg dose of trastuzumab deruxtecan every 3 weeks, until progression of disease or withdrawal from treatment for other reasons.

Arm type	Experimental
Investigational medicinal product name	DS-8201a
Investigational medicinal product code	
Other name	Trastuzumab deruxtecan
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Antibody component covalently conjugated to a drug component, prepared by dilution based on body weight for intravenous (IV) infusion.

Number of subjects in period 1	Trastuzumab Deruxtecan
Started	79
Completed	10
Not completed	69
Physician decision	1
Adverse event, non-fatal	11
Death	2
Progressive Disease	48
Miscellaneous	1
Clinical Progression	4

Withdrawal by subject	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	79	79	
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)	46	46	
From 65-84 years	33	33	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	59.3		
standard deviation	± 11.8	-	
Gender categorical Units: Subjects			
Female	22	22	
Male	57	57	

End points

End points reporting groups

Reporting group title	Trastuzumab Deruxtecan

Reporting group description:

Participants who have centrally confirmed HER2-positive gastric or gastro-esophageal junction cancer received an intravenous (IV) infusion 6.4 mg/kg dose of trastuzumab deruxtecan every 3 weeks, until progression of disease or withdrawal from treatment for other reasons.

Primary: Percentage of Participants With Objective Response Rate (ORR) Based on Independent Central Review Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point title	Percentage of Participants With Objective Response Rate (ORR) Based on Independent Central Review Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma[1]

End point description:

The Objective Response Rate (ORR) was the defined as the percentage of participants who achieved a best overall response of confirmed Complete Response (CR) or Partial Response (PR), assessed by independent central review (ICR) committee based on RECIST version 1.1. CR was defined as a disappearance of all target lesions and PR was defined as at least a 30% decrease in the sum of diameters of target lesions. Confirmed ORR based on ICR is reported. Objective response rate was assessed in the Full Analysis Set at data cut-off dates (09 April 2021 and 08 Nov 2021).

End point type	Primary

End point timeframe:

Up to 23 months

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: Upper CI was not estimable. Curve representing the upper confidence limits for the survivor function was above 0.5.

End point values	Trastuzumab Deruxtecan			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Percentage of Participants				
number (confidence interval 95%)				
Up to 16 months (data cut-off)	38.0 (27.3 to 49.6)			
Up to 23 months (data cut-off)	41.8 (30.8 to 53.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) Based on Independent Central Review Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point title	Progression-Free Survival (PFS) Based on Independent Central Review Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point description:

Progression-free survival (PFS) by independent central review was defined as the time from the date of enrollment to the earlier of the dates of the first objective documentation of disease progression (as per RECIST v1.1) or death due to any cause. Progressive disease was defined as at least a 20% increase in the sum of diameters of target lesions. Progression-free survival (PFS) was assessed in the Full Analysis Set at data cut-off dates (09 April 2021 and 08 Nov 2021).

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Trastuzumab Deruxtecan			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: months				
median (confidence interval 95%)				
Up to 16 months (data cut-off)	5.5 (4.2 to 7.3)			
Up to 23 months (data cut-off)	5.6 (4.2 to 8.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) Based on Investigator Assessment Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point title	Progression-Free Survival (PFS) Based on Investigator Assessment Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point description:

Progression-free survival (PFS) by investigator assessment was defined as the time from the date of enrollment to the earlier of the dates of the first objective documentation of disease progression (as per RECIST v1.1) or death due to any cause. Progressive disease was defined as at least a 20% increase in the sum of diameters of target lesions. Progression-free survival (PFS) was assessed in the Full Analysis Set at data cut-off date of 09 April 2021.

End point type	Secondary

End point timeframe:

Up to 16 months (data cut-off)

End point values	Trastuzumab Deruxtecan			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: months				
median (confidence interval 95%)	5.5 (4.1 to 6.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) Based on Investigator Assessment Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point title	Objective Response Rate (ORR) Based on Investigator Assessment Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point description:

The Objective Response Rate (ORR) was defined as the percentage of participants who achieved a best overall response of confirmed Complete Response (CR) or Partial Response (PR), assessed by investigator assessment based on RECIST version 1.1. CR was defined as a disappearance of all target lesions and PR was defined as at least a 30% decrease in the sum of diameters of target lesions. Confirmed ORR based on investigator assessment is reported. Objective response rate was assessed in the Full Analysis Set at data cut-off dates (09 April 2021 and 08 Nov 2021).

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Trastuzumab Deruxtecan			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Percentage of Participants				
number (confidence interval 95%)				
Up to 16 months (data cut-off)	34.2 (23.9 to 45.7)			
Up to 23 months (data cut-off)	36.7 (26.1 to 48.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point title	Overall Survival (OS) Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point description:

Overall survival (OS) was defined as the time from the date of first dose of study drug to the date of death due to any cause. Overall survival (OS) was assessed in the Full Analysis Set at data cut-off dates (09 April 2021 and 08 Nov 2021).

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Trastuzumab Deruxtecan			
Subject group type	Reporting group			
Number of subjects analysed	79[2]			
Units: months				
median (confidence interval 95%)				
Up to 16 months (data cut-off)	99.9 (11.5 to 99.9)			
Up to 23 months (data cut-off)	12.1 (9.4 to 15.4)			

Notes:

[2] - For 16 months, 99.9=NA, median and upper limit CI not estimable due to insufficient number of events

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point title	Duration of Response (DoR) Following Treatment With DS8201a in Participants With HER2-Positive Unresectable or Metastatic Gastric or Gastro-Esophageal Junction (GEJ) Adenocarcinoma

End point description:

Duration of Response (DOR) was defined as the time from the date of the first documentation of objective response (complete response [CR] or partial response [PR]) to the date of the first objective documentation of progressive disease (PD) or death due to any cause. DoR based on independent central review. Duration of Response (DOR) was assessed in the Full Analysis Set at data cut-off dates (09 April 2021 and 08 Nov 2021).

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Trastuzumab Deruxtecan			
Subject group type	Reporting group			
Number of subjects analysed	79[3]			
Units: months				
median (confidence interval 95%)				
Up to 16 months (data cut-off)	8.1 (4.1 to 99.9)			
Up to 23 months (data cut-off)	8.1 (5.9 to 99.9)			

Notes:

[3] - 99.9=NA, upper limit CI was not estimable. Curve for survivor function was above 0.5.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) were collected from the date of signing the informed consent form up to 47 days after last dose of the study drug, up 23 months.

Adverse event reporting additional description:

A Treatment-emergent adverse event (TEAE) is defined as an AE that occurs, having been absent before the first dose of study drug, or has worsened in severity or seriousness after the initiating the study drug until 47 days after last dose of the study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Trastuzumab Deruxtecan

Reporting group description:

Participants who have centrally confirmed HER2-positive gastric or gastro-esophageal junction cancer received an intravenous (IV) infusion 6.4 mg/kg dose of trastuzumab deruxtecan every 3 weeks, until progression of disease or withdrawal from treatment for other reasons.

Serious adverse events	Trastuzumab Deruxtecan		
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 79 (41.77%)		
number of deaths (all causes)	46		
number of deaths resulting from adverse events	11		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			
subjects affected / exposed	2 / 79 (2.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Lymphangiosis Carcinomatosa			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tumour Haemorrhage			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural			

complications			
Animal Bite			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Exposure To Communicable Disease			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Basal Ganglia Infarction			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular Accident			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Generalised Tonic-Clonic Seizure			
subjects affected / exposed	1 / 79 (1.27%)		
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	2 / 79 (2.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Hyperpyrexia			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	4 / 79 (5.06%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 79 (3.80%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	2 / 79 (2.53%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 79 (1.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 79 (1.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 79 (1.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 79 (1.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	1 / 79 (1.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal Obstruction				

subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Bile Duct Stenosis			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Interstitial Lung Disease			
subjects affected / exposed	2 / 79 (2.53%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Pneumonitis			
subjects affected / exposed	3 / 79 (3.80%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	1 / 1		
Pulmonary Embolism			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	2 / 79 (2.53%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Hydronephrosis			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Obstruction			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19			
subjects affected / exposed	2 / 79 (2.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Pneumonia			
subjects affected / exposed	2 / 79 (2.53%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Bacterial Sepsis			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Covid-19 Pneumonia			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device Related Infection			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	2 / 79 (2.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Wound Infection			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Catheter site infection			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device Occlusion			
subjects affected / exposed	1 / 79 (1.27%)		
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	Trastuzumab Deruxtecan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 79 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 79 (7.59%)		
occurrences (all)	6		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	33 / 79 (41.77%)		
occurrences (all)	60		
Asthenia			
subjects affected / exposed	12 / 79 (15.19%)		
occurrences (all)	17		
Pyrexia			

subjects affected / exposed	9 / 79 (11.39%)		
occurrences (all)	16		
Oedema Peripheral			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	4		
Mucosal inflammation			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	7 / 79 (8.86%)		
occurrences (all)	7		
Cough			
subjects affected / exposed	9 / 79 (11.39%)		
occurrences (all)	13		
Epistaxis			
subjects affected / exposed	8 / 79 (10.13%)		
occurrences (all)	8		
Interstitial Lung Disease			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	4		
Pneumonitis			
subjects affected / exposed	5 / 79 (6.33%)		
occurrences (all)	5		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 79 (6.33%)		
occurrences (all)	5		
Depression			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	4		
Investigations			
Weight Decreased			
subjects affected / exposed	28 / 79 (35.44%)		
occurrences (all)	31		
Platelet Count Decreased			

subjects affected / exposed occurrences (all)	14 / 79 (17.72%) 24		
Neutrophil Count Decreased subjects affected / exposed occurrences (all)	13 / 79 (16.46%) 18		
Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all)	13 / 79 (16.46%) 15		
White Blood Cell Count Decreased subjects affected / exposed occurrences (all)	9 / 79 (11.39%) 12		
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	8 / 79 (10.13%) 8		
Blood Alkaline Phosphatase Increased subjects affected / exposed occurrences (all)	9 / 79 (11.39%) 11		
Blood Bilirubin Increased subjects affected / exposed occurrences (all)	5 / 79 (6.33%) 7		
Weight increased subjects affected / exposed occurrences (all)	5 / 79 (6.33%) 6		
Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 79 (5.06%) 4		
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	7 / 79 (8.86%) 9		
Dizziness subjects affected / exposed occurrences (all)	6 / 79 (7.59%) 7		
Blood and lymphatic system disorders			

Anaemia				
subjects affected / exposed	30 / 79 (37.97%)			
occurrences (all)	47			
Neutropenia				
subjects affected / exposed	8 / 79 (10.13%)			
occurrences (all)	17			
Thrombocytopenia				
subjects affected / exposed	5 / 79 (6.33%)			
occurrences (all)	7			
Gastrointestinal disorders				
Nausea				
subjects affected / exposed	51 / 79 (64.56%)			
occurrences (all)	91			
Vomiting				
subjects affected / exposed	35 / 79 (44.30%)			
occurrences (all)	58			
Diarrhoea				
subjects affected / exposed	29 / 79 (36.71%)			
occurrences (all)	45			
Constipation				
subjects affected / exposed	23 / 79 (29.11%)			
occurrences (all)	36			
Abdominal Pain				
subjects affected / exposed	11 / 79 (13.92%)			
occurrences (all)	14			
Gastrooesophageal Reflux Disease				
subjects affected / exposed	8 / 79 (10.13%)			
occurrences (all)	8			
Ascites				
subjects affected / exposed	5 / 79 (6.33%)			
occurrences (all)	7			
Dysphagia				
subjects affected / exposed	5 / 79 (6.33%)			
occurrences (all)	5			
Abdominal pain upper				

subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all)	5 / 79 (6.33%) 6 4 / 79 (5.06%) 4		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 19 / 79 (24.05%) 19		
Renal and urinary disorders Urinary Retention subjects affected / exposed occurrences (all) Acute Kidney Injury subjects affected / exposed occurrences (all)	 5 / 79 (6.33%) 6 4 / 79 (5.06%) 4		
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all)	 7 / 79 (8.86%) 7		
Infections and infestations Covid-19 subjects affected / exposed occurrences (all) Device related infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 5 / 79 (6.33%) 5 4 / 79 (5.06%) 4 4 / 79 (5.06%) 4		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all) Hypokalaemia	 26 / 79 (32.91%) 34 		

subjects affected / exposed	13 / 79 (16.46%)		
occurrences (all)	16		
Hypoalbuminaemia			
subjects affected / exposed	8 / 79 (10.13%)		
occurrences (all)	10		
Hyponatraemia			
subjects affected / exposed	6 / 79 (7.59%)		
occurrences (all)	9		
Hypophosphataemia			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2020	Updated endpoints to provide clarification, updated study schema, updated inclusion and exclusion criteria, updated guidelines for dose modifications, updated concomitant medications, treatments, and procedures, updated treatment period section, updated PK assessments due to COVID-19 infection, updated PK, biomarker, and AE analyses to provide clarification, added instructions related to COVID-19

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported