Clinical trial results:
A Phase 2, Multicenter, Randomized Study of Trastuzumab Deruxtecan in Subjects with HER2-overexpressing Locally Advanced, Unresectable or Metastatic Colorectal Cancer (DESTINY-CRC02)

Summary

EudraCT number	2020-004782-39
Trial protocol	FR BE IT ES
Global end of trial date	08 October 2024

Results information

Result version number	v2 (current)
This version publication date	24 October 2025
First version publication date	23 February 2024
Version creation reason	• New data added to full data set Study Completion has been achieved, results updated accordingly.

Trial information

Trial identification

Sponsor protocol code	DS8201-A-U207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04744831
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	Medical Director, Daiichi Sankyo Inc., 1 9089927876, CTRinfo_us@daiichisankyo.com
Scientific contact	Medical Director, Daiichi Sankyo Inc., 1 9089927876, CTRinfo_us@daiichisankyo.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	03 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluates the efficacy, safety, and pharmacokinetics of Trastuzumab deruxtecan (T-DXd) in participants with human epidermal growth factor 2 (HER2)-overexpressing locally advanced, unresectable, or metastatic colorectal cancer (mCRC)

Protection of trial subjects:

This 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), including the following:
European Commission Directive (2001/20/EC Apr 2001) and/or
European Commission Directive (2005/28/EC Apr 2005) and/or
United States (US) Food and Drug Administration (FDA) GCP Regulations: Code of Federal Regulations Title 21, parts 11, 50, 54, 56 and 312 as appropriate and/or
Japanese Ministry of Health, Labor and Welfare Ordinance No. 28 (27 March 1997) and/or
The Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics No. 1 (25 November 2014) and/or
Other applicable local regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2021
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	Spain: 4
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Japan: 43
Country: Number of subjects enrolled	Korea, Republic of: 14
Worldwide total number of subjects	122
EEA total number of subjects	43

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)	77
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 122 subjects who met all inclusion criteria and no exclusion criteria were randomized to T-DXd treatment in the United States, Asia-Pacific, and
Europe.

Pre-assignment

Screening details:

Following adequate study explanation by the investigator or their designee, subjects voluntarily offered signed informed consent prior to participation in any study procedures.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	T-DXd 5.4 mg/kg Q3W

Arm description:

Participants were randomized to receive intravenous T-DXd administered at a dose of 5.4 mg/kg every 3 weeks (Q3W).

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

Dosage and administration details:

Intravenous (IV) infusion administered at a dose of 5.4 mg/kg every 3 weeks (Q3W).

Arm title	T-DXd 6.4 mg/kg Q3W

Arm description:

Participants were randomized to receive intravenous T-DXd administered at a dose of 6.4 mg/kg every 3 weeks (Q3W).

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

Dosage and administration details:

Intravenous (IV) infusion administered at a dose of 6.4 mg/kg every 3 weeks (Q3W).

Number of subjects in period 1	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W
Started	83	39
Completed	0	0
Not completed	83	39
Adverse event, serious fatal	2	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	6	4
Progressive Disease	64	28
other	5	1
Clinical Progression	5	5

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	122	122	
Age Categorical Units: Subjects			

Age continuous			
99.99 denotes data is not available as it has been reported in the corresponding arm groups.			
Units: years arithmetic mean standard deviation	 99.99 ± 99.99	 -	
Gender categorical Units: Subjects			
Male	64	64	
Female	58	58	
Race/Ethnicity, Customized Units: Subjects			
White	50	50	
Black or African American	0	0	
Asian	66	66	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Other	6	6	

Subject analysis sets

Subject analysis set title	T-DXd 5.4 mg/kg Q3W
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive intravenous T-DXd administered at a dose of 5.4 mg/kg every 3 weeks (Q3W).

Subject analysis set title	T-DXd 6.4 mg/kg Q3W
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were randomized to receive intravenous T-DXd administered at a dose of 6.4 mg/kg every 3 weeks (Q3W).

Reporting group values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W	
Number of subjects	82	40	
Age Categorical Units: Subjects			

Age continuous			
99.99 denotes data is not available as it has been reported in the corresponding arm groups.			
Units: years			
arithmetic mean	58.5	61.1	
standard deviation	± 13.05	± 12.13	
Gender categorical			
Units: Subjects			
Male	45	19	
Female	37	21	
Race/Ethnicity, Customized			
Units: Subjects			
White	35	15	
Black or African American	0	0	
Asian	42	24	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Other	5	1	

End points

End points reporting groups

Reporting group title	T-DXd 5.4 mg/kg Q3W
Reporting group description:	
Participants were randomized to receive intravenous T-DXd administered at a dose of 5.4 mg/kg every 3 weeks (Q3W).	
Reporting group title	T-DXd 6.4 mg/kg Q3W
Reporting group description:	
Participants were randomized to receive intravenous T-DXd administered at a dose of 6.4 mg/kg every 3 weeks (Q3W).	
Subject analysis set title	T-DXd 5.4 mg/kg Q3W
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants were randomized to receive intravenous T-DXd administered at a dose of 5.4 mg/kg every 3 weeks (Q3W).	
Subject analysis set title	T-DXd 6.4 mg/kg Q3W
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants were randomized to receive intravenous T-DXd administered at a dose of 6.4 mg/kg every 3 weeks (Q3W).	

Primary: Percentage of Participants With Objective Response Rate (ORR) Based on Blinded Independent Central Review Following IV Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2-overexpressing Metastatic Colorectal Cancer

End point title	Percentage of Participants With Objective Response Rate (ORR) Based on Blinded Independent Central Review Following IV Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2-overexpressing Metastatic Colorectal Cancer[1]

End point description:

Confirmed objective response rate (ORR), defined as the number (percentage) of participants with complete response (CR) or partial response (PR), were assessed by blinded independent central review (BICR) based on Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1. CR was defined as the disappearance of all target lesions and PR was defined as at least a 30% decrease in the sum of diameters of target lesions.

End point type	Primary

End point timeframe:

6 months post-dose administration to data cut off, up to 20 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: No statistical analyses for this end point.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40		
Units: percentage of participants				
number (confidence interval 95%)	37.8 (27.3 to 49.2)	27.5 (14.6 to 43.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point title	Duration of Response Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point description:

DoR, defined as time from the initial response (CR or PR) by BICR and Investigator assessment until documented tumor progression or death from any cause. DoR was assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From the first documented evidence of a response (complete or partial) until disease progression or death, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40[2]		
Units: months				
median (confidence interval 95%)				
BICR	5.5 (4.2 to 8.1)	5.5 (3.7 to 99999)		
Investigator	5.6 (4.2 to 8.0)	6.9 (4.9 to 9.9)		

Notes:

[2] - 99999 = Not estimable due to insufficient data.

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed Objective Response Rate by Investigator Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point title	Confirmed Objective Response Rate by Investigator Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point description:

Confirmed objective response rate (ORR), defined as the number (percentage) of participants with complete response (CR) or partial response (PR), were assessed by Investigator assessment based on

RECIST version 1.1. CR was defined as the disappearance of all target lesions and PR was defined as at least a 30% decrease in the sum of diameters of target lesions. ORR was assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From first dose administration to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40		
Units: percentage of participants				
number (confidence interval 95%)	31.7 (21.9 to 42.9)	30.0 (16.6 to 46.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point title	Progression Free Survival Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point description:

Progression Free Survival (PFS) defined as the time from date of randomization/registration until first objective radiographic tumor progression or death from any cause, based on BICR and Investigator assessment according to RECIST version 1.1. PFS was assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From randomization to data cut off, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40		
Units: month				
median (confidence interval 95%)				
BICR	5.8 (4.6 to 7.0)	5.5 (4.2 to 7.0)		
Investigator	5.8 (4.7 to 7.0)	5.7 (4.2 to 8.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2) - Overexpressing Metastatic Colorectal Cancer

End point title	Disease Control Rate Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2) -Overexpressing Metastatic Colorectal Cancer

End point description:

Disease Control Rate (DCR), defined as the proportion of subjects who achieved CR, PR, or SD for a minimum of 6 weeks during study treatment; DCR based on BICR and DCR based on Investigator assessments assessed according to RECIST version 1.1. DCR was assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From first dose administration to data cut off, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40		
Units: percentage of participants				
number (confidence interval 95%)				
BICR	86.6 (77.3 to 93.1)	85.0 (70.2 to 94.3)		
Investigator	89.0 (80.2 to 94.9)	85.0 (70.2 to 94.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2) - Overexpressing Metastatic Colorectal Cancer

End point title	Clinical Benefit Rate Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2) -Overexpressing Metastatic Colorectal Cancer

End point description:

Clinical Benefit Rate (CBR), defined as proportion of subjects who achieved CR, PR, or SD for at least 6 months; CBR based on BICR and CBR based on Investigator assessments will both be determined based on RECIST version 1.1. CBR was assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From first dose administration to data cut off, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40		
Units: percentage of participants				
number (confidence interval 95%)				
BICR	42.5 (34.1 to 56.5)	32.5 (18.6 to 49.1)		
Investigator	51.2 (39.9 to 62.4)	42.5 (27.0 to 59.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Reporting Treatment-emergent Adverse Events Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point title	Percentage of Participants Reporting Treatment-emergent Adverse Events Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point description:

A Treatment-emergent Adverse Events (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 initiating the study drug until 47 days after the last dose of the study drug. Serious AEs with an onset or worsening 48 days or more after the last dose of study drug, if considered related to study treatment. are also TEAEs. TEAEs were assessed in the Safety Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From first dose administration to data cut off, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: percentage of participants				
number (not applicable)	98.8	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point title	Overall Survival Following Intravenous Administration of T-DXd in Participants With Human Epidermal Growth Factor Receptor 2 (HER2)-Overexpressing Metastatic Colorectal Cancer

End point description:

Overall Survival (OS) defined as the time from date of randomization/ registration until death from any cause, according to RECIST version 1.1. OS was assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From randomization to data cut off, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	40[3]		
Units: months				
median (confidence interval 95%)	13.4 (13.4 to 16.8)	99999 (9.9 to 99999)		

Notes:

[3] - 99999 = Not estimable due to insufficient data.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of T-DXd

End point title	Serum Concentration of T-DXd

End point description:

Descriptive statistics will be provided for serum concentration data of T-DXd, DXd, and total anti-HER2 antibody. Serum concentrations were assessed in the Pharmacokinetics Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

C1D1 (Before infusion (BI), end of infusion (EOI) and 5 hours after infusion), C1D8 (7 days after infusion), C1D15 (14 days after infusion), C2D1 (BI and EOI), C3D1 (BI and EOI), C4D1, (BI and EOI), C6D1 (BI and EOI)

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83[4]	39[5]		
Units: ug/L				
geometric mean (geometric coefficient of variation)				
C1D1 - Before Infusion	99999 (± 99999)	116000.00 (± 99999)		

C1D1 - End of Infusion	118452.77 (± 27.5)	134613.79 (± 18.1)		
C1D1 - 5Hrs After Infusion	123433.28 (± 23.0)	142399.71 (± 19.8)		
C1D8 - 7 Days After Infusion	22261.67 (± 38.9)	28142.80 (± 51.5)		
C1D15 - 14 Days After Infusion	8092.08 (± 61.7)	11396.97 (± 60.3)		
C2D1 - Before Infusion	2827.01 (± 118.8)	4420.63 (± 73.0)		
C2D1 - End of Infusion	109777.43 (± 67.2)	135637.46 (± 22.2)		
C3D1 - Before Infusion	4823.41 (± 83.6)	7543.17 (± 74.3)		
C3D1 - End of Infusion	122218.96 (± 25.8)	139264.52 (± 24.7)		
C4D1 - Before Infusion	5846.34 (± 89.5)	11013.81 (± 51.8)		
C4D1 - End of Infusion	124240.37 (± 23.4)	134129.68 (± 30.3)		
C6D1 - Before Infusion	7507.28 (± 74.5)	10793.89 (± 59.0)		
C6D1 - End of Infusion	117769.64 (± 25.3)	35753.88 (± 1079.6)		

Notes:

[4] - 99999 = Not calculated due to concentrations below the lower limit of quantitation

[5] - 99999 = Not calculated due to concentrations below the lower limit of quantitation

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Total Anti-Human Epidermal Growth Factor Receptor 2 (HER2) Antibody

End point title	Serum Concentration of Total Anti-Human Epidermal Growth Factor Receptor 2 (HER2) Antibody

End point description:

Descriptive statistics will be provided for serum concentration data of T-DXd, DXd, and total anti-HER2 antibody. Serum concentrations were assessed in the Pharmacokinetics Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

C1D1 (Before infusion (BI), end of infusion (EOI) and 5 hours after infusion), C1D8 (7 days after infusion), C1D15 (14 days after infusion), C2D1 (BI and EOI), C3D1 (BI and EOI), C4D1, (BI and EOI), C6D1 (BI and EOI)

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: ug/L				
geometric mean (geometric coefficient of variation)				
C1D1 - Before Infusion	5211.18 (± 388.5)	11934.79 (± 2058.9)		

C1D1 - End of Infusion	110871.93 (± 28.8)	121423.37 (± 20.3)		
C1D1 - 5Hrs After Infusion	107339.74 (± 23.4)	124274.05 (± 23.0)		
C1D8 - 7 Days After Infusion	27646.77 (± 40.3)	32741.77 (± 49.9)		
C1D15 - 14 Days After Infusion	10920.88 (± 71.7)	14293.10 (± 63.0)		
C2D1 - Before Infusion	3723.58 (± 123.1)	4841.90 (± 107.5)		
C2D1 - End of Infusion	106755.21 (± 66.0)	127427.43 (± 23.2)		
C3D1 - Before Infusion	6286.00 (± 93.2)	9100.39 (± 90.0)		
C3D1 - End of Infusion	114763.30 (± 22.8)	134111.33 (± 19.5)		
C4D1 - Before Infusion	7388.01 (± 101.8)	14007.95 (± 67.2)		
C4D1 - End of Infusion	113711.08 (± 21.5)	133956.61 (± 30.5)		
C6D1 - Before Infusion	9033.08 (± 94.9)	13535.33 (± 73.5)		
C6D1 - End of Infusion	104328.76 (± 35.4)	37091.52 (± 816.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Active Metabolite MAAA-1181a

End point title	Serum Concentration of Active Metabolite MAAA-1181a

End point description:

Descriptive statistics will be provided for serum concentration data of T-DXd, DXd, and total anti-HER2 antibody. Serum concentrations were assessed in the Pharmacokinetics Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

C1D1 (Before infusion (BI), end of infusion (EOI) and 5 hours after infusion), C1D8 (7 days after infusion), C1D15 (14 days after infusion), C2D1 (BI and EOI), C3D1 (BI and EOI), C4D1, (BI and EOI), C6D1 (BI and EOI)

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83[6]	39[7]		
Units: pg/mL				
geometric mean (geometric coefficient of variation)				
C1D1 - Before Infusion	99999 (± 99999)	6250.00 (± 99999)		
C1D1 - End of Infusion	4101.40 (± 56.6)	4313.38 (± 45.3)		

C1D1 - 5Hrs After Infusion	12063.71 (± 52.8)	15773.44 (± 39.0)		
C1D8 - 7 Days After Infusion	1372.33 (± 75.8)	1761.02 (± 67.1)		
C1D15 - 14 Days After Infusion	475.30 (± 62.4)	602.43 (± 54.1)		
C2D1 - Before Infusion	209.06 (± 74.6)	291.07 (± 55.4)		
C2D1 - End of Infusion	1474.48 (± 71.2)	1649.91 (± 65.8)		
C3D1 - Before Infusion	279.56 (± 64.0)	427.33 (± 89.5)		
C3D1 - End of Infusion	1559.93 (± 52.6)	1647.92 (± 53.1)		
C4D1 - Before Infusion	284.38 (± 81.4)	494.17 (± 61.2)		
C4D1 - End of Infusion	1448.53 (± 48.5)	1404.67 (± 54.1)		
C6D1 - Before Infusion	332.07 (± 81.3)	578.72 (± 55.8)		
C6D1 - End of Infusion	1182.53 (± 36.8)	1512.25 (± 32.3)		

Notes:

[6] - 99999 = Not calculated due to concentrations below the lower limit of quantitation

[7] - 99999 = Not calculated due to concentrations below the lower limit of quantitation

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Positive for Treatment-emergent Anti-drug Antibodies (ADAs) and Neutralizing Antibodies (NAb) in Participants Who Were Administered T-DXd

End point title	Percentage of Participants Positive for Treatment-emergent Anti-drug Antibodies (ADAs) and Neutralizing Antibodies (NAb) in Participants Who Were Administered T-DXd

End point description:

Immunogenicity will be assessed through characterization of incidence and titer of Anti-drug Antibodies (ADAs), the number and percentage of subjects positive for NAb of T-DXd by dose level will also be determined. ADAs and NAbs were assessed in the Immunogenicity Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Secondary

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	39		
Units: percentage of participants				
number (not applicable)				
ADA	1.3	0		
NAb	0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Patient-Reported Outcomes (PROs) in European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30)

End point title	Change From Baseline in Patient-Reported Outcomes (PROs) in European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30)

End point description:

Exploratory outcome, results not included in this submission. The QLQ-C30 is composed of both multi-item scales and single-item measures. These include 5 functional scales, 3 symptom scales, a global health status/QoL scale, and 6 single items. Each of the multi-item scales includes a different set of items and no item occurs in more than 1 scale. All of the scales and single-item measures range in score from 0 to 100. A high scale score represents a higher response level. Patient questionnaires were assessed in the Full Analysis Set at data cut-off date of 01 Nov 2022.

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months.

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: score				

Notes:

[8] - Exploratory outcome, results not included in this submission

[9] - Exploratory outcome, results not included in this submission

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Patient-Reported Outcomes (PROs) in Patient's Global Impression of Treatment Tolerability (PGI-TT)

End point title	Patient-Reported Outcomes (PROs) in Patient's Global Impression of Treatment Tolerability (PGI-TT)

End point description:

Exploratory outcome, results not included in this submission. The PGI-TT item is included to assess how a patient perceives the overall tolerability of the study treatment over the past 7 days. This is a single-item questionnaire, and patients will rate the bother associated with any treatment-related symptoms using response options ranging from “Not at all” to “Very much”.

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: score				

Notes:

[10] - Exploratory outcome, results not included in this submission

[11] - Exploratory outcome, results not included in this submission

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Patient-Reported Outcomes (PROs) in Patient Global Impression of Symptom Severity (PGIC)

End point title	Patient-Reported Outcomes (PROs) in Patient Global Impression of Symptom Severity (PGIC)

End point description:

Exploratory outcome, results not included in this submission. The PGIC item is included to assess how a patient perceives their overall change in health status since the start of study treatment. This is a single-item questionnaire, and patients will choose from response options ranging from "Much Better" to "Much Worse".

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: score				

Notes:

[12] - Exploratory outcome, results not included in this submission

[13] - Exploratory outcome, results not included in this submission

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Patient-Reported Outcomes (PROs) in Patient Global Impression of Symptom Severity (PGIS)

End point title	Patient-Reported Outcomes (PROs) in Patient Global Impression of Symptom Severity (PGIS)

End point description:

Exploratory outcome, results not included in this submission. The PGIS item is included to assess how a patient perceives the overall severity of cancer symptoms over the past 7 days. This is a single-item questionnaire, and patients will choose the response that best describes the severity of their overall cancer symptoms with options ranging from "No Symptoms" to "Very Severe".

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: score				

Notes:

[14] - Exploratory outcome, results not included in this submission

[15] - Exploratory outcome, results not included in this submission

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Inpatient Healthcare Resource Utilization

End point title	Inpatient Healthcare Resource Utilization

End point description:

Exploratory outcome, results not included in this submission. The impact of treatment and disease on healthcare resource use (including inpatient admissions, intensive care unit admissions, and length of stay in hospital) will be captured/collected in this study on an event-driven basis.

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: score				

Notes:

[16] - Exploratory outcome, results not included in this submission

[17] - Exploratory outcome, results not included in this submission

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Patient-Reported Outcomes (PROs) in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Colorectal Cancer 29 (QLQ-CR29)

End point title	Change From Baseline in Patient-Reported Outcomes (PROs) in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Colorectal Cancer 29 (QLQ-CR29)

End point description:

Exploratory outcome, results not included in this submission. EORTC QLQ-CR29 is designed to be administered in addition to EORTC QLQ-C30. The EORTC QLQ-CR29 is a specific questionnaire for

Colorectal Cancer. Scale from 0 to 100, A higher scale represents better function and a higher quality of life.

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: score				

Notes:

[18] - Exploratory outcome, results not included in this submission

[19] - Exploratory outcome, results not included in this submission

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Patient-Reported Outcomes (PROs) in the EuroQol Questionnaire (EQ) of 5 Dimensions (5D) on a Standardized 5- Level (5L) Descriptive Health Status Scale (EQ-5D-5L)

End point title	Patient-Reported Outcomes (PROs) in the EuroQol Questionnaire (EQ) of 5 Dimensions (5D) on a Standardized 5-Level (5L) Descriptive Health Status Scale (EQ-5D-5L)

End point description:

Exploratory outcome, results not included in this submission. The EQ-5D-5L is self-administered and consists of 2 parts, the EQ-5D-5L descriptive system and the EQ-visual analogue scale. On each dimension, a score of 1 indicates no patient problems in that dimension, 2 indicates slight problems in that dimension, 3 indicates moderate problems in that dimension, 4 indicates severe problems in that dimension and 5 indicates extreme problems in that dimension.

End point type	Other pre-specified

End point timeframe:

From baseline to data cut off, up to approximately 19 months

End point values	T-DXd 5.4 mg/kg Q3W	T-DXd 6.4 mg/kg Q3W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: score				

Notes:

[20] - Exploratory outcome, results not included in this submission

[21] - Exploratory outcome, results not included in this submission

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, to the data cut off date of 20 Nov 2023, up to approximately 63 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	25

Reporting groups

Reporting group title	T-DXd 6.4 mg/kg Q3W

Reporting group description:

Participants were randomized/registered to receive intravenous T-DXd administered at a dose of 6.4 mg/kg every 3 weeks (Q3W).

Reporting group title	T-DXd 5.4 mg/kg Q3W

Reporting group description:

Participants were randomized to receive intravenous T-DXd administered at a dose of 5.4 mg/kg every 3 weeks (Q3W).

Serious adverse events	T-DXd 6.4 mg/kg Q3W	T-DXd 5.4 mg/kg Q3W	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 39 (30.77%)	21 / 83 (25.30%)	
number of deaths (all causes)	13	26	
number of deaths resulting from adverse events	1	2	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 39 (2.56%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Inferior vena cava syndrome			

subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 39 (2.56%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 39 (2.56%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthenia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	1 / 39 (2.56%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastritis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 39 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 39 (2.56%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 39 (0.00%)	3 / 83 (3.61%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ileus paralytic			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 39 (2.56%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 39 (2.56%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Sacral pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 39 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 39 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 39 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	T-DXd 6.4 mg/kg Q3W	T-DXd 5.4 mg/kg Q3W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 39 (97.44%)	81 / 83 (97.59%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 39 (7.69%)	1 / 83 (1.20%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 39 (15.38%)	17 / 83 (20.48%)	
occurrences (all)	20	31	

Fatigue			
subjects affected / exposed	6 / 39 (15.38%)	16 / 83 (19.28%)	
occurrences (all)	9	37	
Pyrexia			
subjects affected / exposed	4 / 39 (10.26%)	13 / 83 (15.66%)	
occurrences (all)	8	19	
Malaise			
subjects affected / exposed	5 / 39 (12.82%)	4 / 83 (4.82%)	
occurrences (all)	5	5	
Mucosal inflammation			
subjects affected / exposed	2 / 39 (5.13%)	4 / 83 (4.82%)	
occurrences (all)	2	4	
Oedema peripheral			
subjects affected / exposed	7 / 39 (17.95%)	5 / 83 (6.02%)	
occurrences (all)	8	5	
Dysgeusia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 83 (1.20%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	5 / 39 (12.82%)	5 / 83 (6.02%)	
occurrences (all)	6	5	
Epistaxis			
subjects affected / exposed	3 / 39 (7.69%)	6 / 83 (7.23%)	
occurrences (all)	5	10	
Dyspnoea			
subjects affected / exposed	3 / 39 (7.69%)	6 / 83 (7.23%)	
occurrences (all)	3	7	
Interstitial lung disease			
subjects affected / exposed	2 / 39 (5.13%)	2 / 83 (2.41%)	
occurrences (all)	2	2	
Cough			
subjects affected / exposed	3 / 39 (7.69%)	8 / 83 (9.64%)	
occurrences (all)	4	10	
Investigations			

Neutrophil count decreased			
subjects affected / exposed	16 / 39 (41.03%)	18 / 83 (21.69%)	
occurrences (all)	47	39	
Weight decreased			
subjects affected / exposed	2 / 39 (5.13%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Blood bilirubin increased			
subjects affected / exposed	6 / 39 (15.38%)	3 / 83 (3.61%)	
occurrences (all)	13	5	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 39 (5.13%)	3 / 83 (3.61%)	
occurrences (all)	4	4	
Lymphocyte count decreased			
subjects affected / exposed	2 / 39 (5.13%)	4 / 83 (4.82%)	
occurrences (all)	2	8	
Blood creatinine increased			
subjects affected / exposed	2 / 39 (5.13%)	4 / 83 (4.82%)	
occurrences (all)	3	4	
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 39 (17.95%)	10 / 83 (12.05%)	
occurrences (all)	13	12	
White blood cell count decreased			
subjects affected / exposed	7 / 39 (17.95%)	11 / 83 (13.25%)	
occurrences (all)	22	28	
Platelet count decreased			
subjects affected / exposed	12 / 39 (30.77%)	18 / 83 (21.69%)	
occurrences (all)	25	41	
Alanine aminotransferase increased			
subjects affected / exposed	6 / 39 (15.38%)	8 / 83 (9.64%)	
occurrences (all)	12	13	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 39 (5.13%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Headache			

subjects affected / exposed	2 / 39 (5.13%)	8 / 83 (9.64%)	
occurrences (all)	2	10	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 39 (41.03%)	22 / 83 (26.51%)	
occurrences (all)	43	52	
Neutropenia			
subjects affected / exposed	2 / 39 (5.13%)	8 / 83 (9.64%)	
occurrences (all)	6	22	
Thrombocytopenia			
subjects affected / exposed	1 / 39 (2.56%)	5 / 83 (6.02%)	
occurrences (all)	1	6	
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	2 / 39 (5.13%)	0 / 83 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 39 (5.13%)	7 / 83 (8.43%)	
occurrences (all)	4	9	
Dyspepsia			
subjects affected / exposed	2 / 39 (5.13%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Stomatitis			
subjects affected / exposed	6 / 39 (15.38%)	12 / 83 (14.46%)	
occurrences (all)	13	17	
Vomiting			
subjects affected / exposed	3 / 39 (7.69%)	17 / 83 (20.48%)	
occurrences (all)	4	29	
Diarrhoea			
subjects affected / exposed	11 / 39 (28.21%)	19 / 83 (22.89%)	
occurrences (all)	14	38	
Constipation			
subjects affected / exposed	6 / 39 (15.38%)	20 / 83 (24.10%)	
occurrences (all)	8	20	
Nausea			

subjects affected / exposed	22 / 39 (56.41%)	49 / 83 (59.04%)	
occurrences (all)	36	102	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 39 (5.13%)	1 / 83 (1.20%)	
occurrences (all)	4	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	11 / 39 (28.21%)	19 / 83 (22.89%)	
occurrences (all)	12	22	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 39 (5.13%)	6 / 83 (7.23%)	
occurrences (all)	2	6	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 39 (7.69%)	2 / 83 (2.41%)	
occurrences (all)	4	2	
Urinary tract infection			
subjects affected / exposed	2 / 39 (5.13%)	4 / 83 (4.82%)	
occurrences (all)	2	5	
Pneumonia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 83 (0.00%)	
occurrences (all)	2	0	
COVID-19			
subjects affected / exposed	5 / 39 (12.82%)	14 / 83 (16.87%)	
occurrences (all)	5	16	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	4 / 39 (10.26%)	6 / 83 (7.23%)	
occurrences (all)	5	8	
Decreased appetite			
subjects affected / exposed	6 / 39 (15.38%)	25 / 83 (30.12%)	
occurrences (all)	9	41	

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