Clinical trial results:
A PHASE 2, MULTICENTER, RANDOMIZED STUDY OF TRASTUZUMAB DERUXTECAN IN SUBJECTS WITH HER2 MUTATED METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC) [DESTINY-LUNG02]

Summary

EudraCT number	2020-003427-42
Trial protocol	FR NL IT ES
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	17 April 2024
First version publication date	17 April 2024

Trial information

Trial identification

Sponsor protocol code	DS8201-A-U206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04644237
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@dsi.com
Scientific contact	Medical Director, Daiichi Sankyo Inc., 1 9089927876, 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	22 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluates the safety and efficacy of Trastuzumab deruxtecan (T-DXd) in epidermal growth factor 2 (HER2) mutated metastatic non-small cell lung cancer (NSCLC) subjects.

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 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;
- US Food and Drug Administration (FDA) GCP Regulations: Code of Federal Regulations (CFR) Title 21, parts 11, 50, 54, 56 and 312 as appropriate and/or;
- Japanese Ministry of Health, Labor and Welfare Ordinance No. 28 (27 Mar 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 Nov 2014);
- Other applicable local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 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	Australia: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 53
Country: Number of subjects enrolled	Korea, Republic of: 28
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	152
EEA total number of subjects	50

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)	97
From 65 to 84 years	54
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 152 participants were randomized to T-DXd treatment in 47 clinical sites, including North America, Europe, and Asia-Pacific.

Pre-assignment

Screening details:

Subjects, after having the study explained to them by the investigator or designee, gave voluntary and signed informed consent before participating 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

Blinding implementation details:

The treatment assignment remained blinded to study subjects, investigators, study site personnel (except the unblinded pharmacist and other unblinded staff members as deemed necessary for site operations to maintain the blind), central imaging readers, and the Interstitial Lung Disease Adjudication Committee.

Arms

Are arms mutually exclusive?	Yes
Arm title	Trastuzumab deruxtecan 5.4 mg/kg

Arm description:

Participants randomized to receive trastuzumab deruxtecan 5.4 mg/kg, administered by intravenous infusion 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 infusion
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	Trastuzumab deruxtecan 6.4 mg/kg

Arm description:

Participants randomized to receive trastuzumab deruxtecan 6.4 mg/kg, administered by intravenous infusion 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 infusion
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	Trastuzumab deruxtecan 5.4 mg/kg	Trastuzumab deruxtecan 6.4 mg/kg
Started	102	50
Completed	27	14
Not completed	75	36
Adverse event, serious fatal	3	2
Consent withdrawn by subject	1	2
Physician decision	3	-
Adverse event, non-fatal	15	12
Progressive Disease	47	19
Not Specified	1	-
Randomized but not Treated	1	-
Clinical Progression	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Trastuzumab deruxtecan 5.4 mg/kg
Reporting group description:	
Participants randomized to receive trastuzumab deruxtecan 5.4 mg/kg, administered by intravenous infusion every 3 weeks (Q3W).	
Reporting group title	Trastuzumab deruxtecan 6.4 mg/kg
Reporting group description:	
Participants randomized to receive trastuzumab deruxtecan 6.4 mg/kg, administered by intravenous infusion every 3 weeks (Q3W).	

Reporting group values	Trastuzumab deruxtecan 5.4 mg/kg	Trastuzumab deruxtecan 6.4 mg/kg	Total
Number of subjects	102	50	152
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.8	59.5	
standard deviation	± 11.59	± 12.14	-
Gender categorical Units: Subjects			
Female	65	34	99
Male	37	16	53
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	65	31	96
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	2
White	23	5	28
More than one race	0	0	0
Unknown or Not Reported	14	12	26

End points

End points reporting groups

Reporting group title	Trastuzumab deruxtecan 5.4 mg/kg
Reporting group description:	
Participants randomized to receive trastuzumab deruxtecan 5.4 mg/kg, administered by intravenous infusion every 3 weeks (Q3W).	
Reporting group title	Trastuzumab deruxtecan 6.4 mg/kg
Reporting group description:	
Participants randomized to receive trastuzumab deruxtecan 6.4 mg/kg, administered by intravenous infusion every 3 weeks (Q3W).	

Primary: Percentage of Participants With Confirmed Objective Response Rate by Blinded Independent Central Review Following Intravenous Administration of Trastuzumab Deruxtecan in Participants With Metastatic Non-small Cell Lung Cancer

End point title	Percentage of Participants With Confirmed Objective Response Rate by Blinded Independent Central Review Following Intravenous Administration of Trastuzumab Deruxtecan in Participants With Metastatic Non-small Cell Lung Cancer[1]

End point description:

Confirmed objective response rate (ORR), defined as the proportion of participants with complete response (CR) or partial response (PR), was assessed by blinded independent central review (BICR) based on Response Evaluation Criteria In Solid Tumors (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.

End point type	Primary

End point timeframe:

9 months after the last participant is randomized to data cut off, up to approximately 21 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: The Objective Response Rate for each dose level was estimated along with the 2-sided Clopper-Pearson 95% Confidence Intervals.

End point values	Trastuzumab deruxtecan 5.4 mg/kg	Trastuzumab deruxtecan 6.4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: percentage of participants				
number (confidence interval 95%)	49.0 (39.0 to 59.1)	56.0 (41.3 to 70.0)		

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 to 21 months. For Primary Results, data was collected up until December 23, 2022.

Adverse event reporting additional description:

A treatment-emergent adverse event (TEAE) was defined as an AE that occurred, having been absent before the first dose of study drug, or had worsened after initiating study treatment up until 47 days after the last dose of the study treatment. Safety Analysis Set included all randomized subjects who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Trastuzumab deruxtecan 6.4 mg/kg

Reporting group description:

Participants randomized to receive trastuzumab deruxtecan 6.4 mg/kg, administered by intravenous infusion every 3 weeks (Q3W).

Reporting group title	Trastuzumab deruxtecan 5.4 mg/kg

Reporting group description:

Participants randomized to receive trastuzumab deruxtecan 5.4 mg/kg, administered by intravenous infusion every 3 weeks (Q3W).

Serious adverse events	Trastuzumab deruxtecan 6.4 mg/kg	Trastuzumab deruxtecan 5.4 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 50 (40.00%)	37 / 101 (36.63%)	
number of deaths (all causes)	14	37	
number of deaths resulting from adverse events	2	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			

subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 10	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Malignant neoplasm progression			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	2 / 50 (4.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	2 / 50 (4.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 50 (2.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 50 (2.00%)	4 / 101 (3.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 50 (2.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			
Disorientation			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Troponin I increased			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutrophil count decreased			
subjects affected / exposed	2 / 50 (4.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	2 / 50 (4.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 50 (2.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hydrocephalus			

subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	1 / 50 (2.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 50 (4.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Optic nerve disorder			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 50 (2.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	0 / 50 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 50 (2.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			

subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Meningitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 50 (2.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 50 (6.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Trastuzumab deruxtecan 6.4 mg/kg	Trastuzumab deruxtecan 5.4 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 50 (100.00%)	101 / 101 (100.00%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	4 / 50 (8.00%)	6 / 101 (5.94%)	
occurrences (all)	5	8	
Weight decreased			
subjects affected / exposed	7 / 50 (14.00%)	11 / 101 (10.89%)	
occurrences (all)	7	20	
Alanine aminotransferase increased			

subjects affected / exposed	7 / 50 (14.00%)	14 / 101 (13.86%)	
occurrences (all)	12	27	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 50 (12.00%)	19 / 101 (18.81%)	
occurrences (all)	13	32	
Platelet count decreased			
subjects affected / exposed	12 / 50 (24.00%)	25 / 101 (24.75%)	
occurrences (all)	35	41	
Neutrophil count decreased			
subjects affected / exposed	20 / 50 (40.00%)	32 / 101 (31.68%)	
occurrences (all)	67	132	
Blood bilirubin increased			
subjects affected / exposed	8 / 50 (16.00%)	3 / 101 (2.97%)	
occurrences (all)	12	9	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 50 (2.00%)	13 / 101 (12.87%)	
occurrences (all)	2	17	
Headache			
subjects affected / exposed	3 / 50 (6.00%)	5 / 101 (4.95%)	
occurrences (all)	4	5	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	8 / 50 (16.00%)	12 / 101 (11.88%)	
occurrences (all)	29	29	
Anaemia			
subjects affected / exposed	24 / 50 (48.00%)	37 / 101 (36.63%)	
occurrences (all)	75	101	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	13 / 50 (26.00%)	16 / 101 (15.84%)	
occurrences (all)	39	39	
Chest pain			
subjects affected / exposed	4 / 50 (8.00%)	3 / 101 (2.97%)	
occurrences (all)	6	3	
Oedema peripheral			

subjects affected / exposed	3 / 50 (6.00%)	4 / 101 (3.96%)	
occurrences (all)	3	4	
Pyrexia			
subjects affected / exposed	6 / 50 (12.00%)	12 / 101 (11.88%)	
occurrences (all)	7	18	
Malaise			
subjects affected / exposed	4 / 50 (8.00%)	16 / 101 (15.84%)	
occurrences (all)	7	22	
Fatigue			
subjects affected / exposed	7 / 50 (14.00%)	16 / 101 (15.84%)	
occurrences (all)	16	18	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	41 / 50 (82.00%)	68 / 101 (67.33%)	
occurrences (all)	84	160	
Constipation			
subjects affected / exposed	16 / 50 (32.00%)	37 / 101 (36.63%)	
occurrences (all)	24	55	
Vomiting			
subjects affected / exposed	22 / 50 (44.00%)	31 / 101 (30.69%)	
occurrences (all)	38	63	
Odynophagia			
subjects affected / exposed	3 / 50 (6.00%)	0 / 101 (0.00%)	
occurrences (all)	3	0	
Toothache			
subjects affected / exposed	3 / 50 (6.00%)	0 / 101 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	6 / 50 (12.00%)	7 / 101 (6.93%)	
occurrences (all)	8	10	
Dyspepsia			
subjects affected / exposed	1 / 50 (2.00%)	8 / 101 (7.92%)	
occurrences (all)	1	8	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 50 (6.00%)	4 / 101 (3.96%)	
occurrences (all)	3	4	

Diarrhoea			
subjects affected / exposed	18 / 50 (36.00%)	23 / 101 (22.77%)	
occurrences (all)	30	39	
Stomatitis			
subjects affected / exposed	5 / 50 (10.00%)	15 / 101 (14.85%)	
occurrences (all)	5	22	
Haemorrhoids			
subjects affected / exposed	3 / 50 (6.00%)	3 / 101 (2.97%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	3 / 50 (6.00%)	2 / 101 (1.98%)	
occurrences (all)	3	2	
Dyspnoea			
subjects affected / exposed	9 / 50 (18.00%)	5 / 101 (4.95%)	
occurrences (all)	11	7	
Pneumonitis			
subjects affected / exposed	6 / 50 (12.00%)	6 / 101 (5.94%)	
occurrences (all)	7	7	
Interstitial lung disease			
subjects affected / exposed	6 / 50 (12.00%)	7 / 101 (6.93%)	
occurrences (all)	6	8	
Cough			
subjects affected / exposed	6 / 50 (12.00%)	9 / 101 (8.91%)	
occurrences (all)	6	10	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	3 / 50 (6.00%)	1 / 101 (0.99%)	
occurrences (all)	4	1	
Alopecia			
subjects affected / exposed	17 / 50 (34.00%)	22 / 101 (21.78%)	
occurrences (all)	21	25	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 50 (6.00%)	9 / 101 (8.91%)	
occurrences (all)	4	13	

Back pain			
subjects affected / exposed	2 / 50 (4.00%)	6 / 101 (5.94%)	
occurrences (all)	3	10	
Muscle spasms			
subjects affected / exposed	3 / 50 (6.00%)	4 / 101 (3.96%)	
occurrences (all)	3	4	
Infections and infestations			
Pneumonia			
subjects affected / exposed	6 / 50 (12.00%)	5 / 101 (4.95%)	
occurrences (all)	9	7	
Paronychia			
subjects affected / exposed	1 / 50 (2.00%)	7 / 101 (6.93%)	
occurrences (all)	1	10	
COVID-19			
subjects affected / exposed	8 / 50 (16.00%)	13 / 101 (12.87%)	
occurrences (all)	10	13	
Urinary tract infection			
subjects affected / exposed	5 / 50 (10.00%)	3 / 101 (2.97%)	
occurrences (all)	5	6	
White blood cell count decreased			
subjects affected / exposed	15 / 50 (30.00%)	26 / 101 (25.74%)	
occurrences (all)	48	101	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 50 (6.00%)	13 / 101 (12.87%)	
occurrences (all)	7	24	
Hypomagnesaemia			
subjects affected / exposed	2 / 50 (4.00%)	6 / 101 (5.94%)	
occurrences (all)	2	7	
Decreased appetite			
subjects affected / exposed	25 / 50 (50.00%)	40 / 101 (39.60%)	
occurrences (all)	49	62	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 October 2020	This amendment was primarily driven by an update in the sample size, from 100 to 150 to better characterize the efficacy and safety profiles. Additionally, the anticipated total duration of the study was increased from 25 to 31 months. This amendment update also included other minor updates to provide further clarification or specification.
30 November 2021	This amendment was primarily driven by the incorporation of an interim analyses for early assessment of the efficacy and safety of the 2 doses administered in the study. Other editorial and administrative changes were also made for improved clarity.
08 November 2022	This amendment was primarily driven by an update in the timing of the final analysis. This amendment update also included other editorial updates to provide further clarification or specification.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported