



Clinical trial results:

HERTHENA-Lung01: A Phase 2 Randomized Open-Label Study of Patritumab Deruxtecan (U3-1402) in Subjects With Previously Treated Metastatic or Locally Advanced EGFR-mutated Non-Small Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2020-000730-17
Trial protocol	FR DE NL AT BE IT BG
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	25 May 2024
First version publication date	25 May 2024

Trial information

Trial identification

Sponsor protocol code	U31402-A-U201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04619004
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo, Inc.
Sponsor organisation address	211 Mount Airy Rd., Basking Ridge, United States, 07920
Public contact	Daiichi Sankyo Contact for Clinical Trial Information, Daiichi Sankyo, Inc., +1 908-992-6400, CTRinfo@dsi.com
Scientific contact	Daiichi Sankyo Contact for Clinical Trial Information, 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	20 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 November 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate HER3-DXd antitumor activity, as measured by ORR as assessed by BICR per RECIST v1.1, in subjects with locally advanced or metastatic EGFRm (exon 19 deletion or L858R mutation) NSCLC.

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 ICH consolidated Guideline E6 for GCP (CPMP/ICH/135/95), and applicable regulatory requirements. The initial protocol, protocol amendments, the ICFs, and information sheets were approved by the appropriate and applicable Independent Ethics Committees or Institutional Review Boards.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 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	United States: 65
Country: Number of subjects enrolled	Japan: 59
Country: Number of subjects enrolled	Korea, Republic of: 28
Country: Number of subjects enrolled	Singapore: 6
Country: Number of subjects enrolled	Taiwan: 19
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Spain: 23
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Australia: 20
Worldwide total number of subjects	277
EEA total number of subjects	78

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)	158
From 65 to 84 years	119
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 277 participants were enrolled and randomized to treatment at clinical sites in the United States, Japan, Republic of Korea, Singapore, Taiwan, Austria, Belgium, Bulgaria, France, Germany, Italy, Netherlands, Spain, United Kingdom, and Australia. Two participants did not receive any treatment (1 person in each treatment arm).

Pre-assignment

Screening details:

The Screening Period started on the day of signing the main ICF and had a maximum duration of 35 days. During the Screening Period, the participant's eligibility was determined. The study allowed rescreening once for any participant who failed to meet eligibility criteria upon initial Screening or whose Screening window had elapsed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Patritumab deruxtecan 5.6 mg/kg

Arm description:

Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received patritumab deruxtecan 5.6 mg/kg IV every 3 weeks (Q3W)

Arm type	Experimental
Investigational medicinal product name	Patritumab Deruxtecan (Fixed dose)
Investigational medicinal product code	
Other name	U3-1402, HER3-DXd
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patritumab deruxtecan will be dosed at 5.6 mg/kg as an intravenous (IV) infusion administered on Day 1 of each 21-day cycle.

Arm title	Patritumab deruxtecan Up-Titration
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Arm description:

Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received a patritumab deruxtecan up-titration regimen

Arm type	Experimental
Investigational medicinal product name	Patritumab Deruxtecan (Up-titration)
Investigational medicinal product code	
Other name	U3-1402, HER3-DXd
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patritumab deruxtecan will be dosed as an intravenous (IV) infusion administered at Cycle 1, 3.2 mg/kg; Cycle 2, 4.8 mg/kg; Cycle 3 and subsequent cycles, 6.4 mg/kg administered on Day 1 of each 21-day cycle.

Number of subjects in period 1	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up- Titration
Started	226	51
Completed	87	14
Not completed	139	37
Adverse event, serious fatal	114	28
Consent withdrawn by subject	24	7
Other - Not specified	-	1
Lost to follow-up	1	1

Baseline characteristics

Reporting groups

Reporting group title	Patritumab deruxtecan 5.6 mg/kg
Reporting group description: Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received patritumab deruxtecan 5.6 mg/kg IV every 3 weeks (Q3W)	
Reporting group title	Patritumab deruxtecan Up-Titration
Reporting group description: Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received a patritumab deruxtecan up-titration regimen	

Reporting group values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up-Titration	Total
Number of subjects	226	51	277
Age categorical Units: Subjects			
<65 years	122	36	158
≥65 years	104	15	119
Age continuous Units: years arithmetic mean standard deviation	62.7 ± 9.86	59.8 ± 10.07	-
Gender categorical Units: Subjects			
Female	133	29	162
Male	93	22	115
Race/Ethnicity, Customized Units: Subjects			
Asian	106	32	138
Black or African-American	3	1	4
Native Hawaiian or Other Pacific Islander	1	0	1
White	92	15	107
Other	24	3	27

End points

End points reporting groups

Reporting group title	Patritumab deruxtecan 5.6 mg/kg
Reporting group description: Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received patritumab deruxtecan 5.6 mg/kg IV every 3 weeks (Q3W)	
Reporting group title	Patritumab deruxtecan Up-Titration
Reporting group description: Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received a patritumab deruxtecan up-titration regimen	

Primary: Objective Response Rate (ORR) as Assessed by Blinded Independent Central Review (BICR)

End point title	Objective Response Rate (ORR) as Assessed by Blinded Independent Central Review (BICR) ^[1]
End point description: ORR is defined as the proportion of participants with a best overall response (BOR) of confirmed complete response (CR) or confirmed partial response (PR) as assessed by BICR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. 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 based on RECIST v1.1.	
End point type	Primary
End point timeframe: Data collected from screening until time of disease progression by BICR, death, lost to follow up, study discontinuation, whichever occurs first, assessed 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: No statistical analyses were reported for this endpoint; descriptive analyses were used to assess this outcome.	

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up-Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	50		
Units: participants	64	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
End point description: DoR is defined as the time from the first documented confirmed response (CR or PR) to the date of progression or death due to any cause as assessed by BICR and Investigator per RECIST v1.1, respectively. 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	Secondary

End point timeframe:

Data collected from screening until time of disease progression by BICR, death, lost to follow up, study discontinuation, whichever occurs first, assessed up to approximately 21 months

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up- Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	8		
Units: months				
median (confidence interval 95%)				
Duration of response (BICR)	6.0 (4.4 to 7.2)	7.1 (2.8 to 15.2)		
Duration of response (Investigator)	6.9 (5.6 to 7.2)	5.1 (2.6 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
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End point description:

PFS is defined as the time from the start of study treatment to the first documentation of objective progressive disease (PD) per RECIST v1.1 or death due to any cause. PFS will be determined by BICR and by Investigator, respectively.

End point type	Secondary
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End point timeframe:

Data collected from screening until time of disease progression by BICR, death, lost to follow up, study discontinuation, whichever occurs first, assessed up to approximately 21 months

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up- Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	50		
Units: months				
median (confidence interval 95%)				
Progression-free survival (BICR)	5.5 (5.1 to 5.9)	6.7 (4.2 to 8.8)		
Progression-free survival (Investigator)	5.5 (4.2 to 5.7)	5.3 (4.0 to 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) as Assessed by the Investigator

End point title	Objective Response Rate (ORR) as Assessed by the Investigator
End point description: ORR is defined as the proportion of participants with a BOR of confirmed CR or confirmed PR as assessed by the Investigator per RECIST v1.1. 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	Secondary
End point timeframe: Data collected from screening until time of disease progression, death, lost to follow up, study discontinuation, whichever occurs first, assessed up to approximately 21 months	

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up-Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	50		
Units: participants	56	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description: DCR is defined as the proportion of participants who achieved a BOR of confirmed CR, confirmed PR, or stable disease (SD) as assessed by BICR and by the Investigator per RECIST v1.1, respectively. CR was defined as a disappearance of all target lesions, PR was defined as at least a 30% decrease in the sum of diameters of target lesions, and stable disease (SD) was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD; at least a 20% increase in the sum of diameters of target lesions).	
End point type	Secondary
End point timeframe: Data collected from screening until time of disease progression by BICR, death, lost to follow up, study discontinuation, whichever occurs first, assessed up to approximately 21 months	

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up-Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	50		
Units: participants				
Disease control rate (BICR)	166	38		
Disease control rate (Investigator)	169	37		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR)

End point title	Time to Tumor Response (TTR)
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End point description:

TTR is defined as the time from the start of study treatment to the date of the first documentation of confirmed response (CR or PR) as assessed by BICR and Investigator per RECIST v1.1, respectively. 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	Secondary
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End point timeframe:

Data collected from screening until time of disease progression by BICR, death, lost to follow up, study discontinuation, whichever occurs first, assessed up to approximately 21 months

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up- Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	8		
Units: months				
arithmetic mean (standard deviation)				
Time to response (BICR)	2.2 (± 1.31)	1.7 (± 0.61)		
Time to response (Investigator)	2.5 (± 1.78)	2.1 (± 1.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best percentage change in the sum of diameters (SoD) of measurable tumors

End point title	Best percentage change in the sum of diameters (SoD) of measurable tumors
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End point description:

The best percentage change in the SoD of measurable tumors is defined as the percentage change in the smallest SoD from all post-baseline tumor assessments, taking as reference the baseline SoD.

End point type	Secondary
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End point timeframe:

Data collected from screening until time of disease progression by BICR, death, lost to follow up, study discontinuation, whichever occurs first, assessed up to approximately 21 months

End point values	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up- Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	49		
Units: percentage change from baseline				
arithmetic mean (standard deviation)				
Sum of diameters (BICR)	-25.66 (± 30.39)	-17.48 (± 29.54)		
Sum of diameters (Investigator)	-20.84 (± 27.01)	-11.46 (± 29.25)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from after first dose up to 47 days post last dose, up to approximately 21 months (primary outcome data cutoff date).

Adverse event reporting additional description:

Safety events are reported from the Safety Analysis Set. Treatment-emergent adverse events are reported per the investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Patritumab deruxtecan 5.6 mg/kg
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Reporting group description:

Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and who received patritumab deruxtecan 5.6 mg/kg IV every 3 weeks (Q3W)

Reporting group title	Patritumab deruxtecan Up-Titration
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Reporting group description:

Participants with metastatic or locally advanced NSCLC with an EGFR-activating mutation and received a patritumab deruxtecan up-titration regimen

Serious adverse events	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up-Titration	
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 225 (40.00%)	16 / 50 (32.00%)	
number of deaths (all causes)	114	28	
number of deaths resulting from adverse events	24	5	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			
subjects affected / exposed	3 / 225 (1.33%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			

subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Metastasis to central nervous system			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 225 (1.33%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	11 / 225 (4.89%)	4 / 50 (8.00%)	
occurrences causally related to treatment / all	0 / 11	0 / 4	
deaths causally related to treatment / all	0 / 11	0 / 4	
Asthenia			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			

subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	9 / 225 (4.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	9 / 9	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 225 (1.33%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Pleural effusion			
subjects affected / exposed	4 / 225 (1.78%)	2 / 50 (4.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial obstruction			
subjects affected / exposed	0 / 225 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 225 (0.44%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 225 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Platelet count decreased			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Ankle fracture			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 225 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (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			

Seizure			
subjects affected / exposed	4 / 225 (1.78%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petit mal epilepsy			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			

subjects affected / exposed	0 / 225 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 225 (2.67%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	2 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	5 / 225 (2.22%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	3 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	4 / 225 (1.78%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 225 (0.44%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis haemorrhagic			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 225 (0.44%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 225 (1.33%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	5 / 225 (2.22%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	5 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic duct obstruction			

subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 225 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hypertransaminaemia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic haematoma			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cytolysis			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Musculoskeletal and connective tissue disorders			

Muscular weakness			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 225 (2.22%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	1 / 3	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 225 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	1 / 225 (0.44%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 225 (0.89%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	4 / 225 (1.78%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Patritumab deruxtecan 5.6 mg/kg	Patritumab deruxtecan Up- Titration	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	223 / 225 (99.11%)	49 / 50 (98.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 225 (2.22%)	3 / 50 (6.00%)	
occurrences (all)	5	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	69 / 225 (30.67%)	12 / 50 (24.00%)	
occurrences (all)	79	14	
Malaise			
subjects affected / exposed	15 / 225 (6.67%)	6 / 50 (12.00%)	
occurrences (all)	23	16	
Oedema peripheral			

subjects affected / exposed occurrences (all)	20 / 225 (8.89%) 22	3 / 50 (6.00%) 3	
Pyrexia subjects affected / exposed occurrences (all)	22 / 225 (9.78%) 30	6 / 50 (12.00%) 8	
Asthenia subjects affected / exposed occurrences (all)	41 / 225 (18.22%) 70	7 / 50 (14.00%) 14	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	37 / 225 (16.44%) 40	5 / 50 (10.00%) 7	
Dyspnoea subjects affected / exposed occurrences (all)	40 / 225 (17.78%) 44	2 / 50 (4.00%) 2	
Epistaxis subjects affected / exposed occurrences (all)	22 / 225 (9.78%) 27	1 / 50 (2.00%) 2	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	17 / 225 (7.56%) 17	5 / 50 (10.00%) 5	
Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	38 / 225 (16.89%) 56	9 / 50 (18.00%) 13	
White blood cell count decreased subjects affected / exposed occurrences (all)	48 / 225 (21.33%) 85	9 / 50 (18.00%) 20	
Neutrophil count decreased subjects affected / exposed occurrences (all)	61 / 225 (27.11%) 104	15 / 50 (30.00%) 32	
Platelet count decreased subjects affected / exposed occurrences (all)	65 / 225 (28.89%) 88	13 / 50 (26.00%) 22	
Alanine aminotransferase increased			

subjects affected / exposed	26 / 225 (11.56%)	9 / 50 (18.00%)	
occurrences (all)	39	15	
Blood creatinine increased			
subjects affected / exposed	12 / 225 (5.33%)	3 / 50 (6.00%)	
occurrences (all)	18	4	
Blood lactate dehydrogenase increased			
subjects affected / exposed	13 / 225 (5.78%)	1 / 50 (2.00%)	
occurrences (all)	15	1	
Lymphocyte count decreased			
subjects affected / exposed	16 / 225 (7.11%)	3 / 50 (6.00%)	
occurrences (all)	27	4	
Blood alkaline phosphatase increased			
subjects affected / exposed	21 / 225 (9.33%)	1 / 50 (2.00%)	
occurrences (all)	25	1	
Weight decreased			
subjects affected / exposed	23 / 225 (10.22%)	9 / 50 (18.00%)	
occurrences (all)	24	9	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 225 (2.67%)	4 / 50 (8.00%)	
occurrences (all)	7	4	
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 225 (11.56%)	9 / 50 (18.00%)	
occurrences (all)	28	13	
Dysgeusia			
subjects affected / exposed	14 / 225 (6.22%)	1 / 50 (2.00%)	
occurrences (all)	17	1	
Dizziness			
subjects affected / exposed	13 / 225 (5.78%)	4 / 50 (8.00%)	
occurrences (all)	16	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	74 / 225 (32.89%)	15 / 50 (30.00%)	
occurrences (all)	107	23	
Thrombocytopenia			

subjects affected / exposed occurrences (all)	33 / 225 (14.67%) 59	5 / 50 (10.00%) 5	
Neutropenia subjects affected / exposed occurrences (all)	23 / 225 (10.22%) 35	5 / 50 (10.00%) 13	
Leukopenia subjects affected / exposed occurrences (all)	12 / 225 (5.33%) 17	1 / 50 (2.00%) 3	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	6 / 225 (2.67%) 6	4 / 50 (8.00%) 4	
Gastrointestinal disorders Stomatitis subjects affected / exposed occurrences (all)	26 / 225 (11.56%) 30	7 / 50 (14.00%) 7	
Abdominal pain subjects affected / exposed occurrences (all)	19 / 225 (8.44%) 20	5 / 50 (10.00%) 6	
Vomiting subjects affected / exposed occurrences (all)	60 / 225 (26.67%) 70	11 / 50 (22.00%) 15	
Diarrhoea subjects affected / exposed occurrences (all)	62 / 225 (27.56%) 91	11 / 50 (22.00%) 21	
Nausea subjects affected / exposed occurrences (all)	147 / 225 (65.33%) 215	32 / 50 (64.00%) 48	
Constipation subjects affected / exposed occurrences (all)	77 / 225 (34.22%) 95	15 / 50 (30.00%) 19	
Abdominal pain upper subjects affected / exposed occurrences (all)	14 / 225 (6.22%) 15	3 / 50 (6.00%) 3	
Gastrooesophageal reflux disease			

subjects affected / exposed occurrences (all)	7 / 225 (3.11%) 8	3 / 50 (6.00%) 3	
Dyspepsia subjects affected / exposed occurrences (all)	14 / 225 (6.22%) 19	2 / 50 (4.00%) 6	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	57 / 225 (25.33%) 57	0 / 50 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	13 / 225 (5.78%) 15	0 / 50 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	21 / 225 (9.33%) 25	7 / 50 (14.00%) 7	
Arthralgia subjects affected / exposed occurrences (all)	20 / 225 (8.89%) 22	4 / 50 (8.00%) 4	
Myalgia subjects affected / exposed occurrences (all)	7 / 225 (3.11%) 7	3 / 50 (6.00%) 6	
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	10 / 225 (4.44%) 12	3 / 50 (6.00%) 3	
Pneumonia subjects affected / exposed occurrences (all)	11 / 225 (4.89%) 12	3 / 50 (6.00%) 3	
COVID-19 subjects affected / exposed occurrences (all)	20 / 225 (8.89%) 23	3 / 50 (6.00%) 3	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	92 / 225 (40.89%) 115	21 / 50 (42.00%) 28	

Hypokalaemia			
subjects affected / exposed	37 / 225 (16.44%)	6 / 50 (12.00%)	
occurrences (all)	49	8	
Hyperglycaemia			
subjects affected / exposed	15 / 225 (6.67%)	2 / 50 (4.00%)	
occurrences (all)	18	3	
Hypoalbuminaemia			
subjects affected / exposed	20 / 225 (8.89%)	1 / 50 (2.00%)	
occurrences (all)	27	1	
Hyponatraemia			
subjects affected / exposed	15 / 225 (6.67%)	2 / 50 (4.00%)	
occurrences (all)	18	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2020	Revised number of planned sites, revised eligibility criteria, removed text regarding Independent Monitoring Committee, updated details on tumor assessments, defined new Screening period and procedures for rescreening, revised sample size, modified schedule of events for study assessments, and provided additional details on study/site closure,
30 March 2021	Inclusion criteria were updated, screening assessments were revised, benefits and risk section was modified, highly effective contraception was defined, and additional clarification was provided for the reporting and management of safety events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported