# 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 |

**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 |

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<br>Units: Subjects | | | |
| <65 years | 122 | 36 | 158 |
| ≥65 years | 104 | 15 | 119 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 62.7 | 59.8 | |
| standard deviation | ± 9.86 | ± 10.07 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 133 | 29 | 162 |
| Male | 93 | 22 | 115 |
| Race/Ethnicity, Customized<br>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) |
|---|---|

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 |
|---|---|

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) |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

### 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 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 | 20 / 225 (8.89%) | 3 / 50 (6.00%) | |
| occurrences (all) | 22 | 3 | |
| Pyrexia | | | |
| subjects affected / exposed | 22 / 225 (9.78%) | 6 / 50 (12.00%) | |
| occurrences (all) | 30 | 8 | |
| Asthenia | | | |
| subjects affected / exposed | 41 / 225 (18.22%) | 7 / 50 (14.00%) | |
| occurrences (all) | 70 | 14 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 37 / 225 (16.44%) | 5 / 50 (10.00%) | |
| occurrences (all) | 40 | 7 | |
| Dyspnoea | | | |
| subjects affected / exposed | 40 / 225 (17.78%) | 2 / 50 (4.00%) | |
| occurrences (all) | 44 | 2 | |
| Epistaxis | | | |
| subjects affected / exposed | 22 / 225 (9.78%) | 1 / 50 (2.00%) | |
| occurrences (all) | 27 | 2 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 17 / 225 (7.56%) | 5 / 50 (10.00%) | |
| occurrences (all) | 17 | 5 | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 38 / 225 (16.89%) | 9 / 50 (18.00%) | |
| occurrences (all) | 56 | 13 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 48 / 225 (21.33%) | 9 / 50 (18.00%) | |
| occurrences (all) | 85 | 20 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 61 / 225 (27.11%) | 15 / 50 (30.00%) | |
| occurrences (all) | 104 | 32 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 65 / 225 (28.89%) | 13 / 50 (26.00%) | |
| occurrences (all) | 88 | 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 | 33 / 225 (14.67%) | 5 / 50 (10.00%) | |
| occurrences (all) | 59 | 5 | |
| Neutropenia | | | |
| subjects affected / exposed | 23 / 225 (10.22%) | 5 / 50 (10.00%) | |
| occurrences (all) | 35 | 13 | |
| Leukopenia | | | |
| subjects affected / exposed | 12 / 225 (5.33%) | 1 / 50 (2.00%) | |
| occurrences (all) | 17 | 3 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 6 / 225 (2.67%) | 4 / 50 (8.00%) | |
| occurrences (all) | 6 | 4 | |
| Gastrointestinal disorders | | | |
| Stomatitis | | | |
| subjects affected / exposed | 26 / 225 (11.56%) | 7 / 50 (14.00%) | |
| occurrences (all) | 30 | 7 | |
| Abdominal pain | | | |
| subjects affected / exposed | 19 / 225 (8.44%) | 5 / 50 (10.00%) | |
| occurrences (all) | 20 | 6 | |
| Vomiting | | | |
| subjects affected / exposed | 60 / 225 (26.67%) | 11 / 50 (22.00%) | |
| occurrences (all) | 70 | 15 | |
| Diarrhoea | | | |
| subjects affected / exposed | 62 / 225 (27.56%) | 11 / 50 (22.00%) | |
| occurrences (all) | 91 | 21 | |
| Nausea | | | |
| subjects affected / exposed | 147 / 225 (65.33%) | 32 / 50 (64.00%) | |
| occurrences (all) | 215 | 48 | |
| Constipation | | | |
| subjects affected / exposed | 77 / 225 (34.22%) | 15 / 50 (30.00%) | |
| occurrences (all) | 95 | 19 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 14 / 225 (6.22%) | 3 / 50 (6.00%) | |
| occurrences (all) | 15 | 3 | |
| Gastrooesophageal reflux disease | | | |

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