



Clinical trial results: CDK4/6 inhibition in locally advanced/metastatic chordoma Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-004660-19 |
| Trial protocol | DE |
| Global end of trial date | 22 December 2022 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 02 January 2026 |
| First version publication date | 02 January 2026 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | NCT-2016-415 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03110744 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Ruprecht-Karls-University Heidelberg, Medical Faculty |
| Sponsor organisation address | Im Neuenheimer Feld 672, Heidelberg, Germany, 69120 |
| Public contact | NCT Trial Center, Heidelberg University Hospital, studienzentrale@nct-heidelberg.de |
| Scientific contact | NCT Trial Center, Heidelberg University Hospital, studienzentrale@nct-heidelberg.de |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 11 December 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 December 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 December 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary objective of this phase II trial is to gain first evidence of antitumor activity of palbociclib in adult patients with (locally) advanced or metastasized chordoma not amenable to curative treatment with surgery or radiotherapy.

Protection of trial subjects:

During and following a patient's participation in the trial, the investigator should ensure that adequate medical care was provided to a patient for any AE, including clinically significant laboratory values. The investigator should inform a patient when medical care was needed for intercurrent illness(es) of which the investigator becomes aware.

Background therapy:

not applicable

Evidence for comparator:

not applicable

| | |
|---|-----------------|
| Actual start date of recruitment | 31 January 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 42 |
| Worldwide total number of subjects | 42 |
| EEA total number of subjects | 42 |

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) | 26 |

| | |
|---------------------|----|
| From 65 to 84 years | 16 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

First enrollment (FPI): 31.01.2018

Last Enrollment (LPI): 28.04.2022

Pre-assignment

Screening details:

Screening period (Baseline visit): Day -28 to 0

Period 1

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

Arms

| | |
|--|------------------------|
| Arm title | Palbociclib |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Palbociclib (Ibrance®) |
| Investigational medicinal product code | PD-0332991-00 |
| Other name | |
| Pharmaceutical forms | Capsule, hard + tablet |
| Routes of administration | Oral use |

Dosage and administration details:

oral administration once per day for 21 days in a 28-day cycle

| Number of subjects in period 1 ^[1] | Palbociclib |
|---|-------------|
| Started | 28 |
| Completed | 28 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The given numbers cannot be adapted to the structure of the database.

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Palbociclib |
|-----------------------|-------------|

Reporting group description: -

| Reporting group values | Palbociclib | Total | |
|------------------------|-------------|-------|--|
| Number of subjects | 28 | 28 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 18-44 | 3 | 3 | |
| 45-64 | 15 | 15 | |
| >=65 | 10 | 10 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 58.9 | | |
| standard deviation | ± 12.95 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 21 | 21 | |

Subject analysis sets

| | |
|----------------------------|-------------------|
| Subject analysis set title | full analysis set |
|----------------------------|-------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All enrolled patients who have finished at least one cycle of the study medication and who are evaluable for the primary endpoint are included in the full analysis set under the ITT principle.

The primary endpoint is the disease control rate (DCR) after six cycles of palbociclib, which is defined as the presence of complete response (CR) or partial response (PR) or stable disease (SD) according to RECIST version 1.1.

| | |
|----------------------------|---------------------|
| Subject analysis set title | safety analysis set |
|----------------------------|---------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

All enrolled patients who have received any amount of the study medication are subject of the safety population.

| Reporting group values | full analysis set | safety analysis set | |
|------------------------|-------------------|---------------------|--|
| Number of subjects | 25 | 28 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 18-44 | 2 | 3 | |
| 45-64 | 13 | 15 | |
| >=65 | 10 | 10 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 60.1 | 58.9 | |
| standard deviation | ± 12.32 | ± 12.95 | |

| | | | |
|--------------------|----|----|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 6 | 7 | |
| Male | 19 | 21 | |

End points

End points reporting groups

| | |
|---|---------------------|
| Reporting group title | Palbociclib |
| Reporting group description: - | |
| Subject analysis set title | full analysis set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| All enrolled patients who have finished at least one cycle of the study medication and who are evaluable for the primary endpoint are included in the full analysis set under the ITT principle. The primary endpoint is the disease control rate (DCR) after six cycles of palbociclib, which is defined as the presence of complete response (CR) or partial response (PR) or stable disease (SD) according to RECIST version 1.1. | |
| Subject analysis set title | safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All enrolled patients who have received any amount of the study medication are subject of the safety population. | |

Primary: Disease Control Rate (DCR)

| | |
|---|----------------------------|
| End point title | Disease Control Rate (DCR) |
| End point description: | |
| The primary endpoint is the disease control rate (DCR) after six cycles of palbociclib, which is defined as the presence of complete response (CR) or partial response (PR) or stable disease (SD) according to RECIST version 1.1. | |
| End point type | Primary |
| End point timeframe: | |
| From the six cycle of palbociclib to end of study. | |

| End point values | Palbociclib | full analysis set | safety analysis set | |
|----------------------------------|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 28 | 25 | 28 | |
| Units: rate | | | | |
| number (confidence interval 95%) | | | | |
| DCR | 0.440 (0.244 to 0.651) | 0.440 (0.244 to 0.651) | 0.393 (0.215 to 0.594) | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | DCR analysis |
| Statistical analysis description: | |
| Null hypothesis: the true response rate p is less or equal to a reference rate p_0 is tested against a one-sided alternative, where p is the true response probability, p_0 , the (uninteresting) reference response rate, and p_1 the (desirable) target level. In the final analysis the null hypothesis is rejected and the drug recommended for further development if 8 or more responses are observed in 43 patients. This design yields a type I error rate of ≤ 0.05 and power of $\geq 80\%$ when $p=0.25$ | |
| Comparison groups | Palbociclib v full analysis set v safety analysis set |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 81 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | ≤ 0.05 ^[2] |
| Method | Ratio |

Notes:

[1] - After 8 responders with stable disease (SD), it was decided to terminate the study as sufficient evidence was obtained to reject the null hypothesis. 42 patients were recruited and screened, of whom 28 started treatment with IMP.

[2] - This p-value was used for the sample size calculation and the primary endpoint analysis consisted on a rate.

Secondary: Tumor Response Rate (TRR)

| | |
|-----------------|---------------------------|
| End point title | Tumor Response Rate (TRR) |
|-----------------|---------------------------|

End point description:

The TRR is defined as the sum of complete response (CR) and partial response (PR) according to RECIST version 1.1 after six cycles of study medication.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the six cycle of palbociclib to end of study.

| End point values | Palbociclib | full analysis set | safety analysis set | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 28 | 25 | 28 | |
| Units: Ratio | | | | |
| number (not applicable) | | | | |
| TRR | 0 | 0 | 0 | |

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 in months from first administration of the IMP to progression of disease or death from any cause, whichever occurs first. Patients without the event are censored on the last date of follow-up.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first administration of the IMP to progression of disease or death from any cause, whichever occurs first (up to last patient last visit).

| End point values | full analysis set | safety analysis set | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 25 ^[3] | 28 ^[4] | | |
| Units: months | | | | |
| number (not applicable) | | | | |
| Kaplan Meier Analysis: 25% estimate | 4.0 | 2.8 | | |
| Kaplan Meier Analysis: 50% estimate | 5.8 | 5.6 | | |
| Kaplan Meier Analysis: 75% estimate | 11.1 | 11.1 | | |

Notes:

[3] - 18 patients with event

[4] - 20 patients with event

| | |
|-----------------------------------|--|
| Attachments (see zip file) | PFS safety analysis set/5.3.2_Chordoma_timetoevent.pdf PFS full analysis set/5.3.1_Chordoma_timetoevent.pdf |
|-----------------------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

| | |
|-----------------|-----------------------|
| End point title | Overall survival (OS) |
|-----------------|-----------------------|

End point description:

OS is defined as the time in months from first administration of the IMP to time of death from any cause. Patients without the event are censored on the last date of follow-up.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first administration of the IMP to time of death from any cause (up to last patient last visit).

| End point values | Palbociclib | full analysis set | safety analysis set | |
|-------------------------------------|-------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 28 ^[5] | 25 ^[6] | 28 ^[7] | |
| Units: months | | | | |
| number (not applicable) | | | | |
| Kaplan Meier Analysis: 25% estimate | 10.8 | 13.8 | 10.8 | |
| Kaplan Meier Analysis: 50% estimate | 24.6 | 34.0 | 24.6 | |
| Kaplan Meier Analysis: 75% estimate | 50.1 | 50.1 | 50.1 | |

Notes:

[5] - 14 patients with event

[6] - 12 patients with event

[7] - 14 patients with event

| | |
|-----------------------------------|--|
| Attachments (see zip file) | OS full analysis set/5.4.1_Chordoma_timetoevent.pdf OS safety analysis set/5.4.2_Chordoma_timetoevent.pdf |
|-----------------------------------|--|

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In this trial, all AEs that occur after first administration of the IMP are documented. The individual period of observation ends 28 days after the last dose of the IMP for chordoma.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Safety population |
|-----------------------|-------------------|

Reporting group description: -

| Serious adverse events | Safety population | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 28 (35.71%) | | |
| number of deaths (all causes) | 14 | | |
| number of deaths resulting from adverse events | 2 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastases to peritoneum | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Neoplasm progression | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| tumor pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration | | | |

| | | | |
|---|----------------|--|--|
| site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Social circumstances | | | |
| Social stay hospitalisation | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Catheterisation cardiac | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|----------------|--|--|
| Dislocation of vertebra | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paralysis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Intestinal perforation | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Mechanical ileus | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Hypopituitarism | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteolysis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Catheter site infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Implant site infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Safety population | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 28 (96.43%) | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 9 / 28 (32.14%) | | |
| occurrences (all) | 9 | | |
| Leukopenia | | | |
| subjects affected / exposed | 7 / 28 (25.00%) | | |
| occurrences (all) | 7 | | |
| Neutropenia | | | |
| subjects affected / exposed | 10 / 28 (35.71%) | | |
| occurrences (all) | 10 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | | |
| occurrences (all) | 6 | | |
| Gait disturbance | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Mucosal disorder | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Oedema | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all) Vertigo positional subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 | | |
| Eye disorders Astigmatism subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Dysphagia | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 2 / 28 (7.14%) 2 4 / 28 (14.29%) 4 1 / 28 (3.57%) 1 | | |

| | | | |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Flatulence | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal sounds abnormal | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Lip dry | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 5 / 28 (17.86%) | | |
| occurrences (all) | 5 | | |
| Proctalgia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Toothache | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Endocrine disorders | | | |

| | | | |
|---|----------------------|--|--|
| Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|-------------------------|
| 08 May 2018 | Substantial Amendment 1 |
| 16 November 2020 | Substantial Amendment 2 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported