# Clinical trial results:
# A Phase 3, Open-Label, Randomized Study of Futibatinib Versus Gemcitabine-Cisplatin Chemotherapy as First-Line Treatment of Patients with Advanced Cholangiocarcinoma Harboring FGFR2 Gene Rearrangements

## Summary

| | |
|---|---|
| EudraCT number | 2019-004630-42 |
| Trial protocol | FR PT DE PL IT |
| Global end of trial date | 22 April 2024 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 31 January 2025 |
| First version publication date | 31 January 2025 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | TAS-120-301 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04093362 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Taiho Oncology, Inc. |
| Sponsor organisation address | 101 Carnegie Center, Suite 101, Princeton, New Jersey, United States, 08540 |
| Public contact | Senior Study Manager, Taiho Oncology, Inc, +1 844-878-2446, medicalinformation@taihooncology.com |
| Scientific contact | Senior Study Manager, Taiho Oncology, Inc, +1 844-878-2446, medicalinformation@taihooncology.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 28 April 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 April 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy and safety of futibatinib versus gemcitabine-cisplatin chemotherapy as first-line treatment of subjects with advanced, metastatic, or recurrent unresectable intrahepatic cholangiocarcinoma (iCCA) harboring fibroblast growth factor receptor 2 (FGFR2) gene rearrangements.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 06 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 | Poland: 1 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Brazil: 4 |
| Country: Number of subjects enrolled | Taiwan: 1 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | United States: 2 |
| Worldwide total number of subjects | 10 |
| EEA total number of subjects | 2 |

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) | 5 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 10 subjects took part in the study from 06 January 2021 to 22 April 2023.

### Pre-assignment

Screening details:

Total 10 subjects with advanced cholangiocarcinoma were enrolled & randomised to receive either futibatinib or gemcitabine-cisplatin. The study was later terminated by the sponsor due to poor recruitment.

### 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** | Futibatinib |

Arm description:

Subjects received futibatinib at an oral dose of 20 milligrams (mg), administered once daily (QD) in each 21-day cycle up to a maximum of 649 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Futibatinib |
| Investigational medicinal product code | |
| Other name | TAS-120 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Futibatinib at an oral dose of 20 milligrams (mg), administered daily (QD) on every day of a 21-day cycle.

| | |
|---|---|
| **Arm title** | Gemcitabine-Cisplatin |

Arm description:

Subjects received cisplatin 25 milligrams per square meter (mg/m2) intravenous (IV) infusion followed by gemcitabine 1000 mg/m2 IV infusion on Days 1 and 8 of each 21-day cycle up to a maximum of 155 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cisplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cisplatin 25 mg/m2, IV infusion on Days 1 and 8 of each 21-day cycle.

| | |
|---|---|
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine 1000 mg/m2, IV infusion on Days 1 and 8 of each 21-day cycle.

| **Number of subjects in period 1** | Futibatinib | Gemcitabine-Cisplatin |
|---|---|---|
| Started | 4 | 6 |
| Completed | 0 | 0 |
| Not completed | 4 | 6 |
| Withdrawal of Consent | 1 | - |
| Study Termination | 1 | 1 |
| Death | 1 | 3 |
| Reason not Specified | 1 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Futibatinib |
| Reporting group description: | |
| Subjects received futibatinib at an oral dose of 20 milligrams (mg), administered once daily (QD) in each 21-day cycle up to a maximum of 649 days. | |
| Reporting group title | Gemcitabine-Cisplatin |
| Reporting group description: | |
| Subjects received cisplatin 25 milligrams per square meter (mg/m2) intravenous (IV) infusion followed by gemcitabine 1000 mg/m2 IV infusion on Days 1 and 8 of each 21-day cycle up to a maximum of 155 days. | |

| Reporting group values | Futibatinib | Gemcitabine-Cisplatin | Total |
|---|---|---|---|
| Number of subjects | 4 | 6 | 10 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 69.3 | 56.3 | |
| standard deviation | ± 9.46 | ± 12.77 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 1 | 4 | 5 |
| Male | 3 | 2 | 5 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 3 | 4 |
| Not Hispanic or Latino | 3 | 2 | 5 |
| Unknown or Not Reported | 0 | 1 | 1 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 2 | 0 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 2 | 5 | 7 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 1 | 1 |

## End points

### End points reporting groups

| Reporting group title | Futibatinib |
|---|---|

Reporting group description:

Subjects received futibatinib at an oral dose of 20 milligrams (mg), administered once daily (QD) in each 21-day cycle up to a maximum of 649 days.

| Reporting group title | Gemcitabine-Cisplatin |
|---|---|

Reporting group description:

Subjects received cisplatin 25 milligrams per square meter (mg/m2) intravenous (IV) infusion followed by gemcitabine 1000 mg/m2 IV infusion on Days 1 and 8 of each 21-day cycle up to a maximum of 155 days.

### Primary: Progression-free Survival (PFS)

| End point title | Progression-free Survival (PFS)[1] |
|---|---|

End point description:

PFS was defined as the time from date of randomization to the date of documentation of disease progression by independent central review (ICR), or date of death, whichever occurs first. Response assessments were made based on Response Evaluation Criteria in Solid Tumours (RECIST) guidelines (version 1.1, 2009).
As pre-specified in protocol, a total of 162 PFS events were required to perform PFS analysis. As only 10 subjects were enrolled in this study, hence no data was collected or analysed as planned for this end point.

| End point type | Primary |
|---|---|

End point timeframe:

Up to approximately 28 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: As pre-specified in protocol, a total of 162 PFS events were required to perform PFS analysis. As only 10 subjects were enrolled in this study, hence no data was collected or analysed as planned for this end point.

| End point values | Futibatinib | Gemcitabine-Cisplatin | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[2] | 0[3] | | |
| Units: Subjects | | | | |

Notes:

[2] - Only 10 subjects were enrolled in this study, no data was collected or analysed as planned.

[3] - Only 10 subjects were enrolled in this study, no data was collected or analysed as planned.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Objective Response Rate (ORR)

| End point title | Objective Response Rate (ORR) |
|---|---|

End point description:

ORR was defined as the proportion of subjects experiencing a best overall response of partial response (PR) or complete response (CR) as per RECIST 1.1, based on ICR. PR was defined as at least a 30% decrease in the sum of diameters of the target lesions, taking as a reference the baseline sum diameters and persistence of one or more non-target lesion(s) and/or maintenance of tumour marker level above the normal limits. CR was defined as disappearance of all target lesions. Any pathological lymph node

must have reduction in short axis to less than (<)10 millimeters (mm) and disappearance of all non-target lesions and normalisation of tumour marker level. All lymph nodes must be non-pathological in size (<10-mm short axis). The data for this end point was not collected or analysed as planned because the study was terminated early due to poor recruitment.

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

End point timeframe:

Up to approximately 28 months

| **End point values** | Futibatinib | Gemcitabine-Cisplatin | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[4] | 0[5] | | |
| Units: Subjects | | | | |

Notes:

[4] - The data for this end point was not collected as planned due to poor recruitment.

[5] - The data for this end point was not collected as planned due to poor recruitment.

### 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 was defined as the proportion of subjects experiencing a best overall response of stable disease (SD), PR or CR as per RECIST 1.1, based on central assessment of radiologic images. PR was defined as at least a 30% decrease in the sum of diameters of the target lesions, taking as a reference the baseline sum diameters and persistence of one or more non-target lesion(s) and/or maintenance of tumour marker level above the normal limits. CR was defined as disappearance of all target lesions. Any pathological lymph node must have reduction in short axis to <10 mm and disappearance of all non-target lesions and normalisation of tumour marker level. All lymph nodes must be non-pathological in size (<10-mm short axis). The data for this end point was not collected or analysed as planned because the study was terminated early due to poor recruitment.

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

End point timeframe:

Up to approximately 28 months

| **End point values** | Futibatinib | Gemcitabine-Cisplatin | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[6] | 0[7] | | |
| Units: Subjects | | | | |

Notes:

[6] - The data for this end point was not collected due to poor recruitment.

[7] - The data for this end point was not collected due to poor recruitment.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

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

End point description:

OS was defined as the time from the date of randomisation until the date of death due to any cause. All Treated Population included all subjects who received at least one dose of study drug. The data for this end point was not collected or analysed as planned because the study was terminated early due to poor recruitment.

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

End point timeframe:

Up to approximately 28 months

| End point values | Futibatinib | Gemcitabine-Cisplatin | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[8] | 0[9] | | |
| Units: months | | | | |
| median (full range (min-max)) | ( to ) | ( to ) | | |

Notes:

[8] - The data for this end point was not collected due to poor recruitment.

[9] - The data for this end point was not collected due to poor recruitment.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS) Per Investigator Assessment

| End point title | Progression-Free Survival (PFS) Per Investigator Assessment |
|---|---|

End point description:

PFS per investigator assessment is defined as the time from date of randomisation to the date of disease progression based on investigator assessment of radiographic images or death, whichever occurs first. As pre-specified in protocol, a total of 162 PFS events were required to perform PFS analysis. As only 10 subjects were enrolled in this study, hence no data was collected for this end point.

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

End point timeframe:

Up to approximately 28 months

| End point values | Futibatinib | Gemcitabine-Cisplatin | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[10] | 0[11] | | |
| Units: Subjects | | | | |

Notes:

[10] - Only 10 subjects were enrolled in this study, hence no data was collected for this end point.

[11] - Only 10 subjects were enrolled in this study, hence no data was collected for this end point.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs), and Serious Adverse Events (SAEs)

| End point title | Number of Subjects With Treatment-emergent Adverse Events (TEAEs), and Serious Adverse Events (SAEs) |
|---|---|

End point description:

Adverse event (AE): any untoward medical condition in clinical investigation subject administered drug; it does not necessarily have causal relationship with treatment. TEAE: AE that started orworsened at time of/after first dose of study drug administration &within 30 days after last dose of study drug &does not necessarily have a causal relationship to use of study drug. TEAEs were assessed by Common Terminology Criteria for Adverse Events Version 5.0 (CTCAE v5.0). SAE: untoward medical occurrence that at any dose: results in death,is life-threatening,required in subject hospitalisation or prolongation of existing hospitalisation,results in persistent or significant disability/incapacity, is congenital anomaly/birth defect,important medical event. TEAEs included any clinically significant changes in clinical laboratory tests,vital signs,ophthalmological exams &12lead electrocardiogram (ECG). All Treated Population included all subjects who received at least one dose of study drug.

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

End point timeframe:

Up to approximately 28 months

| **End point values** | Futibatinib | Gemcitabine-Cisplatin | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: Subjects | | | | |
| TEAEs | 4 | 5 | | |
| SAEs | 2 | 3 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to end of study (Up to approximately 28 months)

Adverse event reporting additional description:

All Treated Population included all subjects who received at least one dose of study drug.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | V25.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Futibatinib |

Reporting group description: -

| | |
|---|---|
| Reporting group title | Gemcitabine-Cisplatin |

Reporting group description: -

| Serious adverse events | Futibatinib | Gemcitabine-Cisplatin | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 3 / 5 (60.00%) | |
| number of deaths (all causes) | 1 | 3 | |
| number of deaths resulting from adverse events | 1 | 3 | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal sepsis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Metabolism and nutrition disorders | | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Futibatinib | Gemcitabine-Cisplatin | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 5 / 5 (100.00%) | |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Asthenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| Face oedema | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 1 | 2 | |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 5 (60.00%) | |
| occurrences (all) | 0 | 3 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| Hiccups | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Pulmonary embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| Blood follicle stimulating hormone decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 4 | 2 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 2 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Weight increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Cardiac disorders | | | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Blood and lymphatic system disorders | | | |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 5 (60.00%) | |
| occurrences (all) | 0 | 3 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Eye disorders | | | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Serous retinopathy | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 5 (60.00%) | |
| occurrences (all) | 1 | 4 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 2 | 2 | |
| Ascites | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 1 | 2 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 5 (100.00%) | |
| occurrences (all) | 0 | 6 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 5 (60.00%) | |
| occurrences (all) | 0 | 5 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Gingival bleeding | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Onycholysis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Night sweats | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Petechiae | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Renal and urinary disorders | | | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Endocrine disorders | | | |

| | | | |
|---|---|---|---|
| Adrenal insufficiency | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Paronychia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 12 | 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 2 | 2 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 1 | 3 | |

| | | | |
|---|---|---|---|
| Hypochloraemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 January 2020 | The following changes were made as per Amendment 1: 1. The EudraCT number on the cover page was corrected. 2. The requirement that phosphorus be assessed on Day 4 of Cycle 1 was removed from Table 1 (Schedule of Events) and throughout the protocol (the schedule for all other chemistry assessments remains the same as in the original version). |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The data for the end points related to PFS, OS, ORR, and DCR per Investigator assessment was not collected or analysed as planned because the study was terminated early due to poor recruitment.

Notes: