



Clinical trial results:

A Phase II Single-Arm Study to Investigate Tepotinib Combined With Cetuximab in RAS/BRAF Wild-Type Left-Sided mCRC Patients Having Acquired Resistance to Anti-EGFR Antibody Targeting Therapy Due to MET Amplification (PERSPECTIVE)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2020-001776-15 |
| Trial protocol | GB FR CZ BE IT |
| Global end of trial date | 31 March 2022 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 28 September 2022 |
| First version publication date | 28 September 2022 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | MS202202-0002 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04515394 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Healthcare KGaA, Darmstadt Germany |
| Sponsor organisation address | Frankfurter Strasse 250, Darmstadt, Germany, 64293 |
| Public contact | Communication Centre, Merck Healthcare KGaA, Darmstadt Germany, +49 6151725200, service@merckgroup.com |
| Scientific contact | Communication Centre, Merck Healthcare KGaA, Darmstadt Germany, +49 6151725200, service@merckgroup.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 | 31 March 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 31 March 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to assess the preliminary antitumor activity, safety and tolerability of tepotinib in combination with cetuximab in subjects with RAS/BRAF wild-type left-sided Metastatic Colorectal Cancer (mCRC) having acquired resistance to anti-epidermal growth factor receptor (EGFR) antibody targeted therapy due to mesenchymal epithelial transition (MET) amplification.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 28 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 | Spain: 1 |
| Country: Number of subjects enrolled | United States: 2 |
| Worldwide total number of subjects | 3 |
| EEA total number of subjects | 1 |

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) | 1 |
| From 65 to 84 years | 2 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 57 subjects were screened. Out of which, 3 subjects were enrolled and 2 subjects received treatment in this study..

Period 1

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

Arms

| | |
|-----------|-----------------------|
| Arm title | Tepotinib + Cetuximab |
|-----------|-----------------------|

Arm description:

Subjects received Tepotinib film-coated tablets at a dose of 500 milligrams (mg) orally, once daily (QD) in combination with weekly intravenous infusions of Cetuximab at a dose of 250 milligrams per square meter (mg/m²) until disease progression (according to Response Evaluation Criteria in Solid Tumors Version 1.1 [RECIST v1.1]), death, Adverse event (AE) leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Cetuximab |
| Investigational medicinal product code | MSB0010442D |
| Other name | Erbitux |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received weekly intravenous infusions of Cetuximab at a dose of 250 mg/m² until disease progression (according to [RECIST v1.1]), death, AE leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first.

| | |
|--|--------------------|
| Investigational medicinal product name | Tepotinib |
| Investigational medicinal product code | MSC2156119J |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received Tepotinib initially at 500 mg QD until disease progression (according to [RECIST v1.1]), death, AE leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first.

| Number of subjects in period 1 | Tepotinib + Cetuximab |
|------------------------------------|-----------------------|
| Started | 3 |
| Treated | 2 |
| Completed | 2 |
| Not completed | 1 |
| Subjects did not receive treatment | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Tepotinib + Cetuximab |
|-----------------------|-----------------------|

Reporting group description:

Subjects received Tepotinib film-coated tablets at a dose of 500 milligrams (mg) orally, once daily (QD) in combination with weekly intravenous infusions of Cetuximab at a dose of 250 milligrams per square meter (mg/m²) until disease progression (according to Response Evaluation Criteria in Solid Tumors Version 1.1 [RECIST v1.1]), death, Adverse event (AE) leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first.

| Reporting group values | Tepotinib + Cetuximab | Total | |
|---|-----------------------|-------|--|
| Number of subjects | 3 | 3 | |
| Age Categorical | | | |
| Units: subjects | | | |
| <=18 years | 0 | 0 | |
| Between 18 and 65 years | 1 | 1 | |
| >=65 years | 2 | 2 | |
| Sex: Female, Male | | | |
| Units: subjects | | | |
| Female | 1 | 1 | |
| Male | 2 | 2 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 0 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 3 | 3 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 3 | 3 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|--|-----------------------|
| Reporting group title | Tepotinib + Cetuximab |
| Reporting group description: Subjects received Tepotinib film-coated tablets at a dose of 500 milligrams (mg) orally, once daily (QD) in combination with weekly intravenous infusions of Cetuximab at a dose of 250 milligrams per square meter (mg/m ²) until disease progression (according to Response Evaluation Criteria in Solid Tumors Version 1.1 [RECIST v1.1]), death, Adverse event (AE) leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first. | |
| Subject analysis set title | Tepotinib + Cetuximab |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subjects received Tepotinib film-coated tablets at a dose of 500 milligrams (mg) orally, once daily (QD) in combination with weekly intravenous infusions of Cetuximab at a dose of 250 milligrams per square meter (mg/m ²) until disease progression (according to Response Evaluation Criteria in Solid Tumors Version 1.1 [RECIST v1.1]), death, Adverse event (AE) leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first. | |

Primary: Number of Subjects Who Experienced Dose Limiting Toxicities (DLTs) According to National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 5.0

| | |
|--|--|
| End point title | Number of Subjects Who Experienced Dose Limiting Toxicities (DLTs) According to National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 5.0 ^[1] |
| End point description: DLTs: any of following toxicities and judged by Investigator and/Sponsor to be not attributable to disease/disease-related processes under investigation: Grade (Gr)4 neutropenia for more than 7 days; Gr greater than or equal to [\geq] 3 febrile neutropenia with absolute neutrophil count <1000 per cube millimeter (per mm ³) and a single temperature of >38.3 degree Celsius/a sustained temperature of ≥ 38 degree Celsius for more than 1 hour; Gr4/3 thrombocytopenia with non-traumatic bleeding; Gr3 uncontrolled nausea/vomiting/diarrhea that has not improved within 72 hours despite adequate and optimal treatment; Gr4 vomiting/diarrhea; Gr ≥ 3 skin toxicity that has not resolved to Gr2 after 14 days of adequate treatment. DLT analysis set: all subjects treated in safety run-in period who received at least 75% of tepotinib and cetuximab planned dose and completed DLT period/experienced a DLT during DLT period regardless of received amount of each study intervention. | |
| End point type | Primary |
| End point timeframe: Day 1 to Day 21 of Cycle 1 (each cycle is of 21 days) | |

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: Only descriptive summary statistics was planned for this endpoint.

| End point values | Tepotinib + Cetuximab | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: subjects | | | | |
| number (not applicable) | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Objective Response (OR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Assessed by Investigators

| | |
|-----------------|--|
| End point title | Number of Subjects with Objective Response (OR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Assessed by Investigators ^[2] |
|-----------------|--|

End point description:

OR is defined as a best overall response (BOR) of complete response (CR) or partial response (PR). CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30% reduction from baseline in the sum of the longest diameter (SLD) of all target lesions. Full analysis set (FAS) include all subjects who were administered at least one dose of any study intervention.

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

End point timeframe:

Time from first study treatment assessed up to 218 days

Notes:

[2] - 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: Only descriptive summary statistics was planned for this endpoint.

| | | | | |
|-----------------------------|-----------------------|--|--|--|
| End point values | Tepotinib + Cetuximab | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 2 | | | |
| Units: subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Assessed by Investigator

| | |
|-----------------|---|
| End point title | Duration of Response (DoR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Assessed by Investigator |
|-----------------|---|

End point description:

For subjects with objective response, DoR is the time from when the complete response (CR) or partial response (PR) (whichever is first) criteria are first met until progression disease (PD) or death due to any cause within the period of 2 scheduled tumor assessments (84 or 168 days) after the last tumor assessment, whichever occurs first. PD is defined as at least a 20 percent (%) increase in the sum of the longest diameter (SLD), taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions.

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

End point timeframe:

Time from the first dose of study drug until occurrence of PD, death due to any cause or last tumor assessment (assessed up to 218 days)

| End point values | Tepotinib + Cetuximab | | | |
|----------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[3] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | (to) | | | |

Notes:

[3] - None of the subjects showed objective response.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Assessed by Investigators

| | |
|-----------------|---|
| End point title | Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Assessed by Investigators |
|-----------------|---|

End point description:

PFS is defined as the time (in months) from first administration of study intervention to the date of the first documentation of progression disease (PD) or death due to any cause within the period of 2 scheduled tumor assessments (84 or 168 days) after the last tumor assessment, whichever occurs first. PD is defined as at least a 20 percent (%) increase in the sum of the longest diameter (SLD), taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. Due to early termination of study based on a limited number of subjects (N=2), no data was analyzed statistically, and no derived subject data was generated.

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

End point timeframe:

Time from the first dose of study drug until occurrence of PD, death due to any cause or last tumor assessment (assessed up to 218 days)

| End point values | Tepotinib + Cetuximab | | | |
|----------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[4] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | (to) | | | |

Notes:

[4] - No data was analyzed statistically and no derived subject data was generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Assessed by Investigators

| | |
|-----------------|---|
| End point title | Overall Survival (OS) Assessed by Investigators |
|-----------------|---|

End point description:

OS is defined as the time (in months) from first administration of study intervention to the date of death. Due to early termination of study based on a limited number of subjects (N=2), no data was analyzed statistically, and no derived subject data was generated.

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

End point timeframe:

Time from first study treatment until death, assessed up to 218 days

| End point values | Tepotinib + Cetuximab | | | |
|----------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[5] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | (to) | | | |

Notes:

[5] - No data was analyzed statistically, and no derived subject data was generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related TEAEs

| | |
|-----------------|---|
| End point title | Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related TEAEs |
|-----------------|---|

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a subject/clinical study subject, temporally associated with the use of study intervention, whether considered related to the study intervention or not. A serious AE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. TEAEs were defined as events that started or worsened after first dose of study intervention until 30 days after last dose. TEAEs included both serious and non-serious TEAEs. Treatment-related TEAEs is defined as reasonably related to the study intervention. Safety analysis set (SAF) included all subjects who were administered at least one dose of any study intervention.

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

End point timeframe:

Time from first study treatment up to 30 days after the last dose, assessed up to 226 days

| End point values | Tepotinib + Cetuximab | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 2 | | | |
| Units: subjects | | | | |
| TEAEs | 2 | | | |
| Treatment-related TEAEs | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Changes from Baseline in Vital Signs

| | |
|-----------------|---|
| End point title | Number of Subjects with Clinically Significant Changes from Baseline in Vital Signs |
|-----------------|---|

End point description:

Vital sign assessment included assessments of height, weight, temperature, pulse rate, respiratory rate, and blood pressure. Clinical significance was determined by the investigator. Number of subjects who had any clinically significant changes from baseline in vital signs were reported. Due to early termination of study based on a limited number of subjects (N=2), no data was analyzed statistically, and no derived subject data was generated.

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

End point timeframe:

Time from first study treatment up to 30 days after the last dose, assessed up to 226 days

| | | | | |
|-----------------------------|-----------------------|--|--|--|
| End point values | Tepotinib + Cetuximab | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[6] | | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |

Notes:

[6] - No data was analyzed statistically, and no derived subject data was generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Changes from Baseline in Laboratory Parameters

| | |
|-----------------|---|
| End point title | Number of Subjects with Clinically Significant Changes from Baseline in Laboratory Parameters |
|-----------------|---|

End point description:

Laboratory investigation included hematology, biochemistry, coagulation, routine urinalysis and other screening tests (Follicle-stimulating hormone (FSH) and estradiol, Serum or highly sensitive urine human chorionic gonadotropin (hCG) pregnancy test, Serology (HIV antibody, hepatitis B surface antigen [HBsAg], and hepatitis C virus antibody) and all of the safety labs were performed locally. Clinical significance was determined by the investigator. The number of subjects with clinically significant changes from baseline in laboratory parameters were reported. Due to early termination of study based on a limited number of subjects (N=2), no data was analyzed statistically, and no derived subject data was generated.

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

End point timeframe:

Time from first study treatment up to 30 days after the last dose, assessed up to 226 days

| | | | | |
|-----------------------------|-----------------------|--|--|--|
| End point values | Tepotinib + Cetuximab | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[7] | | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |

Notes:

[7] - No data was analyzed statistically, and no derived subject data was generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Changes from Baseline in 12-Lead Electrocardiogram (ECG) Findings

| | |
|-----------------|--|
| End point title | Number of Subjects with Clinically Significant Changes from Baseline in 12-Lead Electrocardiogram (ECG) Findings |
|-----------------|--|

End point description:

12-lead ECG recordings included heart rate and measures PR, QRS, QT and QTcF intervals. 12-lead ECG recordings were obtained after the participants have rested for at least 5 minutes in semi-supine or supine position. Clinical significance was determined by the investigator. The number of subjects with clinically significant changes from baseline in 12-lead ECG findings were reported. Due to early termination of study based on a limited number of subjects (N=2), no data was analyzed statistically, and no derived subject data was generated.

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

End point timeframe:

Time from first study treatment up to 30 days after the last dose, assessed up to 226 days

| | | | | |
|-----------------------------|-----------------------|--|--|--|
| End point values | Tepotinib + Cetuximab | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[8] | | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |

Notes:

[8] - No data was analyzed statistically, and no derived subject data was generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects With At Least 1 Postive Anti-Drug Antibodies (ADAs) for Cetuximab

| | |
|-----------------|--|
| End point title | Number of subjects With At Least 1 Postive Anti-Drug Antibodies (ADAs) for Cetuximab |
|-----------------|--|

End point description:

Serum samples were analyzed by a validated electrochemiluminescence immunoassay method to detect the presence of antidrug antibodies (ADA). Number of subjects with positive ADA were reported. Immunogenicity analysis set included all subjects who received at least one dose of study intervention and had at least one valid antidrug antibody (ADA) result.

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

End point timeframe:

At Day 1 of cycle 1 (each cycle is of 21 days) and at End of Treatment (14 days after last dose, assessed up to 210 days)

| | | | | |
|-----------------------------|--------------------------|--|--|--|
| End point values | Tepotinib + Cetuximab | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 2 | | | |
| Units: subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time from first study treatment up to 30 days after the last dose, assessed up to 226 days

Adverse event reporting additional description:

Safety analysis set (SAF) included all subjects who were administered at least one dose of any study intervention.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Tepotinib + Cetuximab |
|-----------------------|-----------------------|

Reporting group description:

Subjects received Tepotinib film-coated tablets at a dose of 500 milligrams (mg) orally, once daily (QD) in combination with weekly intravenous infusions of Cetuximab at a dose of 250 milligrams per square meter (mg/m²) until disease progression (according to Response Evaluation Criteria in Solid Tumors Version 1.1 [RECIST v1.1]), death, Adverse event (AE) leading to discontinuation, study withdrawal, or withdrawal of consent, whichever occurs first.

| Serious adverse events | Tepotinib + Cetuximab | | |
|---|--------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Tepotinib + Cetuximab | | |
|---|--------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|----------------|--|--|
| General disorders and administration site conditions | | | |
| oedema peripheral | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| diarrhea | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin toxicity | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| drug eruption | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| dry skin | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| paronychia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Product issues | | | |

| | | | |
|--|---------------------|--|--|
| Device dislocation subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Metabolism and nutrition disorders | | | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Iron deficiency subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 08 March 2021 | <ul style="list-style-type: none">• Added the study acronym "PERSPECTIVE" to study title and short title. Added row on title page indicating the study acronym "PERSPECTIVE".• Added screening window to facilitate protocol adherence.• For ECG assessments, allowed a 60-minute window (from the previous 20-minute window).• Added "The proposed administered dose of 500 mg tepotinib corresponds to 500 mg tepotinib hydrochloride hydrate and is equivalent to 450 mg tepotinib (free base form). The 250 mg tepotinib corresponds to 250 mg tepotinib hydrochloride hydrate and is equivalent to 225 mg tepotinib (free base form)".• To inclusion criterion #2, clarified left-sided CRC tumors, "from splenic flexure to rectum." Included reference to current National Comprehensive Cancer Network (NCCN) CRC v1.2021 guidelines.• To inclusion criterion #2, clarified that advanced tumors are also unresectable.• To inclusion criterion #7b, added "First-line treatment must include a fluoropyrimidine and oxaliplatin or irinotecan and second-line treatment must include a fluoropyrimidine, oxaliplatin, or irinotecan".• To inclusion criterion #11, corrected to add the superscripted numbers to the estimated glomerular filtration rate formula.• Added to exclusion criterion #8 as point "g. Corrected QT interval by Fridericia (QTcF > 480 milliseconds [ms])• Added new exclusion criterion, #16," History of ILD or interstitial pneumonitis including radiation pneumonitis that required steroid treatment".• Added "Grade 4 vomiting or diarrhea" as DLT criteria. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---------------|---|--------------|
| 31 March 2022 | This study was terminated early due to operational challenges identifying suitable participants for screening in the study. | - |

Notes:

Limitations and caveats

None reported