Clinical trial results:
Phase Ib/II Multicenter, Randomized, Open Label Trial to Compare Tepotinib (MSC2156119J) Combined with Gefitinib Versus Chemotherapy as Second-line Treatment in subjects with MET Positive, Locally Advanced or Metastatic Non-small Cell Lung Cancer (NSCLC) Harboring EGFR Mutation and Having Acquired Resistance to Prior EGFR-Tyrosine Kinase Inhibitor (EGFR-TKI) Therapy

Summary

EudraCT number	2016-001604-28
Trial protocol	ES SK BG NL IT
Global end of trial date	14 October 2021

Results information

Result version number	v1 (current)
This version publication date	02 November 2022
First version publication date	02 November 2022

Trial information

Trial identification

Sponsor protocol code	EMR200095-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01982955
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 Center, Merck Healthcare KGaA, Darmstadt,Germany, +49 6151725200,
Scientific contact	Communication Center, Merck Healthcare KGaA, Darmstadt,Germany, +49 6151725200,

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	14 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a multi-center, open-label, randomized, Phase 1b/2 study to determine the recommended phase 2 dose (RP2D) and to evaluate the efficacy in terms of progression free survival (PFS) of Tepotinib when used in combination with gefitinib in subjects with T790M negative, MET positive locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) mutation and having acquired resistance to Prior EGFR-Tyrosine Kinase Inhibitor (EGFR-TKI) Therapy. This study has 2:1 randomization (Tepotinib/Gefitinib arm versus Chemotherapy arm).

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	23 December 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 49
Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Singapore: 7
Worldwide total number of subjects	88
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	56
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 18 subjects were enrolled in Phase 1b part of the study and a total of 70 subjects were enrolled in phase 2 part of the study. Subjects enrolled in phase 1b were not eligible for randomization in phase 2.

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	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg

Arm description:

Subjects received Tepotinib 300 milligram (mg) along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm type	Experimental
Investigational medicinal product name	Tepotinib 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subejcts received Tepotinib 300 mg orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm title	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg

Arm description:

Subjects received Tepotinib 500 mg along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm type	Experimental
Investigational medicinal product name	Tepotinib 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Tepotinib 500 mg tablet orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm title	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)

Arm description:

Subjects randomized to receive Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm type	Experimental

Investigational medicinal product name	Gefitinib 250 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to receive 250 mg Gefitinib tablets orally once daily over a 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Investigational medicinal product name	Tepotinib 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to receive Tepotinib recommended Phase 2 dose 500 mg once daily over a 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm title	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)

Arm description:

Subjects randomized to receive 500 milligram per square meter (mg/m^2) of Pemetrexed as intravenous infusion over 10 minutes in combination with Cisplatin (75 mg/m^2 as an intravenous infusion over 2 hours) or Carboplatin (intravenously at a dose of area under curve (AUC) 5 or AUC6 at the discretion of the Investigator) on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects randomized to receive 500 milligram per square meter (mg/m^2) of Pemetrexed as intravenous infusion over 10 minutes on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects randomized to receive Carboplatin (intravenously at a dose of area under curve (AUC) 5 or AUC 6 at the discretion of the Investigator) on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects randomized to receive Cisplatin (75 mg/m^2 as an intravenous infusion over 2 hours) on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.

Arm title	Phase 2: Single-arm Cohort (MET+ T790M positive)

Arm description:

Subjects with MET+ T790M positive Non-small Cell Lung Cancer (NSCLC) received a Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Arm type	Experimental
Investigational medicinal product name	Gefitinib 250 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with MET+ T790M positive Non-small Cell Lung Cancer (NSCLC) received 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Investigational medicinal product name	Tepotinib 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with MET+ T790M positive Non-small Cell Lung Cancer (NSCLC) received a Tepotinib recommended Phase 2 dose 500 mg once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Number of subjects in period 1	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)
Started	6	12	31
Treated	6	12	31
Completed	6	12	31
Not completed	0	0	0
Randomized but not treated	-	-	-

Number of subjects in period 1	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)
Started	24	15
Treated	23	15
Completed	23	15
Not completed	1	0
Randomized but not treated	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg
Reporting group description:	
Subjects received Tepotinib 300 milligram (mg) along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.	
Reporting group title	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg
Reporting group description:	
Subjects received Tepotinib 500 mg along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.	
Reporting group title	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)
Reporting group description:	
Subjects randomized to receive Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment.	
Reporting group title	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)
Reporting group description:	
Subjects randomized to receive 500 milligram per square meter (mg/m^2) of Pemetrexed as intravenous infusion over 10 minutes in combination with Cisplatin (75 mg/m^2 as an intravenous infusion over 2 hours) or Carboplatin (intravenously at a dose of area under curve (AUC) 5 or AUC6 at the discretion of the Investigator) on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.	
Reporting group title	Phase 2: Single-arm Cohort (MET+ T790M positive)
Reporting group description:	
Subjects with MET+ T790M positive Non-small Cell Lung Cancer (NSCLC) received a Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.	

Reporting group values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)
Number of subjects	6	12	31
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	3	6	21
>=65 years	3	6	10
Sex: Female, Male Units: Subjects			
Female	3	7	20
Male	3	5	11
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	6	12	31
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0

More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	Total
Number of subjects	24	15	88
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	17	9	56
>=65 years	7	6	32
Sex: Female, Male Units: Subjects			
Female	12	10	52
Male	12	5	36
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	24	15	88
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg

Reporting group description:

Subjects received Tepotinib 300 milligram (mg) along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Reporting group title	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg

Reporting group description:

Subjects received Tepotinib 500 mg along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Reporting group title	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)

Reporting group description:

Subjects randomized to receive Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Reporting group title	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)

Reporting group description:

Subjects randomized to receive 500 milligram per square meter (mg/m^2) of Pemetrexed as intravenous infusion over 10 minutes in combination with Cisplatin (75 mg/m^2 as an intravenous infusion over 2 hours) or Carboplatin (intravenously at a dose of area under curve (AUC) 5 or AUC6 at the discretion of the Investigator) on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.

Reporting group title	Phase 2: Single-arm Cohort (MET+ T790M positive)

Reporting group description:

Subjects with MET+ T790M positive Non-small Cell Lung Cancer (NSCLC) received a Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Primary: Phase 1b: Number of Subjects Experiencing at least One Dose Limiting Toxicity (DLT)

End point title	Phase 1b: Number of Subjects Experiencing at least One Dose Limiting Toxicity (DLT)[1][2]

End point description:

Dose limiting toxicity (DLT) using National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 4.0 was defined as toxicities at any dose level and judged to be related to the study treatment by investigator and/or the sponsor. DLTs included Grade 4 neutropenia for more than 7 days; Grade greater than or equal to (>=) 3 febrile neutropenia for more than 1 day; Grade 4 thrombocytopenia or Grade 3 thrombocytopenia with non-traumatic bleeding; Grade >= 3 uncontrolled nausea/vomiting and/or diarrhea despite adequate and optimal treatment and Grade >= 3 any non-hematological adverse event (AE), except the aforementioned gastrointestinal events and alopecia. Number of subjects who experienced DLT during Phase 1b were reported. Dose Limiting Toxicity (DLT) set included all subjects who experienced a DLT during Cycle 1, or received at least 80 percent of all planned doses of treatment during Cycle.

End point type	Primary

End point timeframe:

Day 1 to Day 21 of Cycle 1 (each cycle is 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 statistics was planned to be reported for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	12		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Phase 1b: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs[3][4]

End point description:

An AE was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. 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. The term TEAE is defined as AEs starting or worsening after the first intake of the study drug. TEAEs include both Serious TEAEs and non-serious TEAEs. Number of subjects with TEAEs and serious TEAEs were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Primary

End point timeframe:

Up to 175 Weeks

Notes:

[3] - 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 statistics was planned to be reported for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: subjects				
Any TEAEs	6	12		
Any Serious TEAEs	4	7		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2 (Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by the Investigator

End point title	Phase 2 (Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by the Investigator[5][6]

End point description:

Progression-free survival (assessed by the Investigator) time was defined as the time in months from randomization to either first observation of radiologically confirmed progression disease (PD) by the investigator or occurrence of death due to any cause within 84 days of either randomization or the last tumor assessment. PD is defined as at least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study; and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 millimeter (mm). PFS was measured using Kaplan-Meier (KM) estimates. The Intent-to-treat analysis set in the Phase 2 part of the study included all subjects with treatment group who were randomized to study treatment.

End point type	Primary

End point timeframe:

Up to 328 weeks

Notes:

[5] - 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 statistics was planned to be reported for this endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	24		
Units: Months				
median (confidence interval 90%)	4.86 (3.88 to 6.87)	4.37 (4.17 to 6.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration Versus Time Curve from Time Zero to the Last Sampling Time AUC (0-t) of Tepotinib, its Metabolites and

Gefitinib

End point title	Phase 1b: Area Under the Plasma Concentration Versus Time Curve from Time Zero to the Last Sampling Time AUC (0-t) of Tepotinib, its Metabolites and Gefitinib[7]

End point description:

Area under the plasma concentration versus time curve from time zero to the last sampling time t at which the concentration is at or above the lower limit of quantification (LLLQ). AUC(0-t) was calculated according to the mixed log-linear trapezoidal rule. The Pharmacokinetic (PK) set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here "n=Number Analyzed" signifies those subjects who were evaluable for specified category. Here, "99999" indicate that value was not determined because only 2 subjects had evaluable AUC(0-t) at time point. For statistical reasons, calculation of summary statistics does not make sense for this low sample size. Individual values were 3830 and 3980 ng*h/mL.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: nanogram*hour per milliliter (ng*h/mL)				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1 (n=5, 12)	6280 (± 25.4)	9210 (± 48.4)		
Tepotinib: Day 15 of Cycle 1 (n=6, 9)	15600 (± 19.6)	22200 (± 43.3)		
MSC2571109A: Day 1 of Cycle 1 (n=5, 11)	1680 (± 11.8)	1770 (± 56.7)		
MSC2571109A Day15 of Cycle 1 (n=6, 8)	4420 (± 25.7)	7530 (± 52.6)		
MSC2571107A Day 1 of Cycle 1 (n=5, 11)	248 (± 49.3)	324 (± 57.3)		
MSC2571107A Day 15 of Cycle 1 (n=6, 8)	872 (± 38.5)	1880 (± 76.0)		
Gefitinib: Day 1 of Cycle 1 (n=2, 11)	99999 (± 99999)	2930 (± 45.8)		
Gefitinib: Day 15 of Cycle 1 (n=6, 9)	7690 (± 44.1)	7080 (± 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration-Time Curve within 1 Dosing Interval (AUC 0-tau) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Area Under the Plasma Concentration-Time Curve within 1 Dosing Interval (AUC 0-tau) of Tepotinib, its

	Metabolites and Gefitinib[8]

End point description:

AUC (0-tau) is the area under the plasma concentration time curve within 1 dosing interval. The PK set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here "n=Number Analyzed" signifies those subjects who were evaluable for specified category. Here, "99999" indicate that value was not determined because only 2 subjects had evaluable AUC(0-tau) at time point. For statistical reasons, calculation of summary statistics does not make sense for this low sample size. Individual values were 3830 and 3980 ng*h/mL.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1 (n=5, 12)	6280 (± 25.4)	9210 (± 48.4)		
Tepotinib: Day 15 of Cycle 1 (n=6, 9)	15600 (± 19.6)	22200 (± 43.3)		
MSC2571109A: Day 1 of Cycle 1 (n=5, 11)	1680 (± 11.8)	1770 (± 56.7)		
MSC2571109A: Day 15 of Cycle 1 (n=6, 8)	4420 (± 25.7)	7530 (± 52.6)		
MSC2571107A: Day 1 of Cycle 1 (n=5, 11)	248 (± 49.3)	324 (± 57.3)		
MSC2571107A: Day 15 of Cycle 1 (n=6, 8)	872 (± 38.5)	1880 (± 76.0)		
Gefitinib: Day 1 of Cycle 1 (n=2, 11)	99999 (± 99999)	2930 (± 45.8)		
Gefitinib: Day 15 of Cycle 1 (n=6, 9)	7690 (± 44.1)	7080 (± 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Maximum Observed Plasma Concentration (Cmax) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Maximum Observed Plasma Concentration (Cmax) of Tepotinib, its Metabolites and Gefitinib[9]

End point description:

Cmax is the maximum observed plasma concentration obtained directly from the concentration versus time curve. The PK set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here "n=Number Analyzed" signifies those subjects who were evaluable for specified category. Here, "99999" indicate that value was not determined because only 2 subjects had evaluable

Cmax at time point. For statistical reasons, calculation of summary statistics does not make sense for this low sample size. Individual values were 302 and 305 ng/mL.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Nanogram per Milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1 (n=5, 12)	375 (± 30.4)	575 (± 62.6)		
Tepotinib: Day 15 of Cycle 1 (n=6, 10)	763 (± 22.0)	1050 (± 44.1)		
MSC2571109A: Day 1 of Cycle 1 (n=5, 11)	132 (± 14.7)	149 (± 56.5)		
MSC2571109A: Day 15 of Cycle 1 (n=6, 9)	280 (± 32.0)	444 (± 45.8)		
MSC2571107A: Day 1 of Cycle 1 (n=5, 11)	16.8 (± 56.5)	24.3 (± 62.5)		
MSC2571107A: Day 15 of Cycle 1 (n=6, 9)	44.9 (± 40.5)	94.9 (± 70.8)		
Gefitinib: Day 1 of Cycle 1 (n=2, 11)	99999 (± 99999)	215 (± 48.7)		
Gefitinib: Day 15 of Cycle 1 (n=6, 10)	432 (± 38.3)	366 (± 32.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Average Observed Plasma Concentration (Cavg) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Average Observed Plasma Concentration (Cavg) of Tepotinib, its Metabolites and Gefitinib[10]

End point description:

Cavg is the average plasma concentration within 1 dosing interval obtained directly from the concentration versus time curve. The PK analysis set employed here. "Number of subjects analyzed" signifies subjects who were evaluable for this outcome measure and "n=Number Analyzed" signifies those subjects who were evaluable for specified category.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Tepotinib (n=6, 9)	654 (± 19.4)	924 (± 43.3)		
MSC2571109A (n=6, 8)	185 (± 25.4)	314 (± 52.6)		
MSC2571107A (n=6, 8)	36.4 (± 38.2)	78.3 (± 76.0)		
Gefitinib (n=6, 9)	321 (± 43.9)	295 (± 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Minimum Observed Plasma Concentration (Cmin) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Minimum Observed Plasma Concentration (Cmin) of Tepotinib, its Metabolites and Gefitinib[11]

End point description:

Cmin is minimum observed plasma concentration obtained directly from the concentration versus time curve. The PK analysis set employed here. "Number of subjects analyzed" signifies subjects who were evaluable for this outcome measure and "n=Number Analyzed" signifies those subjects who were evaluable for specified category.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Tepotinib (n=6, 9)	534 (± 18.8)	735 (± 47.6)		

MSC2571109A (n=6, 8)	156 (± 28.8)	270 (± 58.5)		
MSC2571107A (n=6, 8)	32.8 (± 40.1)	68.7 (± 80.1)		
Geftinib (n=6, 9)	231 (± 57.3)	190 (± 43.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Time to Reach Maximum Plasma Concentration (Tmax) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Time to Reach Maximum Plasma Concentration (Tmax) of Tepotinib, its Metabolites and Gefitinib[12]

End point description:

Tmax is time to reach maximum observed plasma concentration obtained directly from the concentration versus time curve. The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here "Number Analyzed" signifies those subjects who were evaluable for specified category. Here "99999" indicate that value can not be determined as only 2 subjects had evaluable tmax at time point. For statistical reasons, calculation of summary statistics does not make sense for this low sample size. Individual values were 4.00 and 4.00 hour.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Hours				
median (full range (min-max))				
Tepotinib: Day 1 of Cycle 1 (n=5, 12)	8.00 (4.00 to 8.00)	9.01 (4.00 to 10.00)		
Tepotinib: Day 15 of Cycle 1 (n=6, 10)	6.00 (0.00 to 8.00)	9.00 (4.00 to 24.00)		
MSC2571109A: Day 1 of Cycle 1 (n=5, 11)	24.00 (23.75 to 24.00)	24.00 (24.00 to 24.00)		
MSC2571109A: Day 15 of Cycle 1 (n=6, 9)	0.00 (0.00 to 24.00)	0.00 (0.00 to 24.00)		
MSC2571107A: Day 1 of Cycle 1 (n=5, 11)	24.00 (23.75 to 24.00)	24.00 (24.00 to 24.00)		
MSC2571107A: Day 15 of Cycle 1 (n=6, 9)	0.13 (0.00 to 8.00)	0.25 (0.00 to 24.00)		
Gefitinib: Day 1 of Cycle 1 (n=2, 11)	99999 (99999 to 99999)	8.00 (4.00 to 8.02)		
Gefitinib: Day 15 of Cycle 1 (n=6, 10)	4.00 (4.00 to 10.00)	8.00 (4.00 to 10.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration-Time Curve From Time Zero to Infinity (AUC 0-infinity) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Area Under the Plasma Concentration-Time Curve From Time Zero to Infinity (AUC 0-infinity) of Tepotinib, its Metabolites and Gefitinib[13]

End point description:

The AUC(0-inf) was estimated by determining the total area under the curve of the concentration versus time curve extrapolated to infinity. The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here, "99999" indicate that value was not determined. Study drug administered once daily with rich PK sampling up to 24 hours. As half-life of study drug exceeding the PK sampling time, Lambda(z) could not be reliably estimated. Therefore, AUC(0-inf) which is dependent on Lambda(z) was not determined.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Tepotinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		

Gefitinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Total Body Clearance From Plasma (CL/F) of Tepotinib and Gefitinib

End point title	Phase 1b: Apparent Total Body Clearance From Plasma (CL/F) of Tepotinib and Gefitinib[14]

End point description:

The CL/f is a measure of the rate at which it was metabolized or eliminated by normal biological processes. Clearance obtained after oral dose was influenced by the fraction of the dose absorbed. The CL/F from plasma was calculated using the formula: Dose divided by area under the concentration time curve from time zero to infinity (AUC0-inf). The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: liter per hour (L/h)				
geometric mean (geometric coefficient of variation)				
Tepotinib	17.3 (± 19.6)	20.3 (± 43.3)		
Gefitinib	32.5 (± 44.1)	35.3 (± 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Volume of Distribution (Vz/F) During the Terminal Phase of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Apparent Volume of Distribution (Vz/F) During the Terminal Phase of Tepotinib, its Metabolites and Gefitinib[15]

End point description:

The Vz/f was defined as the theoretical volume in which the total amount of required to uniformly distribute to produce the desired plasma concentration. Apparent volume of distribution after oral dose (Vz/F) was influenced by the fraction absorbed. The Vz/f was calculated by dividing the dose with area under the concentration time curve from time zero to infinity multiplied with terminal elimination rate constant Lambda(z). Vz/f=Dose/AUC(0-inf) multiply Lambda(z). The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here, "99999" indicate that values was not determined. Study drug administered once daily with rich PK sampling up to 24 hours. As half-life of study drug exceeding the PK sampling time, Lambda(z) could not be reliably estimated. Therefore, Vz/F which is dependent on Lambda(z) was not determined.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Liter				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Tepotinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Volume of Distribution During the Steady State (Vss/F) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Apparent Volume of Distribution During the Steady State (Vss/F) of Tepotinib, its Metabolites and Gefitinib[16]

End point description:

Volume of distribution was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. Vss/f after oral dose was influenced by the fraction absorbed. The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here, "99999" indicate that value was not determined. Study drug administered once daily with rich PK sampling up to 24 hours. As half-life of study drug exceeding the PK sampling time, Lambda(z) could not be reliably estimated. Therefore, Vss/F which is dependent on Lambda(z) was not determined.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Liter				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Tepotinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 15 of cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Terminal Elimination Rate Constant Lambda(z) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Apparent Terminal Elimination Rate Constant Lambda(z) of Tepotinib, its Metabolites and Gefitinib[17]

End point description:

Lambda(z) was determined from the terminal slope of the log-transformed plasma concentration curve

using linear regression method. The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here, "99999" indicate that value was not determined. Study drug administered once daily with rich PK sampling up to 24 hours. As half-life of study drug exceeding the PK sampling time, Lambda(z) could not be reliably estimated. Therefore, Lambda (z) was not determined.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: 1 per hour				
geometric mean (geometric coefficient of variation)				
Tepotinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Tepotinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571109A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
MSC2571107A: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 1 of Cycle 1	99999 (± 99999)	99999 (± 99999)		
Gefitinib: Day 15 of Cycle 1	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Terminal Half-Life (t1/2) of Tepotinib, its Metabolites and Gefitinib

End point title	Phase 1b: Apparent Terminal Half-Life (t1/2) of Tepotinib, its Metabolites and Gefitinib[18]

End point description:

Apparent terminal half-life was defined as the time required for the plasma concentration of drug to decrease 50 percent in the final stage of its elimination. The Pharmacokinetic set included all subjects who had received at least 1 dose of the tepotinib or gefitinib and who had provided at least 1 plasma concentration measurement of tepotinib or gefitinib after the first dose. Here, "99999" indicate that value was not determined. Study drug administered once daily with rich PK sampling up to 24 hours. As

half-life of study drug exceeding the PK sampling time, Lambda(z) could not be reliably estimated. Therefore, t1/2 which is dependent on Lambda(z) was not determined.

End point type	Secondary

End point timeframe:

Pre dose, 0.25, 0.5, 1, 2, 4, 8, 10 and 24 hours post dose on Day 1 and 15 of Cycle 1 (each Cycle is 21 days)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Hours				
median (full range (min-max))				
Tepotinib: Day 1 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
Tepotinib: Day 15 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
MSC2571109A: Day 1 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
MSC2571109A: Day 15 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
MSC2571107A: Day 1 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
MSC2571107A: Day 15 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
Gefitinib: Day 1 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		
Gefitinib: Day 15 of Cycle 1	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Percentage of Subjects With Objective Response Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria

End point title	Phase 1b: Percentage of Subjects With Objective Response Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria[19]

End point description:

Objective response (OR) was defined as percentage of subjects who had achieved complete response or partial response as best overall response according to local radiological assessments from randomization/ first administration of study treatment to first observation of disease progression (PD). CR: defined as disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: defined as at least a 30% decrease in sum of diameters of target lesions taking as reference baseline sum diameters. PD defined as an increase of at least 20% in sum of the diameters of target lesions, taking as reference the

smallest sum of the diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or presence of new lesions. Sum must also demonstrate an absolute increase of at least 5 mm. The safety analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Percentage of subjects				
number (confidence interval 90%)	33.3 (6.3 to 72.9)	33.3 (12.3 to 60.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Percentage of Subjects With Disease Control Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria

End point title	Phase 1b: Percentage of Subjects With Disease Control Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria[20]

End point description:

Disease control defined as CR, PR, or stable disease as best overall response according to local radiological assessments from date of randomization/the first administration of study treatment to the first observation of PD. CR:disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR:at least 30% decrease in sum of diameters of target lesions taking as reference baseline sum diameters. PD: an increase of at least 20% in sum of the diameters of target lesions, taking as reference smallest sum of the diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or presence of new lesions. Sum must also demonstrate an absolute increase of at least 5mm. SD: as any cases that do not qualify for either PR or PD at minimum interval of 42 days after randomization/start of study treatment. The safety analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Percentage of subjects				
number (confidence interval 90%)	50.0 (15.3 to 84.7)	58.3 (31.5 to 81.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Treatment-Related Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related Serious TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03

End point title	Phase 1b: Number of Subjects With Treatment-Related Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related Serious TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03[21]

End point description:

An adverse event (AE) was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. 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. Term TEAE was defined as AEs starting/worsening after first intake of the study drug. TEAEs included both Serious TEAEs and non-serious TEAEs. Treatment-related AE was defined as having a "Possible" or "Related" relationship to study treatment, as assessed by the Investigator. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects				
Any TEAE Related to Tepotinib	6	9		
Any TEAE Related to Gefitinib	5	11		
Any Serious TEAE Related to Tepotinib	0	0		
Any Serious TEAE Related to Gefitinib	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Grade 3/4 Treatment-Emergent Adverse Events (TEAEs) and Grade 3/4 Treatment-Related TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 4.03

End point title	Phase 1b: Number of Subjects With Grade 3/4 Treatment-Emergent Adverse Events (TEAEs) and Grade 3/4 Treatment-Related TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 4.03[22]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in subject which does not necessarily have causal relationship with treatment was any unfavorable and unintended sign (including abnormal laboratory finding), symptom/disease temporally associated with use of medicinal product, whether/not considered related to medicinal product. Term TEAE was defined as AEs starting/worsening after first intake of the study drug. TEAEs included both Serious TEAEs and non-serious TEAEs. Treatment-related TEAE was defined as having a "Possible" or "Related" relationship to study treatment, as assessed by the Investigator. As per NCI-CTCAE, Grade 3 is Severe, Grade 4 is Life-threatening and Grade 5 or Death. Number of subjects with Grade 3/4 TEAEs and Grade 3/4 treatment-related TEAEs were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects				
Any Grade 3/4 TEAE	5	9		
Any Grade 3/4 TEAE Related to Tepotinib	2	4		
Any Grade 3/4 TEAE Related to Gefitinib	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) Leading to Permanent Treatment Discontinuation

End point title	Phase 1b: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) Leading to Permanent Treatment Discontinuation[23]

End point description:

An adverse event (AE) was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. 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. Term TEAE is defined as AEs starting/worsening after first intake of the study drug. TEAEs included both Serious TEAEs and non-serious TEAEs. Number of subjects with TEAEs leading to permanent treatment discontinuation were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects				
TEAE Leading Permanent Tepotinib Discontinuation	0	2		
TEAE Leading Permanent Gefitinib Discontinuation	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Death and Reasons

End point title	Phase 1b: Number of Subjects With Death and Reasons[24]

End point description:

Number of subjects with death due to progressive disease (PD), adverse event (AE) related to study treatment, AE not related to study treatment were reported. An AE was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. PD defined as an increase of at least 20% in the sum of the diameters of target lesions, taking as reference the smallest sum of the diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 mm. Number of subjects with deaths due to PD, AE related to study treatment, AE not related to study treatment were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects				
Death due to PD	0	3		
Death due to AE related to study treatment	0	0		
Death due to AE not related to study treatment	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Laboratory Test Abnormalities of Grade 3 or Higher Severity Based on NCI-CTCAE Version 4.03 Reported as Treatment-Emergent Adverse Events (TEAEs)

End point title	Phase 1b: Number of Subjects With Laboratory Test Abnormalities of Grade 3 or Higher Severity Based on NCI-CTCAE Version 4.03 Reported as Treatment-Emergent Adverse Events (TEAEs)[25]

End point description:

The laboratory measurements included hematology and coagulation, biochemistry and urinalysis. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects				
Amylase increased	2	2		
Lipase increased	1	2		
Neutrophil count decreased	0	1		
Hyperglycemia	0	2		
Hypocalcemia	1	0		
Hyponatremia	0	2		
Hypoproteinemia	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

End point title	Phase 1b: Number of Subjects With Clinically Significant Abnormalities in Vital Signs[26]

End point description:

Vital signs assessment included blood pressure, heart rate, respiratory rate and body temperature. Number of subjects with any clinically significant abnormalities in vital signs were reported. Clinical significance was determined by the investigator. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Clinically Significant Abnormalities in 12-Lead Electrocardiograms (ECG) Findings

End point title	Phase 1b: Number of Subjects With Clinically Significant Abnormalities in 12-Lead Electrocardiograms (ECG) Findings[27]

End point description:

ECG parameters included heart rhythm, pulse rate intervals, QRS, QT intervals, RR intervals and corrected QT(QTc) intervals. Clinical significance was determined by the investigator. Number of subjects with clinically significant abnormalities in 12-lead ECG were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Number of Subjects With Eastern Cooperative Oncology Group (ECOG) Performance Status Score of 2 or Higher Than 2

End point title	Phase 1b: Number of Subjects With Eastern Cooperative Oncology Group (ECOG) Performance Status Score of 2 or Higher Than 2[28]

End point description:

ECOG PS score is widely used by doctors and researchers to assess how a subject's disease is progressing and is used to assess how the disease affects the daily living abilities of the subject and determine appropriate treatment and prognosis. The score ranges from Grade 0 to Grade 5, where Grade 0 = Fully active, able to carry on all pre-disease performance without restriction, Grade 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (like light house work, office work), Grade 2 = Ambulatory and capable of all self-care but unable to carry out any work activities, Grade 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours and Grade 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair, Grade 5 = Death. Number of subjects with ECOG performance status score of 2 or higher than 2 were reported. The safety analysis set was used.

End point type	Secondary

End point timeframe:

Up to 175 weeks

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 1b. Therefore, other arms have not been selected.

End point values	Phase 1b: Tepotinib 300 mg + Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Subjects	2	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Treatment-Related TEAEs and Treatment-Related Serious TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03

End point title	Phase 2: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Treatment-Related TEAEs and Treatment-Related Serious TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03[29]

End point description:

An AE was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. 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 was defined as AEs that started or worsened in severity within the first dosing day of study treatment after the last dose of study treatment. TEAEs include both Serious TEAEs and non-serious TEAEs Treatment related AE was defined as having a "Possible" or "Related" relationship to study treatment, as assessed by the Investigator. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects				
Any TEAE	31	23	13	

Any Treatment-Related TEAE	30	23	11	
Any Serious TEAE	13	8	5	
Any Treatment-Related Serious TEAE	6	7	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Greater than or Equal to (>=) Grade 3 Treatment-Emergent Adverse Events (TEAEs) and >= Grade 3 Treatment-Related TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03

End point title	Phase 2: Number of Subjects With Greater than or Equal to (>=) Grade 3 Treatment-Emergent Adverse Events (TEAEs) and >= Grade 3 Treatment-Related TEAEs According to National Cancer Institute Common Toxicity Criteria for Adverse Events Version 4.03[30]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in subject which does not necessarily have causal relationship with treatment was any unfavorable and unintended sign (including abnormal laboratory finding), symptom/disease temporally associated with use of medicinal product, whether/not considered related to medicinal product. Term TEAE is defined as AEs starting/worsening after first intake of the study drug. TEAEs included both Serious TEAEs and non-serious TEAEs. Treatment-related AE was defined as having a "Possible" or "Related" relationship to study treatment, as assessed by the Investigator. As per NCI-CTCAE, Grade 3 is Severe, Grade 4 is Life-threatening and Grade 5 or Death. Number of subjects with >= Grade 3 TEAEs and >= Grade 3 treatment-related TEAEs were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects				
Any TEAE of >= Grade 3	20	14	7	
Any Treatment-related TEAE of >= Grade 3	16	12	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) Leading to Permanent Treatment Discontinuation

End point title	Phase 2: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) Leading to Permanent Treatment Discontinuation[31]

End point description:

An adverse event (AE) was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. 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. Term TEAE is defined as AEs starting/worsening after first intake of the study drug. TEAEs included both Serious TEAEs and non-serious TEAEs. Number of subjects with TEAEs leading to permanent treatment discontinuation were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects	3	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Death and Reasons

End point title	Phase 2: Number of Subjects With Death and Reasons[32]

End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. PD defined as an increase of at least 20% in the sum of the diameters of target lesions, taking as reference the smallest sum of the diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 mm. Number of subjects with deaths due to PD, AE related to study treatment, unknown reason was reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects				
Death due to disease progression	21	15	8	
Death due to AE related to study treatment	0	0	0	
Unknown	2	5	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects with Laboratory Test Abnormalities of Grade 3 or Higher Severity Based on NCI-CTCAE Version 4.03 Reported as Treatment-Emergent Adverse Events (TEAEs)

End point title	Phase 2: Number of Subjects with Laboratory Test Abnormalities of Grade 3 or Higher Severity Based on NCI-CTCAE Version 4.03 Reported as Treatment-Emergent Adverse Events (TEAEs)[33]

End point description:

The laboratory measurements included hematology and coagulation, biochemistry and urinalysis. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects				
Anaemia	0	7	0	

Neutropenia	0	1	0	
Alanine aminotransferase increased	1	0	0	
Amylase increased	7	2	2	
Gamma-glutamyltransferase increased	0	1	0	
Lipase increased	4	2	1	
Neutrophil count decreased	2	3	0	
White blood cell count decreased	1	2	0	
Hyponatremia	1	3	0	
Hypokalemia	0	2	0	
hypophosphatemia	0	1	0	
Hypoalbuminemia	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

End point title	Phase 2: Number of Subjects With Clinically Significant Abnormalities in Vital Signs[34]

End point description:

Vital signs assessment included blood pressure, heart rate, respiratory rate and body temperature. Number of subjects with any clinically significant abnormalities in vital signs were reported. Clinical significance was determined by the investigator. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Clinically Significant Abnormalities in

12-Lead Electrocardiograms (ECG) Findings

End point title	Phase 2: Number of Subjects With Clinically Significant Abnormalities in 12-Lead Electrocardiograms (ECG) Findings[35]

End point description:

ECG parameters included heart rhythm, pulse rate intervals, QRS, QT intervals, RR intervals and corrected QT(QTc) intervals. Clinical significance was determined by the investigator. Number of subjects with clinically significant abnormalities in 12-lead ECG were reported. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects	2	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Eastern Cooperative Oncology Group (ECOG) Performance Status Score of 2 or Higher Than 2

End point title	Phase 2: Number of Subjects With Eastern Cooperative Oncology Group (ECOG) Performance Status Score of 2 or Higher Than 2[36]

End point description:

ECOG PS score is widely used by doctors and researchers to assess how a subject's disease is progressing, and is used to assess how the disease affects the daily living abilities of the subject, and determine appropriate treatment and prognosis. The score ranges from Grade 0 to Grade 5, where Grade 0 = Fully active, able to carry on all pre-disease performance without restriction, Grade 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (like light house work, office work), Grade 2 = Ambulatory and capable of all self-care but unable to carry out any work activities, Grade 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours and Grade 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair, Grade 5 = Death. Number of subjects with ECOG performance status score of 2 or higher than 2 were reported. The safety analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been

selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	23	15	
Units: Subjects	6	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by Independent Review Committee (IRC)

End point title	Phase 2 (Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by Independent Review Committee (IRC)[37]

End point description:

Progression-free survival (assessed by Independent Review Committee) time was defined as the time in months from randomization to either first observation of radiologically confirmed progression disease (PD) by the IRC or occurrence of death due to any cause within 84 days of either randomization or the last tumor assessment. PD is defined as at least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study; and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 mm. PFS was measured using Kaplan-Meier (KM) estimates. The Intent-to-treat analysis set in the Phase 2 part of the study included all subjects with treatment group who were randomized to study treatment.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	24		
Units: Months				
median (confidence interval 90%)	10.15 (4.24 to 19.32)	4.34 (4.11 to 6.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: (Randomized Part Only): Overall Survival (OS) Time

End point title	Phase 2: (Randomized Part Only): Overall Survival (OS)

End point description:

Overall survival time was measured as time in months between the date of randomization and the date of death. The Intent-to-treat analysis set in the Phase 2 part of the study included all subjects with treatment group who were randomized to study treatment.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	24		
Units: Months				
median (confidence interval 90%)	17.25 (12.12 to 29.14)	19.48 (15.90 to 21.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Randomized Part Only): Percentage of Subjects With Objective Response Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria

End point title	Phase 2 (Randomized Part Only): Percentage of Subjects With Objective Response Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria[39]

End point description:

Objective response was defined as percentage of subjects who had achieved complete response or partial response as best overall response according to local radiological assessments from randomization/the first administration of the study treatment to first observation of disease progression.

CR: defined as disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: defined as at least a 30% decrease in sum of diameters of target lesions taking as reference baseline sum diameters. PD defined as an increase of at least 20% in the sum of diameters of target lesions, taking as reference the smallest sum of diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. Sum must also demonstrate an absolute increase of at least 5 mm. Intent-to-treat analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	24		
Units: Percentage of Subjects				
number (confidence interval 90%)	45.2 (29.7 to 61.3)	33.3 (17.8 to 52.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Randomized Part Only): Percentage of Subjects With Disease Control Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria

End point title	Phase 2 (Randomized Part Only): Percentage of Subjects With Disease Control Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria[40]

End point description:

Disease control defined as CR, PR, or stable disease as best overall response according to local radiological assessments from date of randomization/the first administration of study treatment to first observation of PD. CR: disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR: at least 30% decrease in sum of diameters of target lesions taking as reference baseline sum diameters. PD: an increase of at least 20% in sum of the diameters of target lesions, taking as reference smallest sum of diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or presence of new lesions. Sum must also demonstrate an absolute increase of at least 5mm. SD: as any cases that do not qualify for either PR/PD at minimum interval of 42 days after randomization/start of study treatment. The Intent-to-treat analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	24		
Units: Percentage of Subjects				
number (confidence interval 90%)	83.9 (69.0 to 93.4)	70.8 (52.1 to 85.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Non-Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by Independent Review Committee (IRC)

End point title	Phase 2 (Non-Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by Independent Review Committee (IRC)[41]

End point description:

Progression-free survival (assessed by Independent Review Committee) time was defined as the time in months from randomization to either first observation of radiologically confirmed progression disease by the IRC or occurrence of death due to any cause within 84 days of either randomization or the last tumor assessment. PD is defined as at least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study; and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 mm. PFS was measured using Kaplan-Meier (KM) estimates. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Single-arm Cohort (MET+ T790M positive)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Months				

median (confidence interval 90%)	2.63 (1.38 to 2.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Non-Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by Investigator

End point title	Phase 2 (Non-Randomized Part Only): Progression-free Survival (PFS) Based on Tumor Assessment by Investigator[42]

End point description:

Progression-free survival (assessed by Investigator) time was defined as the time in months from randomization to either first observation of radiologically confirmed progression disease by the Investigator or occurrence of death due to any cause within 84 days of either randomization or the last tumor assessment. PD is defined as at least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study; and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 mm. PFS was measured using Kaplan-Meier (KM) estimates. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Single-arm Cohort (MET+ T790M positive)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Months				
median (confidence interval 90%)	1.41 (1.35 to 4.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: (Non-Randomized Part Only): Overall Survival (OS) Time

End point title	Phase 2: (Non-Randomized Part Only): Overall Survival (OS) Time[43]

End point description:

Overall survival time was measured as time in months between the date of randomization and the date

of death. The safety analysis set included all subjects who had received any dose of the study medication.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Single-arm Cohort (MET+ T790M positive)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Months				
median (confidence interval 90%)	25.86 (13.08 to 39.66)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Non-Randomized Part Only): Percentage of Subjects With Objective Response Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria

End point title	Phase 2 (Non-Randomized Part Only): Percentage of Subjects With Objective Response Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria[44]

End point description:

Objective response (OR) was defined as percentage of subjects who had achieved complete response (CR) or partial response (PR) as best overall response according to local radiological assessments from randomization/the first administration of study treatment to first observation of disease progression (PD). CR: defined as disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: defined as at least a 30% decrease in sum of diameters of target lesions taking as reference the baseline sum diameters. PD defined as an increase of at least 20% in the sum of diameters of target lesions, taking as reference smallest sum of diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or the presence of new lesions. The sum must also demonstrate an absolute increase of at least 5 mm. Safety analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Single-arm Cohort (MET+ T790M positive)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Percentage of Subjects				
number (confidence interval 90%)	0 (0.0 to 18.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 (Non-Randomized Part Only): Percentage of Subjects With Disease Control Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria

End point title	Phase 2 (Non-Randomized Part Only): Percentage of Subjects With Disease Control Based on Tumor Response Assessment According to Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) Criteria[45]

End point description:

Disease control defined as CR, PR, or stable disease(SD) as best overall response according to local radiological assessments from date of randomization/the first administration of study treatment to first observation of PD. CR: disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR: at least 30% decrease in sum of diameters of target lesions taking as reference baseline sum diameters. PD: an increase of at least 20% in sum of the diameters of target lesions, taking as reference smallest sum of diameters of target lesions recorded since treatment started and/or unequivocal progression of existing non-target lesions and/or presence of new lesions. Sum must also demonstrate an absolute increase of at least 5mm. SD: as any cases that do not qualify for either PR/PD at minimum interval of 42 days after randomization/start of study treatment. Safety analysis set was used.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Single-arm Cohort (MET+ T790M positive)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Percentage of Subjects				
number (confidence interval 90%)	40 (19.1 to 64.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) Global Health Status Scale Score at end of Treatment (EOT)

End point title	Phase 2: Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) Global Health Status Scale Score at end of Treatment (EOT)[46]

End point description:

EORTC QLQ-C30 is a 30-question tool used to assess the overall quality of life (QoL) in cancer subjects. It consisted of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, role, cognitive, emotional, social), and 9 symptom scales/items (Fatigue, nausea and vomiting, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, financial impact. The EORTC QLQ-C30 GHS/QoL score ranges from 0 to 100; High score indicates better GHS/QoL. Score 0 represents: very poor physical condition and QoL. Score 100 represents: excellent overall physical condition and QoL. Quality of life (Qol) evaluable population set included ITT subjects in the treatment group in which they actually received the treatment with a baseline and at least 1 evaluable on-treatment QoL questionnaire. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and EOT (up to 110 weeks)

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	21	10	
Units: Units on a Scale				
arithmetic mean (standard deviation)	-16.29 (± 30.691)	-2.78 (± 22.869)	-24.19 (± 24.673)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time-to-Symptom Progression (TTSP)

End point title	Phase 2: Time-to-Symptom Progression (TTSP)[47]

End point description:

TTSP was measured from randomization to symptomatic progression by lung cancer symptom scale (LCSS) used to measure symptom changes relevant to quality of life. It consisted of 9 items focused on cancer symptoms (loss of appetite, fatigue, cough, shortness of breath, blood in sputum, symptoms of cancer, illness affecting normal activity, QoL). For each symptom score distance from left boundary to point where subject has marked line was measured in millimeters. Total scale length was 100 mm. Symptomatic progression was defined as increase/worsening of average symptomatic burden index

(mean of 6 major lung cancer specific symptom scores); Worsening defined as 10% increase of scale breadth from baseline. Score 0 indicate no/minimum symptoms;100 indicates maximum level of symptoms. Quality of life evaluable population set included ITT subjects in treatment group in which they actually received treatment with a baseline and at least 1 evaluable on-treatment QoL questionnaire.

End point type	Secondary

End point timeframe:

Up to 328 weeks

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: It was planned to report data for only Phase 2. Therefore, other arms have not been selected.

End point values	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+ T790 negative)	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	22	15	
Units: Months				
median (confidence interval 90%)	5.75 (1.41 to 11.86)	8.61 (2.83 to 19.42)	2.63 (1.41 to 8.31)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 328 weeks

Adverse event reporting additional description:

The safety analysis set included all subjects who had received any dose of the study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0, 24.0

Reporting groups

Reporting group title	Phase 1b: Tepotinib 300 mg +Gefitinib 250 mg

Reporting group description:

Subjects received Tepotinib 300 milligram (mg) along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Reporting group title	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg

Reporting group description:

Subjects received Tepotinib 500 milligram (mg) along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Reporting group title	Phase 2: Tepotinib 500mg+Gefitinib250mg (MET+T790 negative)

Reporting group description:

Subjects randomized to receive Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Reporting group title	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)

Reporting group description:

Subjects randomized to receive 500 milligram per square meter (mg/m^2) of Pemetrexed as intravenous infusion over 10 minutes in combination with Cisplatin (75 mg/m2 as an intravenous infusion over 2 hours) or Carboplatin (intravenously at a dose of area under curve (AUC) 5 or AUC6 at the discretion of the Investigator) on Day 1 of each 21-day cycle until progressive disease, intolerable toxicity or withdrawal from treatment or up to 6 cycles if or 4 cycles followed by Pemetrexed maintenance monotherapy.

Reporting group title	Phase 2: Single-arm Cohort (MET+ T790M positive)

Reporting group description:

Subjects with MET+ T790M positive Non-small Cell Lung Cancer (NSCLC) received a Tepotinib recommended Phase 2 dose 500 mg once daily along with 250 mg Gefitinib tablets orally once daily over a 21-day treatment cycle until progressive disease, intolerable toxicity or withdrawal from treatment.

Serious adverse events	Phase 1b: Tepotinib 300 mg +Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+T790 negative)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	7 / 12 (58.33%)	13 / 31 (41.94%)
number of deaths (all causes)	1	3	23
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	3 / 31 (9.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea at rest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 23 (34.78%)	5 / 15 (33.33%)	
number of deaths (all causes)	20	10	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Amylase increased			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face Oedema			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Constipation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea paroxysmal nocturnal			

subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea at rest			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes virus infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypophosphataemia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (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	Phase 1b: Tepotinib 300 mg +Gefitinib 250 mg	Phase 1b: Tepotinib 500 mg + Gefitinib 250 mg	Phase 2: Tepotinib 500mg+Gefitinib250 mg (MET+T790 negative)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	12 / 12 (100.00%)	31 / 31 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	5 / 31 (16.13%)
occurrences (all)	1	0	5
Axillary pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	6 / 31 (19.35%)
occurrences (all)	0	0	6
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	5 / 12 (41.67%)	2 / 31 (6.45%)
occurrences (all)	1	5	2

Malaise			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	4 / 31 (12.90%)
occurrences (all)	0	1	4
Oedema peripheral			
subjects affected / exposed	2 / 6 (33.33%)	3 / 12 (25.00%)	12 / 31 (38.71%)
occurrences (all)	2	3	12
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	4 / 31 (12.90%)
occurrences (all)	1	2	4
Local swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Non−cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Social circumstances			
Inadequate diet			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	3 / 6 (50.00%)	1 / 12 (8.33%)	8 / 31 (25.81%)
occurrences (all)	3	1	8
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	8 / 31 (25.81%)
occurrences (all)	0	1	8
Haemoptysis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	4 / 31 (12.90%)
occurrences (all)	1	1	4
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	3 / 6 (50.00%)	5 / 12 (41.67%)	0 / 31 (0.00%)
occurrences (all)	3	5	0
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pulmonary thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Innsomnia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	5 / 31 (16.13%)
occurrences (all)	1	1	5
Investigations			

Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	10 / 31 (32.26%)
occurrences (all)	1	0	10
Amylase increased			
subjects affected / exposed	4 / 6 (66.67%)	2 / 12 (16.67%)	11 / 31 (35.48%)
occurrences (all)	4	2	11
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	5 / 31 (16.13%)
occurrences (all)	1	0	5
Blood albumin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 6 (50.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	3	0	2
Blood creatinine increased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 12 (0.00%)	4 / 31 (12.90%)
occurrences (all)	2	0	4
Blood urea increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	2	0	3
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 6 (50.00%)	1 / 12 (8.33%)	3 / 31 (9.68%)
occurrences (all)	3	1	3
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
International normalised ratio increased			
subjects affected / exposed	3 / 6 (50.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Lipase increased			
subjects affected / exposed	2 / 6 (33.33%)	2 / 12 (16.67%)	8 / 31 (25.81%)
occurrences (all)	2	2	8
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Prothrombin time prolonged			
subjects affected / exposed	3 / 6 (50.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences (all)	3	0	1
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	6 / 31 (19.35%)
occurrences (all)	0	3	6
White blood cell count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Bacterial test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Supraventricular extrasystoles			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Cardiac discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	3 / 31 (9.68%)
occurrences (all)	0	2	3
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	7 / 31 (22.58%)
occurrences (all)	0	1	7
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	5 / 31 (16.13%)
occurrences (all)	0	0	5
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Neutropenia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eyelids pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	3 / 12 (25.00%)	1 / 31 (3.23%)
occurrences (all)	1	3	1
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	3 / 31 (9.68%)
occurrences (all)	0	2	3
Cheilitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	6 / 31 (19.35%)
occurrences (all)	0	3	6
Diarrhoea			

subjects affected / exposed	4 / 6 (66.67%)	10 / 12 (83.33%)	18 / 31 (58.06%)
occurrences (all)	4	10	18
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	2 / 31 (6.45%)
occurrences (all)	1	2	2
Epigastric discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	2 / 12 (16.67%)	7 / 31 (22.58%)
occurrences (all)	2	2	7
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	3 / 12 (25.00%)	9 / 31 (29.03%)
occurrences (all)	2	3	9
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Liver injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			

subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	4 / 31 (12.90%)
occurrences (all)	1	0	4
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	4 / 12 (33.33%)	3 / 31 (9.68%)
occurrences (all)	0	4	3
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	2 / 6 (33.33%)	4 / 12 (33.33%)	4 / 31 (12.90%)
occurrences (all)	2	4	4
Rash			
subjects affected / exposed	3 / 6 (50.00%)	5 / 12 (41.67%)	8 / 31 (25.81%)
occurrences (all)	3	5	8
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Skin fissures			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Acne			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Intertrigo			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Hydronephrosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Ureterolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	4 / 31 (12.90%)
occurrences (all)	1	2	4
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	2 / 31 (6.45%)
occurrences (all)	0	2	2
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	2 / 31 (6.45%)
occurrences (all)	1	1	2
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Neck pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	2	1	0

Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	4 / 12 (33.33%)	11 / 31 (35.48%)
occurrences (all)	2	4	11
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	2 / 31 (6.45%)
occurrences (all)	0	2	2
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Hypermagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 12 (8.33%)	9 / 31 (29.03%)
occurrences (all)	2	1	9
Hypocalcaemia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 12 (8.33%)	6 / 31 (19.35%)
occurrences (all)	2	1	6
Hypochloraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	3 / 31 (9.68%)
occurrences (all)	0	1	3
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	2 / 31 (6.45%)
occurrences (all)	1	2	2
Hypoproteinaemia			

subjects affected / exposed	2 / 6 (33.33%)	0 / 12 (0.00%)	3 / 31 (9.68%)
occurrences (all)	2	0	3
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Phase 2: Pemetrexed+Cisplatin/Carboplatin (MET+T790 negative)	Phase 2: Single-arm Cohort (MET+ T790M positive)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)	13 / 15 (86.67%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 23 (21.74%)	2 / 15 (13.33%)	
occurrences (all)	5	2	
Axillary pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Fatigue			

subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Malaise			
subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Oedema			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 23 (4.35%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Local swelling			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Non−cardiac chest pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Social circumstances			
Inadequate diet			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal dryness			

subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 23 (21.74%)	3 / 15 (20.00%)	
occurrences (all)	5	3	
Dyspnoea			
subjects affected / exposed	2 / 23 (8.70%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Haemoptysis			
subjects affected / exposed	0 / 23 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Pleural effusion			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Productive cough			
subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Rhinorrhoea			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Dyspnoea exertional			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hiccups			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pulmonary thrombosis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			

Innsomnia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Amylase increased			
subjects affected / exposed	4 / 23 (17.39%)	4 / 15 (26.67%)	
occurrences (all)	4	4	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 23 (13.04%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Blood albumin decreased			
subjects affected / exposed	1 / 23 (4.35%)	3 / 15 (20.00%)	
occurrences (all)	1	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 23 (21.74%)	2 / 15 (13.33%)	
occurrences (all)	5	2	
Blood creatinine increased			
subjects affected / exposed	6 / 23 (26.09%)	2 / 15 (13.33%)	
occurrences (all)	6	2	
Blood urea increased			
subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
C-reactive protein increased			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Creatinine renal clearance decreased			
subjects affected / exposed	3 / 23 (13.04%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Electrocardiogram QT prolonged			

subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)		
occurrences (all)	2	1		
Gamma-glutamyltransferase increased				
subjects affected / exposed	4 / 23 (17.39%)	1 / 15 (6.67%)		
occurrences (all)	4	1		
Haemoglobin decreased				
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)		
occurrences (all)	1	1		
International normalised ratio increased				
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)		
occurrences (all)	1	1		
Lipase increased				
subjects affected / exposed	3 / 23 (13.04%)	2 / 15 (13.33%)		
occurrences (all)	3	2		
Neutrophil count decreased				
subjects affected / exposed	9 / 23 (39.13%)	1 / 15 (6.67%)		
occurrences (all)	9	1		
Platelet count decreased				
subjects affected / exposed	6 / 23 (26.09%)	0 / 15 (0.00%)		
occurrences (all)	6	0		
Prothrombin time prolonged				
subjects affected / exposed	2 / 23 (8.70%)	1 / 15 (6.67%)		
occurrences (all)	2	1		
Weight decreased				
subjects affected / exposed	6 / 23 (26.09%)	3 / 15 (20.00%)		
occurrences (all)	6	3		
White blood cell count decreased				
subjects affected / exposed	12 / 23 (52.17%)	2 / 15 (13.33%)		
occurrences (all)	12	2		
Bacterial test positive				
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)		
occurrences (all)	0	0		
Blood glucose increased				

subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pericardial effusion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Cardiac discomfort			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 23 (17.39%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Headache			
subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Cognitive disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Memory impairment			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 23 (69.57%)	4 / 15 (26.67%)	
occurrences (all)	16	4	
Leukopenia			

subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Neutropenia			
subjects affected / exposed	7 / 23 (30.43%)	1 / 15 (6.67%)	
occurrences (all)	7	1	
Thrombocytopenia			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hypoacusis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eyelids pruritus			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Keratitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cheilitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Constipation			

subjects affected / exposed	6 / 23 (26.09%)	3 / 15 (20.00%)	
occurrences (all)	6	3	
Diarrhoea			
subjects affected / exposed	4 / 23 (17.39%)	7 / 15 (46.67%)	
occurrences (all)	4	7	
Dyspepsia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Epigastric discomfort			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	14 / 23 (60.87%)	2 / 15 (13.33%)	
occurrences (all)	14	2	
Stomatitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	11 / 23 (47.83%)	3 / 15 (20.00%)	
occurrences (all)	11	3	
Abdominal discomfort			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Gingival bleeding			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Liver injury			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	2 / 23 (8.70%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Rash			
subjects affected / exposed	0 / 23 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	4	
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Skin fissures			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Skin hyperpigmentation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Acne			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Intertrigo			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Hydronephrosis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Ureterolithiasis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 23 (4.35%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Bone pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Muscle twitching			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Neck pain			

subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Localised infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Folliculitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	

Pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 23 (43.48%)	3 / 15 (20.00%)	
occurrences (all)	10	3	
Hyperglycaemia			
subjects affected / exposed	4 / 23 (17.39%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Hyperkalaemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hypermagnesaemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 23 (4.35%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Hypocalcaemia			
subjects affected / exposed	3 / 23 (13.04%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Hypochloraemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia			
subjects affected / exposed	6 / 23 (26.09%)	2 / 15 (13.33%)	
occurrences (all)	6	2	
Hypomagnesaemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hyponatraemia			
subjects affected / exposed	3 / 23 (13.04%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Hypoproteinaemia			

subjects affected / exposed	5 / 23 (21.74%)	2 / 15 (13.33%)	
occurrences (all)	5	2	
Hypoglycaemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2017	Protocol amendments, including administrative changes was filed by the Sponsor and at the site.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported