Clinical trial results:
A Phase I/II, Open-Label, Multicenter Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Anti-Tumor Activity of YH25448 in Patients with EGFR Mutation Positive Advanced Non-Small Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2019-003106-28
Trial protocol	GB ES
Global end of trial date	14 November 2022

Results information

Result version number	v1 (current)
This version publication date	26 November 2023
First version publication date	26 November 2023

Trial information

Trial identification

Sponsor protocol code	73841937NSC2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04075396
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, South Raritan, New Jersey, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the safety, tolerability, and pharmacokinetics (PK) of YH25448 when given orally to subjects with epidermal growth factor receptor single activating mutation positive (EGFRm+) locally advanced or metastatic non-small cell lung cancer (NSCLC).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	28
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	16
From 65 to 84 years	12

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 29 subjects from outside Korea were enrolled in the study, out of which 28 subjects received study treatment and none completed the study.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lazertinib 240 mg

Arm description:

Subjects with epidermal growth factor receptor single activating mutation positive (EGFRm+) advanced non-small cell lung cancer (NSCLC) with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 240 milligrams (mg) orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 32.7 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.

Arm type	Experimental
Investigational medicinal product name	Lazertinib
Investigational medicinal product code	
Other name	YH25448
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received lazertinib 240 mg tablet once daily.

Arm title	Lazertinib 320 mg

Arm description:

Subjects with EGFRm+ advanced NSCLC with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 320 mg orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 8.3 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.

Arm type	Experimental
Investigational medicinal product name	Lazertinib
Investigational medicinal product code	
Other name	YH25448
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received lazertinib 320 mg tablet once daily.

Number of subjects in period 1	Lazertinib 240 mg	Lazertinib 320 mg
Started	15	13
Completed	0	0
Not completed	15	13
Adverse event, serious fatal	11	9
Consent withdrawn by subject	1	2
Protocol v 11.0 implementation	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Lazertinib 240 mg
Reporting group description:	
Subjects with epidermal growth factor receptor single activating mutation positive (EGFRm+) advanced non-small cell lung cancer (NSCLC) with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 240 milligrams (mg) orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 32.7 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.	
Reporting group title	Lazertinib 320 mg
Reporting group description:	
Subjects with EGFRm+ advanced NSCLC with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 320 mg orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 8.3 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.	

Reporting group values	Lazertinib 240 mg	Lazertinib 320 mg	Total
Number of subjects	15	13	28
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	7	16
From 65 to 84 years	6	6	12
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	60.6	63	
standard deviation	± 11.35	± 12.48	-
Title for Gender Units: subjects			
Female	9	8	17
Male	6	5	11

End points

End points reporting groups

Reporting group title	Lazertinib 240 mg

Reporting group description:

Subjects with epidermal growth factor receptor single activating mutation positive (EGFRm+) advanced non-small cell lung cancer (NSCLC) with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 240 milligrams (mg) orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 32.7 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.

Reporting group title	Lazertinib 320 mg

Reporting group description:

Subjects with EGFRm+ advanced NSCLC with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 320 mg orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 8.3 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.

Primary: Part D: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Part D: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. TEAEs were defined as AEs that started on or after the first dose of study medication and prior to 28-day follow-up period. All TEAEs including serious and non-serious events are reported in this endpoint. The safety analysis population included all subjects who received at least 1 dose of investigational product (IP).

End point type	Primary

End point timeframe:

From Day 1 up to 32.7 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Subjects	15	13		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

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

End point description:

Number of subjects with clinically significant abnormalities in vital signs were reported. Vital signs included pulse rate, systolic blood pressure, diastolic blood pressure, body temperature, height, weight, and body mass index (BMI). Baseline was defined as last non-missing measurement taken prior to reference start date. The safety analysis population included all subjects who received at least 1 dose of IP.

End point type	Primary

End point timeframe:

Baseline up to 32.7 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Number of Subjects With Clinically Significant Abnormalities in Electrocardiogram (ECG) Tests

End point title	Part D: Number of Subjects With Clinically Significant Abnormalities in Electrocardiogram (ECG) Tests[3]

End point description:

Number of subjects with clinically significant abnormalities in ECG tests were reported. ECG variables included heart rate, PR interval, RR interval, QRS interval, QT interval and Fridericia-corrected QT interval (QTcF). Baseline was defined as last non-missing measurement taken prior to reference start date. The safety analysis population included all subjects who received at least 1 dose of IP.

End point type	Primary

End point timeframe:

Baseline up to 32.7 months

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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Number of Subjects With Greater Than or Equal to (>=) Grade 4 Toxicity in Laboratory Tests Based on National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 4.03

End point title	Part D: Number of Subjects With Greater Than or Equal to (>=) Grade 4 Toxicity in Laboratory Tests Based on National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 4.03[4]

End point description:

Number of subjects with >=Grade 4 toxicity in laboratory tests based on NCI-CTCAE version 4.03 were reported. Safety laboratory assessments included clinical chemistry, hematology and urinalysis. As per NCI-CTCAE version 4.03: Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death. Baseline was defined as last non-missing measurement taken prior to reference start date. The safety analysis population included all subjects who received at least 1 dose of IP.

End point type	Primary

End point timeframe:

Baseline up to 32.7 months

Notes:

[4] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Subjects	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Number of Subjects With Clinically Significant Abnormalities in Physical Examination

End point title	Part D: Number of Subjects With Clinically Significant Abnormalities in Physical Examination[5]

End point description:

Number of subjects with clinically significant abnormalities in physical examination was reported. Physical examination included general appearance, skin, head and neck (including ears, eyes, nose and throat), respiratory, cardiovascular, abdomen, lymph nodes, thyroid, muscular-skeletal (including spine and extremities) and neurological systems. Baseline was defined as last non-missing measurement taken prior to reference start date. Safety analysis population: all subjects who received at least 1 dose of IP.

End point type	Primary

End point timeframe:

Baseline up to 32.7 months

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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Subjects	11	5		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to 24 Hours (AUC[0-24]) for Single Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to 24 Hours (AUC[0-24]) for Single Dose of Lazertinib[6]

End point description:

AUC(0-24) was defined as area under the plasma concentration time curve from time zero to 24 hours. AUC(0-24) for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10 and 24 hours post-dose on Day 1 of Cycle 0

Notes:

[6] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: h*ng/mL				
arithmetic mean (standard deviation)	3253.58 (± 916.67)	4097.34 (± 1261.96)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the Last Quantifiable Concentration (AUC[0-last]) for Single Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the Last Quantifiable Concentration (AUC[0-last]) for Single Dose of Lazertinib[7]

End point description:

AUC(0-last) was defined as area under the plasma concentration-time curve from time zero to time of last quantifiable concentration. AUC(0-last) for single dose of lazertinib was reported in this endpoint. Pharmacokinetic (PK) analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[7] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Hour*nanograms per millilitre(h*ng/mL)				
arithmetic mean (standard deviation)	5907.56 (± 2218.84)	7664.99 (± 2057.13)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUC[0-Infinity]) for Single Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUC[0-Infinity]) for Single Dose of Lazertinib[8]

End point description:

AUC(0-infinity) was defined as area under the plasma concentration time curve from time zero to infinite time. AUC(0-infinity) for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[8] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: h*ng/mL				
arithmetic mean (standard deviation)	6504.88 (± 2542.12)	8869.21 (± 2642.17)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Time to Reach Maximum Observed Plasma Concentration (Tmax) for Single Dose of Lazertinib

End point title	Part D: Time to Reach Maximum Observed Plasma Concentration (Tmax) for Single Dose of Lazertinib[9]

End point description:

Tmax was defined as time to reach the maximum observed plasma concentration. Tmax for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[9] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Hours				
median (full range (min-max))	2.00 (0.92 to 4.15)	2.50 (1.07 to 4.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Maximum Observed Plasma Concentration (Cmax) for Single Dose of Lazertinib

End point title	Part D: Maximum Observed Plasma Concentration (Cmax) for Single Dose of Lazertinib[10]

End point description:

Cmax was defined as maximum observed plasma concentration. Cmax for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[10] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)	441.04 (± 135.45)	524.13 (± 271.58)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Apparent Terminal Elimination Rate Constant (lambda[z]) for Single Dose of Lazertinib

End point title	Part D: Apparent Terminal Elimination Rate Constant (lambda[z]) for Single Dose of Lazertinib[11]

End point description:

Lambda(z) was defined as terminal elimination rate constant. Lambda(z) for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[11] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Per hour (1/h)				
arithmetic mean (standard deviation)	0.02 (± 0.01)	0.01 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Apparent Terminal Half-Life (t1/2) for Single Dose of Lazertinib

End point title	Part D: Apparent Terminal Half-Life (t1/2) for Single Dose of Lazertinib[12]

End point description:

T1/2 was defined the time measured for the plasma concentration of a drug to decrease by half of its initial concentration. T1/2 for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[12] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Hours				
median (full range (min-max))	51.12 (18.75 to 70.71)	63.98 (52.30 to 97.74)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Maximum Observed Plasma Concentration at Steady State (Cmax,ss) for Multiple Dose of Lazertinib

End point title	Part D: Maximum Observed Plasma Concentration at Steady State (Cmax,ss) for Multiple Dose of Lazertinib[13]

End point description:

Cmax,ss was defined as maximum observed plasma concentration at steady state. Cmax,ss for multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

Notes:

[13] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: ng/mL				
arithmetic mean (standard deviation)	509.92 (± 236.66)	632.00 (± 279.88)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the end of Dosing Interval at Steady State (AUCss[0-last]) for Multiple Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the end of Dosing Interval at Steady

	State (AUCss[0-last]) for Multiple Dose of Lazertinib[14]

End point description:

AUCss(0-last) was defined as area under the plasma concentration time curve from time zero to time of the end of dosing interval at steady state. AUCss(0-last) for multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

Notes:

[14] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: h*ng/mL				
arithmetic mean (standard deviation)	7025.10 (± 4181.22)	9249.58 (± 4924.51)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Apparent Plasma Clearance (CL/F) for Single Dose of Lazertinib

End point title	Part D: Apparent Plasma Clearance (CL/F) for Single Dose of Lazertinib[15]

End point description:

CL/F was defined as apparent plasma clearance. CL/F for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[15] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Litres per hour (L/h)				
arithmetic mean (standard deviation)	41.92 (± 15.56)	39.38 (± 12.96)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Apparent Volume of Distribution (Vd/F) for Single Dose of Lazertinib

End point title	Part D: Apparent Volume of Distribution (Vd/F) for Single Dose of Lazertinib[16]

End point description:

Vd/F was defined as apparent volume of distribution. Vd/F for single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

Notes:

[16] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Litres				
arithmetic mean (standard deviation)	2990.36 (± 1188.45)	3822.19 (± 984.29)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Time to Reach Maximum Observed Plasma Concentration at Steady State (Tmax,ss) for Multiple Dose of Lazertinib

End point title	Part D: Time to Reach Maximum Observed Plasma Concentration at Steady State (Tmax,ss) for Multiple Dose of Lazertinib[17]

End point description:

Tmax,ss was defined as time to reach maximum observed plasma concentration at steady state. Tmax,ss for multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

Notes:

[17] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: Hours				
median (full range (min-max))	3.15 (1.75 to 9.00)	3.97 (2.22 to 9.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Accumulation Ratio (Rac) for Multiple Dose of Lazertinib

End point title	Part D: Accumulation Ratio (Rac) for Multiple Dose of

End point description:

Accumulation ratio was calculated as AUCss(0-last) divided by AUC(0-24), where AUCss(0-last) was defined as area under the plasma concentration time curve from time zero to end of dosing interval at steady state and AUC(0-24) was defined area under the plasma concentration time curve from time zero to 24 hours time. Rac for multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 10 and 24 hours post dose on Day 1 of Cycle 0 and Cycle 2

Notes:

[18] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	4		
Units: Ratio				
arithmetic mean (standard deviation)	2.26 (± 0.61)	2.36 (± 1.08)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Apparent Plasma Clearance at Steady State (CLss/F) for Multiple Dose of Lazertinib

End point title	Part D: Apparent Plasma Clearance at Steady State (CLss/F) for Multiple Dose of Lazertinib[19]

End point description:

CLss/F was defined as apparent plasma clearance at steady state. CLss/F for multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

Notes:

[19] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: Litres per hour (L/h)				
arithmetic mean (standard deviation)	44.25 (± 21.39)	50.10 (± 37.21)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Trough Concentrations (Ctrough) for Multiple Dose of Lazertinib at Cycle 1 Day 1

End point title	Part D: Trough Concentrations (Ctrough) for Multiple Dose of Lazertinib at Cycle 1 Day 1[20]

End point description:

Ctrough was defined as pre-dose plasma concentration. Ctrough for multiple dose of lazertinib at Cycle 1 Day 1 was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 1 of Cycle 1

Notes:

[20] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: ng/mL				
arithmetic mean (standard deviation)	6.41 (± 4.55)	10.91 (± 5.99)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Trough Concentrations (Ctrough) for Multiple Dose of Lazertinib at Cycle 1 Day 8

End point title	Part D: Trough Concentrations (Ctrough) for Multiple Dose of

	Lazertinib at Cycle 1 Day 8[21]

End point description:

Ctrough was defined as pre-dose plasma concentration. Ctrough for multiple dose of lazertinib at Cycle 1 Day 8 was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 8 of Cycle 1

Notes:

[21] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	10		
Units: ng/mL				
arithmetic mean (standard deviation)	154.62 (± 87.60)	225.47 (± 168.22)		

Statistical analyses

No statistical analyses for this end point

Primary: Part D: Trough Concentrations (Ctrough) for Multiple Dose of Lazertinib at Cycle 1 Day 15

End point title	Part D: Trough Concentrations (Ctrough) for Multiple Dose of Lazertinib at Cycle 1 Day 15[22]

End point description:

Ctrough was defined as pre-dose plasma concentration. Ctrough for multiple dose of lazertinib at Cycle 1 Day 15 was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Pre-dose on Day 15 of Cycle 1

Notes:

[22] - 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 data was planned to be analyzed for this endpoint.

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: ng/mL				
arithmetic mean (standard deviation)	177.40 (± 99.23)	263.74 (± 145.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the Last Quantifiable Concentration (AUC[0-last]) of Metabolite M7 After Single Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the Last Quantifiable Concentration (AUC[0-last]) of Metabolite M7 After Single Dose of Lazertinib

End point description:

AUC(0-last) was defined as area under the plasma concentration-time curve from time zero to time of last quantifiable concentration. AUC(0-last) of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: h*ng/mL				
arithmetic mean (standard deviation)	216.350 (± 126.357)	208.908 (± 128.968)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUC[0-Infinity]) of Metabolite M7 After Single Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite Time (AUC[0-Infinity]) of Metabolite M7 After Single Dose of Lazertinib

End point description:

AUC(0-infinity) was defined as area under the plasma concentration time curve from time zero to infinite time. AUC(0-infinity) of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: h*ng/mL				
arithmetic mean (standard deviation)	281.172 (± 144.163)	263.373 (± 166.254)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to 24 Hours (AUC[0-24]) of Metabolite M7 After Single Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to 24 Hours (AUC[0-24]) of Metabolite M7 After Single Dose of Lazertinib

End point description:

AUC(0-24) was defined as area under the plasma concentration time curve from time zero to 24 hours. AUC(0-24) of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10 and 24 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: h*ng/mL				
arithmetic mean (standard deviation)	86.692 (± 52.492)	74.523 (± 33.137)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Apparent Terminal Half-Life (t1/2) of Metabolite M7 After Single Dose of Lazertinib

End point title	Part D: Apparent Terminal Half-Life (t1/2) of Metabolite M7 After Single Dose of Lazertinib

End point description:

T1/2 was defined the time measured for the plasma concentration of a drug to decrease by half of its initial concentration. T1/2 of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: Hours (h)				
median (full range (min-max))	41.205 (18.042 to 86.989)	50.019 (13.256 to 74.867)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Metabolite M7 After Single Dose of Lazertinib

End point title	Part D: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Metabolite M7 After Single Dose of Lazertinib

End point description:

Tmax was defined as time to reach the maximum observed plasma concentration. Tmax of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: Hours				
median (full range (min-max))	4.020 (2.070 to 10.080)	4.150 (3.080 to 22.350)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Maximum Observed Plasma Concentration (Cmax) of Metabolite

M7 After Single Dose of Lazertinib

End point title	Part D: Maximum Observed Plasma Concentration (Cmax) of Metabolite M7 After Single Dose of Lazertinib

End point description:

Cmax was defined as maximum observed plasma concentration. Cmax of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: ng/mL				
arithmetic mean (standard deviation)	5.838 (± 3.946)	4.774 (± 2.257)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Maximum Observed Plasma Concentration at Steady State (Cmax,ss) of Metabolite M7 After Multiple Dose of Lazertinib

End point title	Part D: Maximum Observed Plasma Concentration at Steady State (Cmax,ss) of Metabolite M7 After Multiple Dose of Lazertinib

End point description:

Cmax,ss was defined as maximum observed plasma concentration at steady state. Cmax,ss of metabolite M7 after multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: ng/mL				
arithmetic mean (standard deviation)	7.866 (± 4.213)	8.319 (± 7.418)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the end of Dosing Interval at Steady State (AUCss[0-last]) of Metabolite M7 After Multiple Dose of Lazertinib

End point title	Part D: Area Under the Plasma Concentration Time Curve From Time Zero to the Time of the end of Dosing Interval at Steady State (AUCss[0-last]) of Metabolite M7 After Multiple Dose of Lazertinib

End point description:

AUCss(0-last) was defined as area under the plasma concentration-time curve from time zero to time of the end of dosing interval at steady state. AUCss(0-last) of metabolite M7 after multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: h*ng/mL				
arithmetic mean (standard deviation)	148.335 (± 89.794)	168.765 (± 159.476)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Apparent Terminal Elimination Rate Constant (lambda [z]) of Metabolite M7 After Single Dose of Lazertinib

End point title	Part D: Apparent Terminal Elimination Rate Constant (lambda [z]) of Metabolite M7 After Single Dose of Lazertinib

End point description:

Lambda(z) was defined as terminal elimination rate constant. Lambda(z) of metabolite M7 after single dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: Per hour (1/h)				
arithmetic mean (standard deviation)	0.017 (± 0.008)	0.021 (± 0.016)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Metabolic Ratio (MR) of Metabolite M7 and Lazertinib After Single Dose of Lazertinib

End point title	Part D: Metabolic Ratio (MR) of Metabolite M7 and Lazertinib After Single Dose of Lazertinib

End point description:

MR was defined as ratio of the AUC(0-infinity) of metabolite M7 and AUC(0-infinity) of lazertinib, where AUC(0-infinity) was defined as area under the plasma concentration time curve from time zero to infinite time. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10, 24 and 48 hours post-dose on Day 1 of Cycle 0

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: Ratio				
arithmetic mean (standard deviation)	0.042 (± 0.022)	0.027 (± 0.015)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Time for Maximum Observed Plasma Concentration at Steady State (Tmax,ss) of Metabolite M7 After Multiple Dose of Lazertinib

End point title	Part D: Time for Maximum Observed Plasma Concentration at

	Steady State (Tmax,ss) of Metabolite M7 After Multiple Dose of Lazertinib

End point description:

Tmax,ss was defined as time to reach the maximum observed plasma concentration at steady state. Tmax,ss of metabolite M7 after multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: Hours				
median (full range (min-max))	6.330 (2.250 to 9.000)	4.350 (3.930 to 24.070)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Accumulation Ratio (Rac) of Metabolite M7 After Multiple Dose of Lazertinib

End point title	Part D: Accumulation Ratio (Rac) of Metabolite M7 After Multiple Dose of Lazertinib

End point description:

Accumulation ratio was calculated as AUCss(0-last) divided by AUC(0-24), where AUCss(0-last) was defined as area under the plasma concentration time curve from time zero to end of dosing interval and AUC(0-24) was defined area under the plasma concentration time curve from time zero to 24 hours. Rac of metabolite M7 after multiple dose of lazertinib was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 4, 10 and 24 hours post dose on Day 1 Cycle 0 and Cycle 2

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	4		
Units: Ratio				
arithmetic mean (standard deviation)	1.976 (± 0.617)	2.270 (± 1.300)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Trough Concentrations (Ctrough) of Metabolite M7 After Multiple Dose of Lazertinib at Days 1, 8, and 15 of Cycle 1

End point title	Part D: Trough Concentrations (Ctrough) of Metabolite M7 After Multiple Dose of Lazertinib at Days 1, 8, and 15 of Cycle 1

End point description:

Ctrough was defined as pre-dose plasma concentration. Ctrough of Metabolite M7 after multiple dose of lazertinib at Days 1, 8 and 15 of Cycle 1 was reported in this endpoint. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint and 'n' (number analysed) refers to all subjects evaluable at time points.

End point type	Secondary

End point timeframe:

Pre-dose on Days 1, 8 and 15 of Cycle 1

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	10		
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 Cycle 1 (n = 13, 9)	0.257 (± 0.237)	0.358 (± 0.321)		
Day 8 Cycle 1 (n = 14, 10)	4.928 (± 3.005)	5.791 (± 4.650)		
Day 15 Cycle 1 (n = 13, 9)	5.356 (± 3.604)	6.340 (± 4.741)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part D: Metabolic Ratio at Steady State (MRss) of Metabolite M7 and Lazertinib After Multiple Dose of Lazertinib

End point title	Part D: Metabolic Ratio at Steady State (MRss) of Metabolite M7 and Lazertinib After Multiple Dose of Lazertinib

End point description:

MRss was defined as ratio of the AUCss(0-last) of metabolite M7 and AUCss(0-last) of lazertinib, where AUCss(0-last) was defined as area under the plasma concentration time curve from time zero to time of end of dosing interval at steady state. PK analysis population included all subjects who had at least 1 measurable concentration collected post dose. Here 'N' (number of subjects analysed) refers to the

number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 of Cycle 1 up to pre-dose on Day 1 of Cycle 47

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	6		
Units: Ratio				
arithmetic mean (standard deviation)	0.021 (± 0.006)	0.016 (± 0.009)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

ORR: percentage of subjects who had at least 1 confirmed partial or complete response (PR/CR) as per Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 prior to disease progression/recurrence. CR: disappearance of target and non-target lesions and normalization of tumour markers. Pathological lymph nodes must have short axis measures <10 millimetre (mm). PR: >=30% decrease in sum of measures (longest diameter for tumour lesions and short axis measure for nodes) of target lesions, taking as reference baseline sum of diameters. Non-target lesions must be non-progressive disease (PD). PD: >=20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to relative 20% increase, sum must also demonstrate an absolute increase of >=5mm. Appearance of one/more new lesions was considered progression. Evaluable for response population: all subjects in safety analysis population who had a baseline RECIST version 1.1 assessment.

End point type	Secondary

End point timeframe:

Up to 33.7 months

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Percentage of subjects				
number (confidence interval 95%)	26.7 (4.3 to 49.0)	7.7 (0.0 to 22.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the time from the date of first dose of study drug to the earliest date of disease progression per RECIST version 1.1, or death due to any cause, whichever occurs first. PD = at least a 20% increase in the sum of diameters of measured lesions taking as references the smallest sum of diameters recorded on study (including baseline) and an absolute increase of >=5 mm or appearance of at least 1 new lesion. The safety analysis population included all subjects who received at least 1 dose of IP. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to 33.7 months

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Months				
median (full range (min-max))	3.1 (1.3 to 11.2)	4.2 (0.0 to 7.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

DOR: time between date of first documented confirmed response (PR/CR) and date of first documented progression or death, whichever occurred first. CR: disappearance of target and non-target lesions and normalization of tumour markers. Pathological lymph nodes short axis measures <10mm. PR: >=30% decrease in sum of measures (tumour lesions-longest diameter and nodes-short axis)of target lesions, taking as reference baseline sum of diameters. PD: >=20% increase in sum of diameters of measured lesions taking as references smallest sum of diameters recorded on study(including baseline),absolute increase of >=5mm/appearance of at least 1 new lesion. Unequivocal progression of existing non-target lesions. Evaluable for response population: all subjects in safety analysis population who had baseline RECIST version 1.1 assessment. N=number of subjects evaluable for this endpoint. 99999=median is not reached; lower and upper limit of confidence interval could not be calculated for 1 subject.

End point type	Secondary

End point timeframe:

Up to 33.7 months

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	1		
Units: Months				
median (confidence interval 95%)	99999 (5.6 to 99999)	2.8 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline in Tumour Size

End point title	Percentage Change from Baseline in Tumour Size

End point description:

Tumour size was defined as the sum lengths of the longest diameters of the target lesion. Percentage change in tumour size was determined for subjects with measurable disease at baseline. Baseline for RECIST was defined as the last evaluable assessment prior to starting treatment. Evaluable for response population: all subjects in safety analysis population who had a baseline RECIST version 1.1 assessment. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to 33.7 months

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: Percentage change in tumour size				
arithmetic mean (standard deviation)	-5.37 (± 37.68)	9.56 (± 42.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR: percentage of subjects with a best overall response (BOR), extracranial and intracranial response of CR, PR or stable disease(SD). As per RECIST version 1.1 CR: disappearance of target and non-target lesions and normalization of tumour markers. Pathological lymph nodes must have short axis measures <10mm. PR: >=30% decrease in sum of measures (longest diameter for tumour lesions and short axis measure for nodes) of target lesions, taking as reference baseline sum of diameters. Non-target lesions must be non-PD. PD: >=20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to relative 20% increase, sum must also demonstrate >=5mm absolute increase. Appearance of one/more new lesions was considered progression. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Evaluable for response

population: all subjects in safety analysis population who had baseline RECIST version 1.1 assessment.

End point type	Secondary

End point timeframe:

Up to 33.7 months

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Percentage of subjects				
number (confidence interval 95%)	60.0 (35.2 to 84.8)	53.8 (26.7 to 80.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from the date of first dose to date of death due to any cause. The safety analysis population included all subjects who received at least 1 dose of IP. Here 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to 33.7 months

End point values	Lazertinib 240 mg	Lazertinib 320 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: Months				
median (full range (min-max))	9.1 (2.6 to 24.3)	7.7 (3.4 to 12.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality: Day 1 up to 33.7 months; Serious and other adverse events: Day 1 up to 32.7 months

Adverse event reporting additional description:

The safety analysis population included all subjects who received at least 1 dose of investigational product (IP).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Lazertinib 320 mg

Reporting group description:

Subjects with EGFRm+ advanced NSCLC with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 320 mg orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 8.3 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment

Reporting group title	Lazertinib 240 mg

Reporting group description:

Subjects with epidermal growth factor receptor single activating mutation positive (EGFRm+) advanced non-small cell lung cancer (NSCLC) with or without asymptomatic brain metastasis received lazertinib tablet at a dose of 240 milligrams (mg) orally on Day 1 of Cycle 0, which spans 7 days, followed by a once daily dose in each subsequent 21-day treatment cycle, for a maximum duration of up to 32.7 months. Subjects were then followed up for safety for 28 days after the last dose of study treatment.

Serious adverse events	Lazertinib 320 mg	Lazertinib 240 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	10 / 15 (66.67%)	
number of deaths (all causes)	9	11	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 13 (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	
Cardiac disorders			

Palpitations			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Adrenalectomy			
subjects affected / exposed	0 / 13 (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	
Nervous system disorders			
Cognitive Disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	0 / 13 (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	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (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	
Pain			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 13 (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	
Nausea			

subjects affected / exposed	0 / 13 (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	
Vomiting			
subjects affected / exposed	0 / 13 (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	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 13 (15.38%)	3 / 15 (20.00%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone Pain			
subjects affected / exposed	0 / 13 (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	
Muscular Weakness			
subjects affected / exposed	0 / 13 (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	
Pain in Extremity			
subjects affected / exposed	0 / 13 (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	
Pathological Fracture			
subjects affected / exposed	0 / 13 (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	

Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 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	Lazertinib 320 mg	Lazertinib 240 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	15 / 15 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hot Flush			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Oedema Peripheral			

subjects affected / exposed	2 / 13 (15.38%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Medical Device Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Induration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gait Disturbance			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Fatigue			
subjects affected / exposed	3 / 13 (23.08%)	1 / 15 (6.67%)	
occurrences (all)	4	1	
Chest Pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Asthenia			
subjects affected / exposed	2 / 13 (15.38%)	3 / 15 (20.00%)	
occurrences (all)	2	4	
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Dysphonia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	3 / 13 (23.08%)	4 / 15 (26.67%)	
occurrences (all)	3	4	
Epistaxis			

subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Pleural Effusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pulmonary Embolism			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Psychiatric disorders			
Affect Lability			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Confusional State			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Depressed Mood			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Disorientation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Sleep Disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 13 (15.38%)	3 / 15 (20.00%)	
occurrences (all)	2	8	
Amylase Increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Aspartate Aminotransferase Increased			

subjects affected / exposed	1 / 13 (7.69%)	4 / 15 (26.67%)	
occurrences (all)	1	11	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Blood Bilirubin Increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	3	
Blood Creatinine Increased			
subjects affected / exposed	3 / 13 (23.08%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Blood Magnesium Decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Blood Sodium Decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Lymphocyte Count Decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neutrophil Count Decreased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Platelet Count Decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Troponin I Increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Troponin Increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Weight Decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	

White Blood Cell Count Decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dysarthria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Epilepsy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	3 / 13 (23.08%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Hypoaesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Memory Impairment			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neuropathy Peripheral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neurotoxicity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Peripheral Sensory Neuropathy			

subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Taste Disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Thrombocytopenia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Leukopenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	2 / 13 (15.38%)	7 / 15 (46.67%)	
occurrences (all)	5	12	
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vertigo Positional			

subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eye disorders			
Vision Blurred			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Dry Eye			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Abdominal Pain Upper			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Abdominal Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	7 / 13 (53.85%)	7 / 15 (46.67%)	
occurrences (all)	12	11	
Dry Mouth			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	3 / 13 (23.08%)	2 / 15 (13.33%)	
occurrences (all)	4	2	
Glossitis			

subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gingival Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	8 / 13 (61.54%)	4 / 15 (26.67%)	
occurrences (all)	9	5	
Skin and subcutaneous tissue disorders			
Skin Lesion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Skin Hyperpigmentation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dermatitis Acneiform			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dry Skin			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Erythema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Onychoclasis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Onychomadesis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Papule			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Paronychia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	6	
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	3 / 13 (23.08%)	4 / 15 (26.67%)	
occurrences (all)	4	4	
Rash Macular			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Rash Maculo-Papular			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Solar Dermatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chromaturia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Polyuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 13 (23.08%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Back Pain			

subjects affected / exposed	3 / 13 (23.08%)	3 / 15 (20.00%)	
occurrences (all)	3	3	
Muscle Rigidity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Muscular Weakness			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Pain in Extremity			
subjects affected / exposed	2 / 13 (15.38%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Covid-19			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Appetite Disorder			

subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Decreased Appetite			
subjects affected / exposed	3 / 13 (23.08%)	2 / 15 (13.33%)	
occurrences (all)	5	2	
Hypercalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hyperkalaemia			
subjects affected / exposed	1 / 13 (7.69%)	3 / 15 (20.00%)	
occurrences (all)	1	4	
Hypermagnesaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hyponatraemia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Polydipsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2019	The overall reason for this amendment was to change the standard for causality assessment, time schedule for vital sign and electrocardiogram (ECG) assessment for Part D, and reflect other changes to unify protocol for Korea and outside Korea. Sponsor name for Part D was changed from Yuhan to Janssen.
13 April 2021	The overall reason for amendment was to re-insert safety assessments for Part D after primary database lock (DBL) (19 Apr 2021) to allow protocol consistency across part D countries following a request from the Medicines and Healthcare Products Regulatory Agency (MHRA).
19 November 2021	The overall reason for this amendment was to removed requirement for long-term follow-up of subjects in Part D.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study Parts A, B, and C were sponsored by Yuhan Corporation under protocol identifier (ID) YH25448-201 and Part D was sponsored by Janssen Research and Development, LLC under protocol ID 73841937NSC2001. Therefore, only Part D results are reported.

Notes: