Clinical trial results:
A phase III randomized, controlled, open-label, multicenter, global study of capmatinib in combination with osimertinib versus platinum - pemetrexed based doublet chemotherapy in patients with locally advanced or metastatic NSCLC harboring EGFR activating mutations who have progressed on prior EGFRTKI therapy and whose tumors are T790M mutation negative and harbor MET amplification (GEOMETRY-E)

Summary

EudraCT number	2020-003677-21
Trial protocol	DE ES SI PL IT BG HU HR
Global end of trial date	27 December 2022

Results information

Result version number	v1 (current)
This version publication date	20 October 2023
First version publication date	20 October 2023

Trial information

Trial identification

Sponsor protocol code	CINC280L12301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04816214
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis, +41 6133241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis, +41 6133241111, novartis.email@novartis.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	27 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 December 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study aimed to evaluate the anticancer activity of capmatinib in combination with osimertinib compared to platinum-pemetrexed based doublet chemotherapy as second line treatment in patients with advanced or metastatic non-small-cell lung cancer (NSCLC) with EGFR mutation, T790M negative, MET amplified, who progressed following EGFR tyrosine kinase inhibitors (TKIs). A run-in part was conducted to determine the recommended dose of capmatinib and osimertinib for the randomized part.

On 11-May-2022, Novartis decided to halt enrollment for this study due to a business consideration unrelated to any safety concerns. Ongoing patients in the run-in part were allowed to continue treatment through other post-trial drug supply options, as applicable. On 27-Dec-2022 the last patient was transitioned off the study, and following the study protocol this date was declared the Global end of trial date. Randomized part was not initiated.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Korea, Republic of: 2
Worldwide total number of subjects	6
EEA total number of subjects	0

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)	4
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In the Run-in part, subjects were enrolled at 4 investigative sites in 3 countries. The study was terminated early based on Sponsor's decision unrelated to safety concerns and the randomized part of the study was not initiated.

Pre-assignment

Screening details:

A total of 23 subjects were screened of which 6 subjects were enrolled in the run-in part of the study.

Period 1

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

Arms

Arm title	Run-in Part: Capmatinib + Osimertinib

Arm description:

Subjects received a starting dose of capmatinib 400 mg, orally, twice daily (BID) in combination with osimertinib 80 mg, orally, once daily (QD)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	
Other name	INC280
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg of capmatinib administered BID

Investigational medicinal product name	Osimertinib
Investigational medicinal product code	
Other name	Tagrisso, Tagrix
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

80 mg of osimertinib administered QD

Number of subjects in period 1	Run-in Part: Capmatinib + Osimertinib
Started	6
Completed	0
Not completed	6
Death	1
Progressive Disease	4
Study Terminated by Sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	Run-in Part: Capmatinib + Osimertinib
Reporting group description:	
Subjects received a starting dose of capmatinib 400 mg, orally, twice daily (BID) in combination with osimertinib 80 mg, orally, once daily (QD)	

Reporting group values	Run-in Part: Capmatinib + Osimertinib	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 61.7 ± 7.76	 -	
Gender categorical Units: Subjects			
Female	4	4	
Male	2	2	
Race Units: Subjects			
Asian	6	6	

End points

End points reporting groups

Reporting group title	Run-in Part: Capmatinib + Osimertinib

Reporting group description:

Subjects received a starting dose of capmatinib 400 mg, orally, twice daily (BID) in combination with osimertinib 80 mg, orally, once daily (QD)

Primary: Run-in Part: Number of Partipants With Dose Limiting Toxicities (DLTs)

End point title	Run-in Part: Number of Partipants With Dose Limiting Toxicities (DLTs)[1]

End point description:

A DLT was defined as an adverse event (AE) or abnormal laboratory value assessed as unrelated to disease, progressive disease, inter-current illness, or concomitant medications, that despite optimal therapeutic intervention that occurred within the first 21 days of treatment with capmatinib in combination with osimertinib. FAS included all participants who received any component of the study treatment.

End point type	Primary

End point timeframe:

Up to 21 Days (3 weeks)

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 statistical analysis was planned to be reported for this endpoint.

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Number of Participants With at Least One Dose Interruption and Dose Reduction of Each Study Drug

End point title	Run-in Part: Number of Participants With at Least One Dose Interruption and Dose Reduction of Each Study Drug

End point description:

Number of participants with at least one dose interruption and dose reduction were reported for each study drug. Safety set included all participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

From the first dose until last dose of study treatment, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: subjects				
Dose Interruption: Capmatinib	5			
Dose Interruption: Osimertinib	4			
Dose Reduction: Capmatinib	3			
Dose Reduction: Osimertinib	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Dose Intensity of Each Study Drug

End point title	Run-in Part: Dose Intensity of Each Study Drug

End point description:

Dose intensity was computed as the ratio of actual cumulative dose (milligrams) received and actual duration of exposure (weeks) to study drug. Safety set included all participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

From the first dose until last dose of study treatment, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: milligrams per week (mg/week)				
arithmetic mean (standard deviation)				
Capmatinib	5042.8 (± 947.28)			
Osimertinib	534.9 (± 41.29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Median Duration of Exposure to Each Study Drug

End point title	Run-in Part: Median Duration of Exposure to Each Study Drug

End point description:

Duration of exposure is defined as the time (in weeks) between the first and the last dose of study treatment. Safety set included all participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

From the first dose until last dose of study treatment, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: weeks				
median (full range (min-max))				
Capmatinib	23.5 (1 to 39)			
Osimertinib	24.0 (1 to 39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Maximum Plasma Concentration (Cmax) of Capmatinib

End point title	Run-in Part: Maximum Plasma Concentration (Cmax) of Capmatinib

End point description:

Blood samples were collected. Cmax of capmatinib was calculated from plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics. PK analysis set included all participants who provided at least one evaluable PK concentration. 'Number of subjects analysed' indicates the number of participants with data available for endpoint analysis. 'Number analysed (n)' indicates the number of participants with data available at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, and 8 hours post-dose on Days 1 and 15 of Cycle 1 (Cycle = 21 days)

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=6)	5510 (± 2380)			
Day 15 (n=5)	5750 (± 1050)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Maximum Plasma Concentration (Cmax) of Osimertinib and Its Metabolites (AZ5104 and AZ7550)

End point title	Run-in Part: Maximum Plasma Concentration (Cmax) of Osimertinib and Its Metabolites (AZ5104 and AZ7550)

End point description:

Blood samples were colllected. Cmax of osimertinib and its metabolites (AZ5104 and AZ7550) was calculated from plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics. PK analysis set included all participants who provided at least one evaluable PK concentration. 'Number of subjects analysed' indicates the number of participants with data available for endpoint analysis. 'Number analysed (n)' indicates the number of participants with data available at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose on Days 1 and 15 of Cycle 1 (Cycle = 21 days)

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: ng/mL				
arithmetic mean (standard deviation)				
Osimertinib: Day 1 (n=5)	99.5 (± 57.0)			
Osimertinib: Day 15 (n=5)	265 (± 113)			
AZ5104: Day 1 (n=5)	4.86 (± 3.22)			
AZ5104: Day 15 (n=5)	22.0 (± 9.23)			
AZ7550: Day 1 (n=5)	3.61 (± 1.53)			
AZ7550: Day 15 (n=4)	33.0 (± 11.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Time to Maximum Plasma Concentration (Tmax) of Capmatinib

End point title	Run-in Part: Time to Maximum Plasma Concentration (Tmax) of Capmatinib

End point description:

Blood samples were colllected. Tmax of capmatinib was calculated from plasma concentration-time data

using non-compartmental methods and summarized using descriptive statistics. Actual recorded sampling times were considered for the calculations. PK analysis set included all participants who provided at least one evaluable PK concentration. 'Number of subjects analysed' indicates the number of participants with data available for endpoint analysis. 'Number analysed (n)' indicates the number of participants with data available at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, and 8 hours post-dose on Days 1 and 15 of Cycle 1 (Cycle = 21 days)

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
median (full range (min-max))				
Day 1 (n=6) Day 15 (n=5)	1.92 (0.983 to 3.021) 1.00 (0.917 to 1.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Time to Maximum Plasma Concentration (Tmax) of Osimertinib and Its Metabolites (AZ5104 and AZ7550)

End point title	Run-in Part: Time to Maximum Plasma Concentration (Tmax) of Osimertinib and Its Metabolites (AZ5104 and AZ7550)

End point description:

Blood samples were collected. Tmax of osimertinib and its metabolites (AZ5104 and AZ7550) was calculated from plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.
Actual recorded sampling times were considered for the calculations. PK analysis set included all participants who provided at least one evaluable PK concentration. 'Number of participants analysed' indicates the number of subjects with data available for endpoint analysis. 'Number analysed (n)' indicates the number of participants with data available at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose on Days 1 and 15 of Cycle 1 (Cycle = 21 days)

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hours				
median (full range (min-max))				

Osimertinib: Day 1 (n=5)	6.00 (2.90 to 23.1)			
Osimertinib: Day 15 (n=5)	4.00 (0.00 to 7.33)			
AZ5104: Day 1 (n=5)	23.1 (22.3 to 23.5)			
AZ5104: Day 15 (n=5)	4.00 (0.00 to 7.13)			
AZ7550: Day 1 (n=5)	5.68 (2.90 to 23.1)			
AZ7550: Day 15 (n=4)	2.25 (0.00 to 6.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Area Under the Curve to the Last Measurable Concentration (AUClast) of Capmatinib

End point title	Run-in Part: Area Under the Curve to the Last Measurable Concentration (AUClast) of Capmatinib

End point description:

Blood samples were collected. AUClast of capmatinib was calculated from plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics. PK analysis set included all participants who provided at least one evaluable PK concentration. 'Number of subjects analysed' indicates the number of participants with data available for endpoint analysis. 'Number analysed (n)' indicates the number of participants with data available at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, and 8 hours post-dose on Days 1 and 15 of Cycle 1 (Cycle = 21 days)

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanograms*hours/milliliter (ng*hr/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=6)	20100 (± 6080)			
Day 15 (n=5)	21300 (± 7050)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Area Under the Curve to the Last Measurable Concentration

(AUClast) of Osimertinib and Its Metabolites (AZ5104 and AZ7550)	
End point title	Run-in Part: Area Under the Curve to the Last Measurable Concentration (AUClast) of Osimertinib and Its Metabolites (AZ5104 and AZ7550)

End point description:

Blood samples were collected. AUClast of osimertinib and its metabolites (AZ5104 and AZ7550) was calculated from plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics. PK analysis set included all participants who provided at least one evaluable PK concentration.'Number of subjects analysed' indicates the number of participants with data available for endpoint analysis. 'Number analysed (n)' indicates the number of participants with data available at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours post-dose on Days 1 and 15 of Cycle 1 (Cycle = 21 days)

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Osimertinib: Day 1 (n=5)	1790 (± 1030)			
Osimertinib: Day 15 (n=5)	1380 (± 900)			
AZ5104: Day 1 (n=5)	82.9 (± 59.4)			
AZ5104: Day 15 (n=5)	136 (± 56.8)			
AZ7550: Day 1 (n=5)	47.1 (± 46.3)			
AZ7550: Day 15 (n=4)	112 (± 111)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Overall Response Rate (ORR) as per investigator assessment	
End point title	Run-in Part: Overall Response Rate (ORR) as per investigator assessment

End point description:

ORR was defined as the percentage of participants with a confirmed best overall response (BOR) of complete response (CR) or partial response (PR), as per investigator judgment and according to Response Evaluation Criteria in Solid Tumors 1.1 (RECIST v1.1). Criteria for CR: Disappearance of all lesions and pathologic lymph nodes; PR: ≥30% decrease in the sum of longest diameters (SLD) of the target lesions or no new lesions or no progression of non-target lesions. Full Analysis Set (FAS) included all participants who received any component of the study treatment.

End point type	Secondary

End point timeframe:

Up to end of study, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of subjects				
number (confidence interval 95%)	50.0 (11.8 to 88.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Duration of Response (DOR) as per investigator assessment

End point title	Run-in Part: Duration of Response (DOR) as per investigator assessment

End point description:

DOR was defined as the time from first documented response of CR or PR to the date of first documented progressive disease (PD) or death due to any cause. Criteria for CR: Disappearance of all lesions and pathologic lymph nodes; PR: ≥30% decrease in the SLD of the target lesions or no new lesions or no progression of non-target lesions; PD: ≥20% increase in SLD compared to the smallest SLD in the study, or progression of non-target lesions or new lesions. FAS included all participants who received any component of the study treatment. 'Number of subjects analysed' indicates the number of participants with CR or PR. 9999= Upper limit of 95% confidence interval (CI) was not estimable due to an insufficient number of subjects with events.

End point type	Secondary

End point timeframe:

Up to disease progression or death or end of study, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: months				
median (confidence interval 95%)	6.93 (2.50 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Time to Response (TTR) as per investigator assessment

End point title	Run-in Part: Time to Response (TTR) as per investigator assessment

End point description:

TTR was defined as the duration of time between the date of first dose of treatment and the date of the first documented response of either CR or PR as per investigator judgment and according to RECIST v1.1 criteria. Criteria for CR: Disappearance of all lesions and pathologic lymph nodes; PR: ≥30% decrease in SLD of the target lesions or no new lesions or no progression of non-target lesions. FAS included all participants who received any component of the study treatment. 'Number of subjects analysed' indicates the number of participants with CR or PR. 9999= Median and the upper limit of 95% CI were not estimable due to an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of treatment up to end of study, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: months				
median (confidence interval 95%)	9999 (1.41 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Disease Control Rate (DCR) as per investigator assessment

End point title	Run-in Part: Disease Control Rate (DCR) as per investigator assessment

End point description:

DCR was defined as the percentage of participants with a BOR of CR, PR and stable disease (SD) as per investigator judgment and according to RECIST v1.1. Criteria for CR: Disappearance of all lesions and pathologic lymph nodes; PR: ≥30% decrease in SLD of the target lesions or no new lesions or no progression of non-target lesions; SD: Neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease. FAS included all participants who received any component of the study treatment.

End point type	Secondary

End point timeframe:

From randomisation up to end of study, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of subjects				
number (confidence interval 95%)	66.7 (22.3 to 95.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in Part: Progression-Free Survival (PFS) as per investigator assessment

End point title	Run-in Part: Progression-Free Survival (PFS) as per investigator assessment

End point description:

PFS was defined as the time (in months) from first dose of treatment to the date of the first documented PD or death due to any cause as per investigator judgment and according to RECIST v1.1. PFS was censored if no PFS event (progression or death) was observed. Progression was defined as a ≥20% increase in SLD compared to smallest SLD in the study, or progression of non-target lesions or new lesions. FAS included all participants who received any component of the study treatment. 9999= The upper limit of 95% CI was not estimable due to an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of treatment until first documented progression or death or end of study, assessed up to 39 weeks

End point values	Run-in Part: Capmatinib + Osimertinib			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: months				
median (confidence interval 95%)	4.58 (0.99 to 9999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of treatment until 30 days after last dose of study treatment, assessed up to 39 weeks

Adverse event reporting additional description:

Safety set included all participants who received at least one dose of study treatment. Due to early study termination, the randomized part of the study was not conducted. Hence safety data was not collected in the randomized part of the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Run-in Part: Capmatinib + Osimertinib

Reporting group description:

Subjects received a starting dose of capmatinib 400 mg, orally, BID in combination with osimertinib 80 mg, orally, QD for a maximum of 39 weeks.

Serious adverse events	Run-in Part: Capmatinib + Osimertinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
COVID-19			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Run-in Part: Capmatinib + Osimertinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

Respiratory, thoracic and mediastinal disorders Pleural effusion subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Investigations Lipase increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Cardiac disorders Pericardial effusion subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Eye disorders Cataract subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 2 / 6 (33.33%) 4		

Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 1 / 6 (16.67%) 2		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 3 / 6 (50.00%) 3		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Infections and infestations Paronychia subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Metabolism and nutrition disorders Hypoalbuminaemia subjects affected / exposed occurrences (all) Decreased appetite subjects affected / exposed occurrences (all)	 3 / 6 (50.00%) 3 1 / 6 (16.67%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2021	Amendment 1: • Revised inclusion and exclusion criteria: Removed the requirements of T790M negative results for subjects previously treated with osimertinib; Allowed subjects who had previously received 3rd generation EGFR TKIs other than osimertinib to participate in this study; Excluded subjects with known druggable molecular alterations, known EGFR T790M positive status, and who received live vaccines within 30 days prior to the first dose of study treatment. • Updated the biomarker collection schedule for the randomisation part to add one additional time point (Cycle 1 Day 1) and adjusted the schedule of sample collections to start at Cycle 2 instead of Cycle 4.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated as Novartis decided to halt enrolment on 11 May 2022. This was a business decision and not related to any safety concerns.

Notes: