Clinical trial results:
A double-blind, placebo controlled, randomized, phase II study evaluating the efficacy and safety of capmatinib and spartalizumab vs capmatinib and placebo as 1st line treatment for advanced NSCLC patients with MET exon14 skipping mutations

Summary

EudraCT number	2019-003097-11
Trial protocol	DE FR BE IT
Global end of trial date	26 January 2023

Results information

Result version number	v1
This version publication date	16 December 2023
First version publication date	16 December 2023

Trial information

Trial identification

Sponsor protocol code	CINC280J12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04323436
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis, 41 613241111, 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	26 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the trial were:
• Run-in part: To evaluate the anti-tumor activity of capmatinib in combination with spartalizumab
• Randomized part: To compare the efficacy of capmatinib in combination with spartalizumab versus capmatinib plus placebo

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	19 August 2020
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	Belgium: 8
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	31
EEA total number of subjects	24

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	6
From 65 to 84 years	24
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants took part in 15 investigative sites in 9 countries.

Pre-assignment

Screening details:

Screening evaluations were performed within 28 days prior to the first dose of study treatment.
The study enrollment was halted during the Run-in part per sponsor's decision. Following the study enrollment halt, spartalizumab treatment was discontinued and the Randomized part was not initiated.

Period 1

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

Blinding implementation details:

The run-in part (part 1) was open label. The randomized part (part 2) was not initiated.

Arms

Arm title	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W

Arm description:

Capmatinib 400 mg orally twice daily (BID) in combination with spartalizumab 400 mg intravenously every 28 days (Q4W) in the run-in part.

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab 400 mg intravenously every 28 days (Q4W)

Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib 400 mg orally twice daily (BID)

Number of subjects in period 1	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W
Started	31
Treated with capmatinib + spartalizumab	28
Treated with capmatinib only	3

Completed	0
Not completed	31
Physician decision	2
Subject decision	3
Transfer to another study or alternative treatment	8
Death	1
Adverse event	7
Progressive disease	10

Baseline characteristics

Reporting groups	
Reporting group title	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W

Reporting group description:

Capmatinib 400 mg orally twice daily (BID) in combination with spartalizumab 400 mg intravenously every 28 days (Q4W) in the run-in part.

Reporting group values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W	Total	
Number of subjects	31	31	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	6	6	
From 65-84 years	24	24	
85 years and over	1	1	
Age Continuous Units: years			
arithmetic mean	71.6		
standard deviation	± 9.50	-	
Sex: Female, Male Units: participants			
Female	16	16	
Male	15	15	
Race/Ethnicity, Customized Units: Subjects			
White	23	23	
Black or African American	1	1	
Asian	6	6	
Unknown	1	1	

End points

End points reporting groups

Reporting group title	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W

Reporting group description:

Capmatinib 400 mg orally twice daily (BID) in combination with spartalizumab 400 mg intravenously every 28 days (Q4W) in the run-in part.

Primary: Randomized part: Progression-Free Survival (PFS) by BIRC as per RECIST 1.1

End point title	Randomized part: Progression-Free Survival (PFS) by BIRC as per RECIST 1.1[1]

End point description:

PFS is defined as the time from the date of start of treatment to the date of the first documented progression or death due to any cause. Tumor response based on blinded independent review committee (BIRC) assessment per RECIST v1.1.

End point type	Primary

End point timeframe:

Up to 6 years

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: No statistical analysis were planned for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Run-in part: Overall Response Rate (ORR) by investigator assessment as per RECIST 1.1

End point title	Run-in part: Overall Response Rate (ORR) by investigator assessment as per RECIST 1.1[2]

End point description:

Tumor response was based on local investigator assessment as per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1. ORR per RECIST v1.1 is defined as the percentage of participants with a best overall response of Complete Response (CR) or Partial Response (PR).
For RECIST v1.1, CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Primary

End point timeframe:

From start of treatment until end of study, assessed up to 2.5 years

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: No statistical analysis were planned for this endpoint.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 95%)	35.5 (19.2 to 54.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Number of participants with dose reductions and dose interruptions of spartalizumab

End point title	Run-in part: Number of participants with dose reductions and dose interruptions of spartalizumab

End point description:

Number of participants with at least one dose reduction of spartalizumab and number of participants with at least one dose interruption of spartalizumab. Dose reductions were not allowed for spartalizumab.

End point type	Secondary

End point timeframe:

From first dose of spartalizumab to last dose, up to 0.9 years

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: participants				
At least one dose reduction	0			
At least one dose interruption	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Number of participants with dose reductions and dose

interruptions of capmatinib	
End point title	Run-in part: Number of participants with dose reductions and dose interruptions of capmatinib

End point description:

Number of participants with at least one dose reduction of capmatinib and number of participants with at least one dose interruption of capmatinib.

End point type	Secondary

End point timeframe:

From first dose of capmatinib to last dose, up to 2.4 years

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: participants				
At least one dose reduction	19			
At least one dose interruption	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Dose intensity of capmatinib	
End point title	Run-in part: Dose intensity of capmatinib

End point description:

Dose intensity of capmatinib was calculated as actual cumulative dose in milligrams divided by duration of exposure in days.

End point type	Secondary

End point timeframe:

From first dose of capmatinib to last dose, up to 2.4 years

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: mg/day				
arithmetic mean (standard deviation)	595.9 (± 173.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Dose intensity of spartalizumab

End point title	Run-in part: Dose intensity of spartalizumab

End point description:

Dose intensity of spartalizumab was calculated as actual cumulative dose in milligrams divided by duration of exposure in days and then multiplied by the duration of one cycle (28 days).

End point type	Secondary

End point timeframe:

From first dose of spartalizumab to last dose, up to 0.9 years

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: mg/cycle				
arithmetic mean (standard deviation)	365.6 (± 51.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Disease Control Rate (DCR) by investigator assessment as per RECIST 1.1

End point title	Run-in part: Disease Control Rate (DCR) by investigator assessment as per RECIST 1.1

End point description:

DCR is defined as the percentage of participants with a best overall response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), and non-CR/non-progressive disease (for subjects without target lesions). Tumor response was based on local investigator assessment per RECIST v1.1. For RECIST v1.1, CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters; SD= Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progression).

End point type	Secondary

End point timeframe:

From start of treatment until end of study, assessed up to 2.5 years

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 95%)	77.4 (58.9 to 90.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Maximum observed plasma concentration (Cmax) of capmatinib

End point title	Run-in part: Maximum observed plasma concentration (Cmax) of capmatinib

End point description:

Pharmacokinetic (PK) parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed plasma concentration following a dose.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 8 hours after morning dose on Cycle 3 Day 1. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	2730 (± 74.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Time to reach maximum plasma concentration (Tmax) of

capmatinib

End point title	Run-in part: Time to reach maximum plasma concentration (Tmax) of capmatinib

End point description:

PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) plasma concentration following a dose. Actual recorded sampling times were considered for the calculations.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 8 hours after morning dose on Cycle 3 Day 1. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: hours				
median (full range (min-max))	1.75 (1.00 to 3.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Progression-Free Survival (PFS) by investigator assessment as per RECIST 1.1

End point title	Run-in part: Progression-Free Survival (PFS) by investigator assessment as per RECIST 1.1

End point description:

PFS is defined as the time from the date of start of treatment to the date of the first documented progression or death due to any cause. If a patient did not have an event, PFS was censored at the date of the last adequate tumor assessment. Tumor response was based on investigator assessment per RECIST v1.1.
PFS was analyzed using Kaplan-Meier estimates.
Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating ‘not available’). Therefore, not available values because of insufficient number of participants with events are indicated as ‘999’.

End point type	Secondary

End point timeframe:

From start of treatment until end of study, assessed up to 2.5 years

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: months				
median (confidence interval 95%)	16.5 (7.4 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Maximum observed serum concentration (Cmax) of spartalizumab

End point title	Run-in part: Maximum observed serum concentration (Cmax) of spartalizumab

End point description:

Pharmacokinetic (PK) parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed serum concentration following a dose.

End point type	Secondary

End point timeframe:

pre-infusion and 1, 72, 168, 336 and 672 hours after completion of the spartalizumab infusion on Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: µg/mL				
geometric mean (geometric coefficient of variation)	135 (± 28.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of capmatinib

End point title	Run-in part: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of capmatinib

End point description:

PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 8 hours after morning dose on Cycle 3 Day 1. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	10000 (± 61.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Area under the plasma concentration-time curve from time zero to the end of a dosing interval (AUCtau) of capmatinib

End point title	Run-in part: Area under the plasma concentration-time curve from time zero to the end of a dosing interval (AUCtau) of capmatinib

End point description:

PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUCtau calculation. A dosing interval (tau) is defined as 12 hours.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 8 hours after morning dose on Cycle 3 Day 1. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	12900 (± 96.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Time to reach maximum serum concentration (Tmax) of spartalizumab

End point title	Run-in part: Time to reach maximum serum concentration (Tmax) of spartalizumab

End point description:

PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) serum concentration following a dose. Actual recorded sampling times were considered for the calculations.

End point type	Secondary

End point timeframe:

pre-infusion and 1, 72, 168, 336 and 672 hours after completion of the spartalizumab infusion on Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: hours				
median (full range (min-max))	1.67 (0.917 to 164)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Area under the serum concentration-time curve from time zero to the end of a dosing interval (AUCtau) of spartalizumab

End point title	Run-in part: Area under the serum concentration-time curve from time zero to the end of a dosing interval (AUCtau) of spartalizumab

End point description:

PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUCtau calculation. A dosing interval (tau) is defined as 28 days.

End point type	Secondary

End point timeframe:

pre-infusion and 1, 72, 168, 336 and 672 hours after completion of the spartalizumab infusion on Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: hr*µg/mL				
geometric mean (geometric coefficient of variation)	49700 (± 47.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Run-in part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab

End point title	Run-in part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab

End point description:

PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.

End point type	Secondary

End point timeframe:

pre-infusion and 1, 72, 168, 336 and 672 hours after completion of the spartalizumab infusion on Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.

End point values	Run-in part: Capmatinib 400mg BID + Spartalizumab 400mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: hr*µg/mL				
geometric mean (geometric coefficient of variation)	52900 (± 64.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Overall Survival (OS)

End point title	Randomized part: Overall Survival (OS)

End point description:

OS is defined as the time from date of start of treatment to date of death due to any cause.

End point type	Secondary

End point timeframe:

Up to 12 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Dose intensity of capmatinib and spartalizumab

End point title	Randomized part: Dose intensity of capmatinib and spartalizumab

End point description:

Dose intensity is defined as the ratio of actual cumulative dose and duration of exposure.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Number of participants with dose reductions and dose interruptions of capmatinib and spartalizumab

End point title	Randomized part: Number of participants with dose reductions and dose interruptions of capmatinib and spartalizumab

End point description:

Number of participants with at least one dose reduction of capmatinib and spartalizumab and number of

participants with at least one dose interruption of capmatinib and spartalizumab.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Progression-Free Survival (PFS) by investigator assessment as per RECIST 1.1

End point title	Randomized part: Progression-Free Survival (PFS) by investigator assessment as per RECIST 1.1

End point description:

PFS is defined as the time from the date of start of treatment to the date of the first documented progression or death due to any cause. Tumor response based on investigator assessment per RECIST v1.1.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Disease Control Rate (DCR) by BIRC and investigator assessment as per RECIST 1.1

End point title	Randomized part: Disease Control Rate (DCR) by BIRC and investigator assessment as per RECIST 1.1

End point description:

DCR is defined as the percentage of participants with a best overall response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), and non-CR/non-progressive disease (for subjects without target lesions). Tumor response based on BIRC and local investigator assessment per RECIST v1.1.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Overall Response Rate (ORR) by BIRC and investigator assessment as per RECIST 1.1

End point title	Randomized part: Overall Response Rate (ORR) by BIRC and investigator assessment as per RECIST 1.1

End point description:

ORR is defined as the percentage of participants with a best overall response of Complete Response (CR) and Partial Response (PR). Tumor response based on BIRC and local investigator assessment per RECIST v1.1.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Time to response (TTR) by BIRC and investigator assessment as per RECIST 1.1

End point title	Randomized part: Time to response (TTR) by BIRC and investigator assessment as per RECIST 1.1

End point description:

TTR is defined as the time from the date of start of treatment to the first documented response of either CR or PR, which must be subsequently confirmed, according to RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Duration of Response (DOR) by BIRC and investigator assessment as per RECIST 1.1

End point title	Randomized part: Duration of Response (DOR) by BIRC and investigator assessment as per RECIST 1.1

End point description:

DOR is defined as the time from the date of first documented response (CR or PR) to the first documented progression per RECIST 1.1 or death due to any cause.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Change from baseline in EORTC QLQ-C30

End point title	Randomized part: Change from baseline in EORTC QLQ-C30

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) contains 30 items and is composed of both multi-item scales and single-item measures. These include 5 functional scales (physical, role, emotional, cognitive, and social functioning), 3 symptom scales (fatigue, nausea/vomiting, and pain), 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial impact) and a global health status/QoL scale. All scales and single-item measures range in score from 0 to 100. For the functional and the global QoL scales, a higher score indicates better health. For the symptom scales, a higher score indicates more symptom burden. The QLQC30 summary score (0-100) is calculated as the mean of 13 of the 15 QLQC30 scale and item scores (excluding global QoL and financial impact), with a higher score indicating a better health-related QoL.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Change from baseline in EORTC QLQ-LC13

End point title	Randomized part: Change from baseline in EORTC QLQ-LC13

End point description:

EORTC QLQ-LC13 is used in conjunction with the EORTC QLQ-C30 and provides information on an additional 13 items specifically related to lung cancer. The five domains of the LC13 include pain, dyspnea, coughing and hemoptysis, and are based on their presence over the past week. All but the pain domain are scored on a 4 point Likert scale ranging from "not at all" to "very much". Pain score is based on its presence, hence yes or no. Scores are averaged and transformed to 0 to 100. A higher score indicates a higher presence of symptoms.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Change from baseline in EQ-5D-5L

End point title	Randomized part: Change from baseline in EQ-5D-5L

End point description:

The EQ-5D-5L is a standardized measure of health utility that provides a single index value for one's health status. The EQ-5D-5L contains one item for each of five dimensions of health-related quality of life (HRQOL) (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Response options for each item vary from having no problems to extreme problems. Subject responses to the five dimensions of HRQOL reflect a specific health state that corresponds to a population preference weight for that state on a continuous scale of 0 (death) to 1 (perfect health). A visual analog scale (ranging from 0 to 100) is also included to capture subject's rating of their overall health status. Higher scores of the EQ-5D-5L represent better health states.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Time to definitive 10 points deterioration symptom scores for pain in chest, coughing and dyspnea per QLQ-LC13 questionnaire

End point title	Randomized part: Time to definitive 10 points deterioration symptom scores for pain in chest, coughing and dyspnea per QLQ-LC13 questionnaire

End point description:

EORTC QLQ-LC13 is used in conjunction with the EORTC QLQ-C30 and provides information on an additional 13 items specifically related to lung cancer. The five domains of the LC13 include pain in chest, dyspnea, coughing and hemoptysis, and are based on their presence over the past week. All but the pain domain are scored on a 4 point Likert scale ranging from "not at all" to "very much". Pain score is based on its presence, hence yes or no. Scores are averaged and transformed to 0 to 100. A higher score indicates a higher presence of symptoms.
The time to definitive 10 points deterioration is defined as the time from the date of randomization to the date of event, which is defined as at least 10 points relative to baseline worsening of the corresponding scale score or death due to any cause.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Time to definitive deterioration in global health status/QoL, shortness of breath and pain per EORTC QLQ-C30

End point title	Randomized part: Time to definitive deterioration in global health status/QoL, shortness of breath and pain per EORTC QLQ-C30

End point description:

The EORTC QLQ-C30 contains 30 items and is composed of both multi-item scales and single-item measures. These include 5 functional scales (physical, role, emotional, cognitive, and social functioning), 3 symptom scales (fatigue, nausea/vomiting, and pain), 6 single items (dyspnea, insomnia, appetite

loss, constipation, diarrhea, and financial impact) and a global health status/QoL scale. All scales and single-item measures range in score from 0 to 100. For the functional and the global QoL scales, a higher score indicates better health. For the symptom scales, a higher score indicates more symptom burden.
The time to definitive 10 points deterioration is defined as the time from the date of randomization to the date of event, which is defined as at least 10 points relative to baseline worsening of the corresponding scale score or death due to any cause.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Maximum observed concentration (Cmax) of capmatinib and spartalizumab

End point title	Randomized part: Maximum observed concentration (Cmax) of capmatinib and spartalizumab

End point description:

Pharmacokinetic (PK) parameters calculated based on capmatinib and spartalizumab concentrations in plasma and serum, respectively, by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Time to reach maximum concentration (Tmax) of capmatinib and spartalizumab

End point title	Randomized part: Time to reach maximum concentration (Tmax) of capmatinib and spartalizumab

End point description:

Pharmacokinetic (PK) parameters calculated based on capmatinib and spartalizumab concentrations in plasma and serum, respectively, by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Area under the concentration-time curve from time zero to the end of a dosing interval (AUCtau) of capmatinib and spartalizumab

End point title	Randomized part: Area under the concentration-time curve from time zero to the end of a dosing interval (AUCtau) of capmatinib and spartalizumab

End point description:

Pharmacokinetic (PK) parameters calculated based on capmatinib and spartalizumab concentrations in plasma and serum, respectively, by using non-compartmental methods.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of capmatinib and spartalizumab

End point title	Randomized part: Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of capmatinib and spartalizumab

End point description:

Pharmacokinetic (PK) parameters calculated based on capmatinib and spartalizumab concentrations in plasma and serum, respectively, by using non-compartmental methods.

End point type	Secondary

End point timeframe:

Up to 6 years

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Number of participants with anti-spartalizumab antibodies

End point title	Randomized part: Number of participants with anti-spartalizumab antibodies

End point description:

Immunogenicity (IG) evaluated in serum samples. The assay to quantify and assess the IG was a validated homogeneous enzyme-linked immunosorbent assay (ELISA).

End point type	Secondary

End point timeframe:

Baseline (pre-dose), up to 6 years

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of spartalizumab+capmatinib (or capmatinib single agent for patients who did not receive spartalizumab) to 150 days after last dose of spartalizumab or 30 days after last dose of capmatinib, whichever was longer, up to maximum 2.5 years.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Capmatinib + Spartalizumab (Prior discontinuing spartalizumab)

Reporting group description:

Run-in part. Capmatinib 400 mg BID in combination with spartalizumab 400 mg Q4W before the discontinuation of spartalizumab

Reporting group title	Capmatinib only

Reporting group description:

Run-in part. Immediately following the discontinuation of spartalizumab (and enrollment halt), enrolled subjects who had not started study treatment received capmatinib single agent treatment from the start

Reporting group title	Capmatinib + Spartalizumab (After discontinuing spartalizumab)

Reporting group description:

Run-in part. Capmatinib 400 mg BID in combination with spartalizumab 400 mg Q4W after the discontinuation of spartalizumab

Serious adverse events	Capmatinib + Spartalizumab (Prior discontinuing spartalizumab)	Capmatinib only	Capmatinib + Spartalizumab (After discontinuing spartalizumab)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 28 (39.29%)	1 / 3 (33.33%)	8 / 28 (28.57%)
number of deaths (all causes)	4	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Inferior vena cava syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oedema peripheral			

subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium colitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Capmatinib + Spartalizumab (Prior discontinuing spartalizumab)	Capmatinib only	Capmatinib + Spartalizumab (After discontinuing spartalizumab)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 28 (89.29%)	3 / 3 (100.00%)	18 / 28 (64.29%)
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	2 / 28 (7.14%)
occurrences (all)	0	1	3
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Chest pain			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	2	3	1
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	1	1	1
Fatigue			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	3 / 28 (10.71%)
occurrences (all)	3	1	6
Oedema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	4 / 28 (14.29%)
occurrences (all)	1	0	5
Oedema peripheral			
subjects affected / exposed	11 / 28 (39.29%)	3 / 3 (100.00%)	15 / 28 (53.57%)
occurrences (all)	13	12	19
Swelling			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			

Scrotal oedema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	3 / 28 (10.71%)
occurrences (all)	0	1	3
Dyspnoea			
subjects affected / exposed	1 / 28 (3.57%)	2 / 3 (66.67%)	4 / 28 (14.29%)
occurrences (all)	1	2	5
Pleural effusion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Pneumonitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 28 (28.57%)	1 / 3 (33.33%)	6 / 28 (21.43%)
occurrences (all)	11	1	4
Amylase increased			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	4 / 28 (14.29%)
occurrences (all)	3	0	7
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 28 (32.14%)	1 / 3 (33.33%)	6 / 28 (21.43%)
occurrences (all)	13	2	10

Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	1	1	2
Blood bilirubin increased			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	2 / 28 (7.14%)
occurrences (all)	5	1	2
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	4 / 28 (14.29%)
occurrences (all)	1	0	4
Blood creatinine increased			
subjects affected / exposed	10 / 28 (35.71%)	2 / 3 (66.67%)	11 / 28 (39.29%)
occurrences (all)	15	2	22
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	2	1	1
Lipase increased			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	5 / 28 (17.86%)
occurrences (all)	3	2	8
Lymphocyte count decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Platelet count decreased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Weight decreased			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	3	1	0
Weight increased			

subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	4 / 28 (14.29%)
occurrences (all)	2	1	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	3	1	0
Headache			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	2 / 28 (7.14%)
occurrences (all)	3	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 28 (10.71%)
occurrences (all)	1	0	3
Thrombocytopenia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	2	2	1
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	8 / 28 (28.57%)	2 / 3 (66.67%)	1 / 28 (3.57%)
occurrences (all)	8	3	1
Nausea			
subjects affected / exposed	9 / 28 (32.14%)	1 / 3 (33.33%)	2 / 28 (7.14%)
occurrences (all)	11	1	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	1	1	1
Gastritis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	2	0	2
Dry mouth			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Stomatitis			

subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	5 / 28 (17.86%)
occurrences (all)	0	3	6
Vomiting			
subjects affected / exposed	5 / 28 (17.86%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences (all)	5	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Pruritus			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Dermatitis acneiform			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	2
Rash maculo-papular			
subjects affected / exposed	4 / 28 (14.29%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	4	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	3	0	2
Back pain			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	2 / 28 (7.14%)
occurrences (all)	2	1	2
Muscle spasms			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Pain in extremity			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	4 / 28 (14.29%)
occurrences (all)	1	0	6
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 28 (0.00%)	2 / 3 (66.67%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	3 / 28 (10.71%)
occurrences (all)	0	1	3
Respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	2 / 3 (66.67%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 28 (14.29%)	1 / 3 (33.33%)	2 / 28 (7.14%)
occurrences (all)	4	2	5
Hyperkalaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 3 (66.67%)	5 / 28 (17.86%)
occurrences (all)	1	2	10
Hypokalaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	3 / 28 (10.71%)
occurrences (all)	0	1	3
Hyponatraemia			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 28 (10.71%)
occurrences (all)	1	0	3
Hypophosphataemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	1 / 28 (3.57%)
occurrences (all)	0	4	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2021	The main purpose of this protocol amendment was to modify the study conduct and data analysis following the sponsor's decision to halt study enrollment on 28-Jul-2021, as communicated to Health Authorities as per local requirements. The enrollment halt decision was based on lack of tolerability observed in capmatinib and spartalizumab combination treatment arm in the Part 1 of the trial. Immediately following the enrollment halt, below procedural changes were performed: • All ongoing subjects were discontinued from spartalizumab treatment and continue to receive single agent capmatinib, given the proven tolerability and efficacy of capmatinib monotherapy in this study indication. • Enrolled subjects who had not started study treatment were to receive capmatinib single agent treatment from the start. In addition, blinded and independent centralized tumor assessment was no longer required. Updates in several sections were implemented.

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/#/

Notes: