NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Capmatinib

Trial Indication(s)

Non-small cell lung cancer (NSCLC)

Protocol Number

CINC280D2201

Protocol Title

Phase II multicenter randomized two-arm study of capmatinib and spartalizumab combination therapy vs docetaxel in pretreated adult patients with EGFR wild-type ALK rearrangement negative advanced/metastatic non-small cell lung cancer

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: December 2018 (Actual)
Primary Completion Date: September 2020 (Actual)
Study Completion Date: September 2020 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a two-part prospectively designed, multicenter, open-label, randomized phase II study. The main aim of this study was to evaluate the safety and efficacy of capmatinib in combination with spartalizumab in adult participants with epidermal growth factor receptor (EGFR) wild type (for exon 19 deletions and exon 21 L858R substitution mutations), anaplastic lymphoma kinase (ALK) rearrangement negative in locally advanced (stage IIIB, not eligible for definitive chemo-radiation) or metastatic (stage IV) non-small cell lung cancer (NSCLC) after failure of platinum doublet and checkpoint inhibitor treatment.

The trial consisted in two parts:

- Part 1: Run-in. Prior to the randomized part of the study, a run-in to assess the safety and tolerability as well as preliminary efficacy of the capmatinib and spartalizumab combination was conducted. Participants were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days. A review was planned to take place after all participants had at least 24 weeks of follow-up. The decision to expand the study to the randomized part was to be based on the safety, tolerability and preliminary efficacy of the capmatinib and spartalizumab combination
- Part 2: Randomized. Subjects were planned to be randomized to one of the following arms in a 2:1 ratio: 1) combination of capmatinib 400 mg BID and spartalizumab 400 mg i.v. once every 28 days; 2) docetaxel 75 mg/m2 i.v. following local guidelines as per standard of care and product labels. Based on the safety, tolerability, and preliminary efficacy results obtained in the first part of the study, the randomized part was not opened.

For the run-in part of the study, the treatment period began on Cycle 1 Day 1 and continued in 28-day cycles until disease progression, unacceptable toxicity, withdrawal of informed consent, pregnancy, lost to follow-up, or death irrespective of

start of new anti-neoplastic therapy. After treatment discontinuation, all subjects were followed for safety evaluations during the safety follow-up period, and the subject's status was collected every 8 weeks as part of the survival follow-up.

Centers

8 centers in 6 countries: United States(1), France(2), Belgium(1), Spain(2), Germany(1), Israel(1)

Objectives:

Primary Objectives:

- Run-in part: To assess safety and tolerability of capmatinib and spartalizumab combination
- Randomized part: To assess the overall survival of combination of capmatinib and spartalizumab in comparison to docetaxel

Secondary Objectives (run-in and randomized part):

- To assess the objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), duration of response (DOR), and time to response (TTR) of the capmatinib and spartalizumab combination and that of docetaxel
- To characterize the pharmacokinetics of capmatinib and spartalizumab as a combination therapy in this participant population
- To evaluate the prevalence and incidence of immunogenicity

Given that the randomized part of this study was not opened, none of the participants received docetaxel and so no analysis was performed for docetaxel endpoints.

Test Product (s), Dose(s), and Mode(s) of Administration

Capmatinib was administered orally as film-coated tablets, at a dose of 400 mg on a twice daily dosing schedule. Spartalizumab was administered via intravenous infusion, at a dose of 400 mg once every 28 days.

Statistical Methods

Given that the randomized part of the study was not opened, the final analysis was not performed for all endpoints. As none of the participants received docetaxel, no analysis was performed for docetaxel endpoints.

Data were summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum) for quantitative data and/or contingency tables (frequencies and percentages) for qualitative data for demographic and baseline characteristics, efficacy measurements, safety measurements, and all relevant pharmacokinetic (PK) and immunogenicity measurements. The final analysis of study data was based on all participant data of the run-in part when all participants discontinued the study.

Primary endpoints

- Adverse events (AEs) and Serious Adverse Events (SAEs), including changes from baseline in vital signs and laboratory results qualifying and reported as AEs were summarized by number and percentage of subjects having at least one AE. The Common Terminology Criteria for Adverse Events (CTCAE) v5.0 was used to grade the severity of the AEs: Grade 1: mild; Grade 2: moderate; Grade 3: severe or medically significant; Grade 4: life-threatening consequences: Grade 5: Death.
- Dose-limiting toxicities (DLTs) defined as an AE or abnormal laboratory value assessed as unrelated to disease progression, inter-current illness, or concomitant medications that met certain criteria as defined in the protocol, were also summarized by number and percentage of subjects having at least one AE
- The number and percentage of participants who had dose reductions and/or interruptions was summarized for all subjects. Relative dose intensity was calculated as the ratio of dose intensity and planned dose intensity

Secondary endpoints

- Efficacy: The overall/objective response rate (ORR), disease control rate (DCR), progression free survival (PFS), duration of response (DOR), and time to response (TTR) of the capmatinib and spartalizumab combination based on response evaluation criteria in solid tumors (RECIST) 1.1 as per local Investigator's assessment were assessed. ORR and DCR were summarized with accompanying 95% confidence interval (CI). The survival distribution of PFS was estimated using the Kaplan-Meier method. The medians of PFS and 95% confidence intervals of the medians were presented.

- Pharmacokinetics: The secondary objective for PK was to characterize the PK of capmatinib and spartalizumab as a combination therapy in this population. The respective Pharmacokinetic analysis set (PAS) for each study drug was used in the PK data analysis. Descriptive statistics for spartalizumab and capmatinib concentrations were presented at each scheduled time point.
- Immunogenicity: Immunogenicity was characterized descriptively by tabulating anti-drug antibodies (ADA) prevalence at baseline and ADA incidence on-treatment. Sample ADA status was listed.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
-Histologically confirmed locally advanced/metastatic (stage IIIB/IV), EGFR wild-type, ALK rearrangement negative, non-small cell lung cancer
-Subject had demonstrated progression following one prior platinum doublet and one prior PD-(L)1 checkpoint inhibitor (either alone or in combination, the most recent treatment regimen must have contained a PD-(L)1 checkpoint inhibitor)
-Subjects must be candidates for single agent docetaxel
-Subjects must have at least one lesion evaluable by RECIST 1.1

Exclusion Criteria:
-Prior treatment with a MET inhibitor or HGF (Hepatocyte growth factor) targeting therapy
-Any untreated central nervous system (CNS) lesion. Any CNS lesions not remaining stable for ≥ 4 weeks after treatment
-Use of any live vaccines against infectious diseases within 12 weeks of initiation of study treatment.

Other protocol-defined inclusion/exclusion criteria might apply.

Participant Flow Table

Overall Study

	Run-in part: capmatinib + spartalizumab	Randomized part: capmatinib + spartalizumab	Randomized part: docetaxel	Total
Arm/Group Description	Participants (enrolled in the run-in part)	Participants (enrolled in the randomized	Participants (enrolled in the	

	were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days	part) treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days	randomized part) treated with docetaxel 75mg/m2 i.v. following local guidelines as per standard of care and product labels once every 21 days	
Started	18	0[1]	0[1]	18
Completed	0	0	0	0
Not Completed	18	0	0	18
Progressive disease	10	0	0	10
Adverse Event	5	0	0	5
Clinical progression	2	0	0	2
Participant refused to take investigational product	1	0	0	1

[1] Randomized part was not opened

Baseline Characteristics

	Run-in part: capmatinib + spartalizumab	**Randomized part: capmatinib + spartalizumab**	**Randomized part: docetaxel**	**Total**

Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days	Participants (enrolled in the randomized part) treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days	Participants (enrolled in the randomized part) treated with docetaxel 75mg/m2 i.v. following local guidelines as per standard of care and product labels once every 21 days	
Number of Participants [units: participants]	18	0	0	18
Age Continuous (units: Years) Mean ± Standard Deviation				
	61.2±10.52			61.2±10.52
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)				
Female	7	0	0	7
Male	11	0	0	11
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)				
White	17	0	0	17
Missing	1	0	0	1

Primary Outcome Result(s)

Run-in part: Percentage of participants with Dose Limiting Toxicities (DLTs)

(Time Frame: From the day of the first dose of study medication up to 56 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Run-in part: Percentage of participants with Dose Limiting Toxicities (DLTs) (units: Participants) Count of Participants (Not Applicable)	
	1 (5.56%)

Run-in part: Percentage of participants with adverse events (AEs)

(Time Frame: From the day of the first dose of study medication to 150 days after the last dose of spartalizumab, or 30 days after the last dose of capmatinib (whichever is later) up to maximum duration of approximately 1.7 years)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Run-in part: Percentage of participants with adverse events (AEs) (units: Participants) Count of Participants (Not Applicable)	
AEs- All grades	18 (100%)
AEs- Grade ≥3	11 (61.11%)
Treatment-related AEs- All grades	14 (77.78%)
Treatment related AEs- Grade ≥3	1 (5.56%)
Serious AEs (SAEs)- All grades	10 (55.56%)
SAEs- Grade ≥3	7 (38.89%)

Treatment-related SAEs- All grades	3 (16.67%)
Treatment-related SAEs- Grade ≥3	0 (%)
Fatal SAEs- All grades	1 (5.56%)
Fatal SAEs- Grade ≥3	1 (5.56%)
AEs leading to discontinuation- All grades	5 (27.78%)
AEs leading to discontinuation- Grade ≥3	3 (16.67%)
Treatment-related AEs leading to discontinuation- All grades	3 (16.67%)
Treatment-related AEs leading to discontinuation- Grade ≥3	1 (5.56%)
AEs leading to dose adjustment/interruption- All grades	9 (50%)
AEs leading to dose adjustment/interruption- Grade ≥3	5 (27.78%)
AEs requiring additional therapy- All grades	16 (88.89%)
AEs requiring additional therapy- Grade ≥3	8 (44.44%)

Run-in part: Percentage of participants with at least one dose reduction.

(Time Frame: From the day of the first dose of study medication to end of treatment, assessed up to maximum duration of 68 weeks)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Run-in part: Percentage of participants with at least one dose reduction. (units: Participants) Count of Participants (Not Applicable)	
Capmatinib	6 (33.33%)

Run-in part: Percentage of participants with at least one dose interruption

(Time Frame: From the day of the first dose of study medication to end of treatment, assessed up to maximum duration of 68 weeks)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part)

	were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Run-in part: Percentage of participants with at least one dose interruption (units: Participants) Count of Participants (Not Applicable)	
Capmatinib	8 (44.44%)
Spartalizumab	3 (16.67%)

Run-in part: Relative dose intensity received by participants

(Time Frame: From the day of the first dose of study medication to end of treatment, assessed up to maximum duration of 68 weeks)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg

	intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Run-in part: Relative dose intensity received by participants (units: Percentage of dose received) Median (Full Range)	
Capmatinib	99.6 (27.8 to 100.0)
Spartalizumab	100.0 (75.0 to 133.3)

Randomized part: Overall survival (OS)

(Time Frame: From start of treatment to death due to any cause, assessed until the end of the study (up to a planned duration of 18 months))

	Randomized part: capmatinib + spartalizumab	**Randomized part: docetaxel**
Arm/Group Description	Participants (enrolled in the randomized part) treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days	Participants (enrolled in the randomized part) treated with docetaxel 75mg/m2 i.v. following local guidelines as per standard of care and product labels once every 21 days

Number of Participants Analyzed [units: participants]	0[1]	0[1]
Randomized part: Overall survival (OS) (units: Months) Median (95% Confidence Interval)		

[1]Results are not available because the randomized part never started

Secondary Outcome Result(s)

Objective response rate (ORR) based on RECIST 1.1 and as per investigator assessment

(Time Frame: From start of treatment until end of treatment, assessed up to 68 weeks (run-in part))

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18

Objective response rate (ORR) based on RECIST 1.1 and as per investigator assessment (units: Percentage of participants) Number (95% Confidence Interval)	
	0 (0.0 to 18.5)

Disease control rate (DCR) based on RECIST 1.1 and as per investigator assessment

(Time Frame: From start of treatment until end of treatment, assessed up to 68 weeks (run-in part))

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Disease control rate (DCR) based on RECIST 1.1 and as per investigator assessment (units: Percentage of	

participants) Number (95% Confidence Interval)	
	27.8 (9.7 to 53.5)

Progression free survival (PFS)

(Time Frame: From start of treatment until the first documented radiological progression or death, whichever comes first, assessed up to 68 weeks (run-in part))

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
Progression free survival (PFS) (units: Months) Median (95% Confidence Interval)	
	1.9 (1.7 to 3.6)

Time to response (TTR) based on RECIST 1.1 and as per investigator assessment

(Time Frame: From start of treatment to the first documented response of either complete response or partial response, assessed up to 68 weeks (run-in part))

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	0
Time to response (TTR) based on RECIST 1.1 and as per investigator assessment (units: Months) Number (95% Confidence Interval)	

Duration of response (DOR) based on RECIST 1.1 and as per investigator assessment

(Time Frame: From first documented response (CR or PR) to first documented progression or death, whichever came first, assessed up to 68 weeks (run-in part))

	Run-in part: capmatinib + spartalizumab

Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	0
Duration of response (DOR) based on RECIST 1.1 and as per investigator assessment (units: Months) Median (95% Confidence Interval)	

AUClast of capmatinib

(Time Frame: Cycle 3 day 1 at predose, 0.5 hours (h), 1h, 2h, 4h and 8h postdose. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice

	daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	8
AUClast of capmatinib (units: nanogram*hour/milliliter (ng*hr/mL)) Geometric Mean (Geometric Coefficient of Variation)	
	11500 (47.3%)

AUCtau of capmatinib

(Time Frame: Cycle 3 day 1 at predose, 0.5 hours (h), 1h, 2h, 4h and 8h postdose. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days

Number of Participants Analyzed [units: participants]	5
AUCtau of capmatinib (units: nanogram*hour/milliliter (ng*hr/mL)) Geometric Mean (Geometric Coefficient of Variation)	
	12800 (48.5%)

Maximum plasma concentration (Cmax) of capmatinib

(Time Frame: Cycle 3 day 1 at predose, 0.5 hours (h), 1h, 2h, 4h and 8h postdose. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	8
Maximum plasma concentration (Cmax) of capmatinib	

(units: nanogram/milliliter (ng/mL)) Geometric Mean (Geometric Coefficient of Variation)	
	3260 (44.6%)

Time to reach maximum (Tmax) plasma concentration of capmatinib

(Time Frame: Cycle 3 day 1 at predose, 0.5 hours (h), 1h, 2h, 4h and 8h postdose. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	8
Time to reach maximum (Tmax) plasma concentration of capmatinib (units: hour (h)) Median (Full Range)	
	1.42 (0.983 to 2.00)

AUClast of spartlizumab

(Time Frame: Cycle 3 day 1 (at predose and 1 hour postdose), cycle 3 day 4, cycle 3 day 8, cycle 3 day 15. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	7
AUClast of spartlizumab (units: microgram*day/milliliter (µg*day/mL)) Geometric Mean (Geometric Coefficient of Variation)	
	1720 (64.5%)

AUCtau of spartlizumab

(Time Frame: Cycle 3 day 1 (at predose and 1 hour postdose), cycle 3 day 4, cycle 3 day 8, cycle 3 day 15. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	7
AUCtau of spartlizumab (units: microgram*day/milliliter (µg*day/mL)) Geometric Mean (Geometric Coefficient of Variation)	
	2110 (35.1%)

Maximum plasma concentration (Cmax) of spartlizumab

(Time Frame: Cycle 3 day 1 (at predose and 1 hour postdose), cycle 3 day 4, cycle 3 day 8, cycle 3 day 15. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part)

	were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	8
Maximum plasma concentration (Cmax) of spartlizumab (units: microgram/milliliter (µg/mL)) Geometric Mean (Geometric Coefficient of Variation)	
	138 (23.2%)

Time to reach maximum (Tmax) plasma concentration of spartlizumab

(Time Frame: Cycle 3 day 1 (at predose and 1 hour postdose), cycle 3 day 4, cycle 3 day 8, cycle 3 day 15. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab

	400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	8
Time to reach maximum (Tmax) plasma concentration of spartlizumab (units: hour (h)) Median (Full Range)	
	1.13 (1.00 to 1.53)

Spartalizumab antidrug antibodies (ADA) prevalence at baseline

(Time Frame: Cycle 1 Day 1 at predose. Each Cycle is 28 days)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days

Number of Participants Analyzed [units: participants]	17
Spartalizumab antidrug antibodies (ADA) prevalence at baseline (units: Participants) Count of Participants (Not Applicable)	
	3 (17.65%)

Spartalizumab ADA Incidence On-treatment

(Time Frame: Predose at Cycle (C)1 Day (D)1, C2D1, C3D1, C4D1, C6D1, C8D1, C10D1, C12D1, thereafter every 6 cycles until discontinuation, and end of treatment (EOT), 30-day and 150-day after EOT)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	14
Spartalizumab ADA Incidence On-treatment (units: Participants)	

Count of Participants (Not Applicable)
3 (21.43%)

Post-hoc: All Collected Deaths

(Time Frame: On-treatment deaths due to any cause were collected from first dose of study medication to 150 days after the last dose of spartalizumab, or 30 days after the last dose of capmatinib, whichever is later, up to a maximum duration of approximately 1.7 years. Total deaths were collected from first dose of study treatment until end of post-treatment efficacy or survival follow, up to maximum duration of approximately 1.7 years)

	Run-in part: capmatinib + spartalizumab
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Number of Participants Analyzed [units: participants]	18
All Collected Deaths (units: Participants)	
Total Deaths	12
On-treatment Deaths	5

Safety Results

All-Cause Mortality

	Run-in part: capmatinib + spartalizumab N = 18
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Total participants affected	5 (27.78%)

Serious Adverse Events by System Organ Class

Time Frame	On-treatment adverse events were collected from first dose of study medication to 150 days after the last dose of spartalizumab, or 30 days after the last dose of capmatinib, whichever is later, up to a maximum duration of approximately 1.7 years.
Additional Description	Any sign or symptom that occurs during the study treatment plus 150 days after the last dose of spartalizumab or 30 days after the last dose of capmatinib (on-treatment). Analysis performed on the safety set in the run-in part: all participants who received at least one dose of spartalizumab [including incomplete infusion] or of capmatinib. No safety data is available for part 2 because it was not opened.
Source Vocabulary for Table Default	MedDRA (23.0)

Assessment Type for Table Default	Systematic Assessment

	Run-in part: capmatinib + spartalizumab N = 18
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Total participants affected	10 (55.56%)
Cardiac disorders	
Cardiac failure congestive	1 (5.56%)
Ventricular arrhythmia	1 (5.56%)
General disorders and administration site conditions	
Fatigue	3 (16.67%)
General physical health deterioration	1 (5.56%)
Pyrexia	1 (5.56%)

Immune system disorders	
Anaphylactic reaction	1 (5.56%)
Drug hypersensitivity	1 (5.56%)
Infections and infestations	
Abdominal infection	1 (5.56%)
Pneumonia	1 (5.56%)
Respiratory tract infection	1 (5.56%)
Metabolism and nutrition disorders	
Decreased appetite	1 (5.56%)
Respiratory, thoracic and mediastinal disorders	
Bronchial obstruction	1 (5.56%)
Dyspnoea	1 (5.56%)
Haemoptysis	1 (5.56%)
Respiratory failure	1 (5.56%)
Vascular disorders	
Deep vein thrombosis	1 (5.56%)

Other Adverse Events by System Organ Class

Time Frame	On-treatment adverse events were collected from first dose of study medication to 150 days after the last dose of spartalizumab, or 30 days after the last dose of capmatinib, whichever is later, up to a maximum duration of approximately 1.7 years.
Additional Description	Any sign or symptom that occurs during the study treatment plus 150 days after the last dose of spartalizumab or 30 days after the last dose of capmatinib (on-treatment). Analysis performed on the safety set in the run-in part: all participants who received at least one dose of spartalizumab [including incomplete infusion] or of capmatinib. No safety data is available for part 2 because it was not opened.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Run-in part: capmatinib + spartalizumab N = 18
Arm/Group Description	Participants (enrolled in the run-in part) were treated with capmatinib 400 mg twice daily (BID) and spartalizumab 400 mg intravenously (i.v.) once every 28 days
Total participants affected	18 (100.00%)
Blood and lymphatic system disorders	
Anaemia	2 (11.11%)

Cardiac disorders	
Pericardial effusion	1 (5.56%)
Stress cardiomyopathy	1 (5.56%)
Eye disorders	
Eyelid oedema	1 (5.56%)
Gastrointestinal disorders	
Abdominal pain	1 (5.56%)
Cheilitis	1 (5.56%)
Constipation	2 (11.11%)
Diarrhoea	5 (27.78%)
Dry mouth	1 (5.56%)
Dyspepsia	1 (5.56%)
Dysphagia	2 (11.11%)
Nausea	7 (38.89%)
Stomatitis	1 (5.56%)
Vomiting	5 (27.78%)
General disorders and administration site conditions	
Asthenia	4 (22.22%)
Axillary pain	1 (5.56%)
Chest pain	2 (11.11%)
Fatigue	4 (22.22%)
Oedema peripheral	4 (22.22%)
Pain	1 (5.56%)

Pyrexia	4 (22.22%)
Infections and infestations	
Herpes zoster	1 (5.56%)
Osteomyelitis	1 (5.56%)
Pneumonia	1 (5.56%)
Investigations	
Alanine aminotransferase increased	2 (11.11%)
Amylase increased	1 (5.56%)
Aspartate aminotransferase increased	2 (11.11%)
Blood alkaline phosphatase increased	1 (5.56%)
Blood creatinine increased	5 (27.78%)
Blood magnesium decreased	1 (5.56%)
C-reactive protein increased	2 (11.11%)
Creatinine renal clearance decreased	1 (5.56%)
Gamma-glutamyltransferase increased	1 (5.56%)
Lipase increased	2 (11.11%)
Lymphocyte count decreased	2 (11.11%)

Weight decreased	3 (16.67%)
Metabolism and nutrition disorders	
Decreased appetite	2 (11.11%)
Dehydration	1 (5.56%)
Hyperglycaemia	1 (5.56%)
Hypoalbuminaemia	1 (5.56%)
Hypomagnesaemia	1 (5.56%)
Musculoskeletal and connective tissue disorders	
Arthralgia	1 (5.56%)
Muscle spasms	1 (5.56%)
Musculoskeletal chest pain	1 (5.56%)
Pain in extremity	1 (5.56%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Cancer pain	1 (5.56%)
Nervous system disorders	
Dizziness	1 (5.56%)
Dysgeusia	1 (5.56%)
Headache	1 (5.56%)
Lethargy	1 (5.56%)
Somnolence	1 (5.56%)

Psychiatric disorders	
Anxiety	2 (11.11%)
Confusional state	1 (5.56%)
Depression	1 (5.56%)
Sleep disorder	1 (5.56%)
Renal and urinary disorders	
Renal pain	1 (5.56%)
Reproductive system and breast disorders	
Nipple pain	1 (5.56%)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm	1 (5.56%)
Cough	1 (5.56%)
Dysphonia	1 (5.56%)
Dyspnoea	5 (27.78%)
Dyspnoea exertional	1 (5.56%)
Pleural effusion	2 (11.11%)
Productive cough	1 (5.56%)
Skin and subcutaneous tissue disorders	
Hyperhidrosis	1 (5.56%)
Pruritus	2 (11.11%)
Rash macular	1 (5.56%)

Vascular disorders	
Hypotension	1 (5.56%)

Other Relevant Findings

None

Conclusion:

No pharmacokinetic drug-drug interactions were observed between capmatinib and spartalizumab.

The capmatinib and spartalizumab combination was well tolerated, presented no new safety signals.

A preliminary efficacy assessment was made. The part 1 preliminary efficacy data of the combination of capmatinib and spartalizumab suggested a low probability of observing efficacy superiority to the control arm data with docetaxel in the planned part 2 randomized section of the trial. As a result, the trial was completed after part 1 and the part 2 randomized section of the study was not opened.

Date of Clinical Trial Report

19-Mar-2021