



Clinical trial results:

A phase Ib/II, open-label, multi-center study of INC280 in combination with PDR001 or PDR001 single agent in advanced hepatocellular carcinoma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-005417-76 |
| Trial protocol | DE IT |
| Global end of trial date | 24 June 2021 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v2 (current) |
| This version publication date | 12 August 2023 |
| First version publication date | 11 June 2022 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CINC280X2108 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02795429 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4056, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 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 | 24 June 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 June 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the trial were:

- Phase Ib part: To characterize the safety and tolerability of capmatinib in combination with spartalizumab and identify the maximum tolerated dose (MTD) and/or the recommended phase 2 dose (RP2D).
- Phase II part: To compare the efficacy of capmatinib in combination with spartalizumab vs. spartalizumab single agent.

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 | 15 June 2016 |
| 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 | China: 4 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | France: 19 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | Hong Kong: 15 |
| Country: Number of subjects enrolled | Italy: 25 |
| Country: Number of subjects enrolled | Korea, Republic of: 7 |
| Country: Number of subjects enrolled | Taiwan: 6 |
| Worldwide total number of subjects | 89 |
| EEA total number of subjects | 49 |

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) | 43 |
| From 65 to 84 years | 45 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in 18 investigative sites in 8 countries.

Pre-assignment

Screening details:

The screening period began once patients had signed the study informed consent. Screening evaluations were performed within 21 days prior to the first dose of study medication. After screening, the treatment period started on Cycle 1 Day 1.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W |

Arm description:

Capmatinib 200 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib

| | |
|--|-----------------------|
| 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 300 mg was administered via intravenous (i.v.) infusion once every 3 weeks (Q3W)

| | |
|--|------------|
| 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 200 mg was administered orally as a tablet twice daily (BID)

| | |
|------------------|--|
| Arm title | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W |
|------------------|--|

Arm description:

Capmatinib 300 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib

| | |
|--|--------------|
| Arm type | Experimental |
| 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 300 mg was administered orally as a tablet twice daily (BID)

| | |
|--|--|
| 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 300 mg was administered via intravenous (i.v.) infusion once every 3 weeks (Q3W) | |
| Arm title | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Arm description: | |
| Capmatinib 400 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| 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 300 mg was administered via intravenous (i.v.) infusion once every 3 weeks (Q3W) | |
| 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 was administered orally as a tablet twice daily (BID) | |
| Arm title | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Arm description: | |
| Capmatinib 400 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase II | |
| Arm type | Experimental |
| 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 was administered orally as a tablet twice daily (BID) | |
| 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 300 mg was administered via intravenous (i.v.) infusion once every 3 weeks (Q3W) | |
| Arm title | Phase II: Spartalizumab 300 mg Q3W |
| Arm description: | |
| Spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase II | |
| Arm type | Active comparator |

| | |
|--|-----------------------|
| 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 300 mg was administered via intravenous (i.v.) infusion once every 3 weeks (Q3W)

| Number of subjects in period 1 | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|---------------------------------------|--|---|--|
| Started | 6 | 10 | 11 |
| Completed | 0 | 0 | 0 |
| Not completed | 6 | 10 | 11 |
| Physician decision | - | - | 2 |
| Death | 1 | - | 1 |
| Adverse event | 1 | 2 | 1 |
| Progressive disease | 3 | 7 | 6 |
| Subject/guardian decision | 1 | 1 | 1 |

| Number of subjects in period 1 | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W |
|---------------------------------------|--|--|
| Started | 32 | 30 |
| Completed | 0 | 0 |
| Not completed | 32 | 30 |
| Physician decision | 1 | 5 |
| Death | 2 | 1 |
| Adverse event | 2 | 1 |
| Progressive disease | 26 | 20 |
| Subject/guardian decision | 1 | 3 |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 200 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| Reporting group title | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 300 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| Reporting group title | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 400 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| Reporting group title | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 400 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase II | |
| Reporting group title | Phase II: Spartalizumab 300 mg Q3W |
| Reporting group description: Spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase II | |

| Reporting group values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|---|--|---|--|
| Number of subjects | 6 | 10 | 11 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 2 | 6 | 5 |
| From 65-84 years | 4 | 4 | 6 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 68.5 | 63.2 | 64.6 |
| standard deviation | ± 7.42 | ± 10.24 | ± 8.99 |

| | | | |
|---|---|---|---|
| Sex: Female, Male Units: participants | | | |
| Female | 0 | 2 | 2 |
| Male | 6 | 8 | 9 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 3 | 3 | 4 |
| White | 3 | 7 | 6 |
| Unknown | 0 | 0 | 1 |

| Reporting group values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | Total |
|---|--|--|-------|
| Number of subjects | 32 | 30 | 89 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 15 | 15 | 43 |
| From 65-84 years | 16 | 15 | 45 |
| 85 years and over | 1 | 0 | 1 |
| Age Continuous Units: years | | | |
| arithmetic mean | 64.8 | 63.4 | |
| standard deviation | ± 10.02 | ± 9.97 | - |
| Sex: Female, Male Units: participants | | | |
| Female | 3 | 5 | 12 |
| Male | 29 | 25 | 77 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 12 | 12 | 34 |
| White | 10 | 10 | 36 |
| Unknown | 10 | 8 | 19 |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 200 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| Reporting group title | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 300 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| Reporting group title | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 400 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase Ib | |
| Reporting group title | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Reporting group description: Capmatinib 400 mg administered orally on a continuous twice daily (BID) dosing schedule in combination with spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase II | |
| Reporting group title | Phase II: Spartalizumab 300 mg Q3W |
| Reporting group description: Spartalizumab 300 mg administered intravenously once every 3 weeks (Q3W) in Phase II | |

Primary: Phase Ib: Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period

| | |
|--|---|
| End point title | Phase Ib: Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period ^{[1][2]} |
| End point description: Number of participants with AEs and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. The on-treatment period is defined from the day of first administration of study treatment up to 30 days after the date of its last administration. AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. For CTCAE v4.03, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE. | |
| End point type | Primary |
| End point timeframe: From first dose of study medication up to 30 days after last dose, with a maximum duration of 3.3 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 primary endpoint.

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 10 | 11 | |
| Units: participants | | | | |
| AEs | 6 | 10 | 10 | |
| Treatment-related AEs | 5 | 7 | 10 | |
| AEs with grade ≥ 3 | 6 | 7 | 7 | |
| Treatment-related AEs with grade ≥ 3 | 4 | 4 | 6 | |
| SAEs | 1 | 1 | 6 | |
| Treatment-related SAEs | 0 | 0 | 5 | |
| Fatal SAEs | 1 | 0 | 1 | |
| Treatment-related fatal SAEs | 0 | 0 | 1 | |
| AEs leading to discontinuation | 3 | 4 | 4 | |
| Treatment-related AEs leading to discontinuation | 2 | 1 | 4 | |
| AEs leading to dose adjustment/interruption | 3 | 6 | 7 | |
| AEs requiring additional therapy | 6 | 9 | 10 | |
| AE due to infusion reaction | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase Ib: Number of participants with Dose-Limiting Toxicities (DLTs) during the first 2 cycles of treatment

| | |
|-----------------|--|
| End point title | Phase Ib: Number of participants with Dose-Limiting Toxicities (DLTs) during the first 2 cycles of treatment ^{[3][4]} |
|-----------------|--|

End point description:

A dose-limiting toxicity (DLT) is defined as an adverse event or abnormal laboratory value of Common Terminology Criteria for Adverse Events (CTCAE) grade ≥ 3 assessed as unrelated to disease, disease progression, inter-current illness or concomitant medications that occurs within the first 2 cycles of treatment with capmatinib in combination with spartalizumab during the dose escalation part of the study. Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher. The duration of one treatment cycle is 21 days.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

42 days

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis were planned for this primary endpoint.

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 8 | 9 | |
| Units: participants | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase Ib: Number of participants with dose reductions and dose interruptions of capmatinib and spartalizumab

| | |
|-----------------|--|
| End point title | Phase Ib: Number of participants with dose reductions and dose interruptions of capmatinib and spartalizumab ^{[5][6]} |
|-----------------|--|

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.

No dose modifications (i.e. dose reduction) were allowed for spartalizumab.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose of study medication up to last dose, with a maximum duration of 3.2 years

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis were planned for this primary endpoint.

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|---------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 10 | 11 | |
| Units: participants | | | | |
| Capmatinib dose reduction | 2 | 4 | 8 | |
| Capmatinib dose interruption | 4 | 6 | 8 | |
| Spartalizumab dose reduction | 0 | 0 | 0 | |
| Spartalizumab dose interruption | 4 | 4 | 7 | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase Ib: Dose intensity of capmatinib

| | |
|-----------------|--|
| End point title | Phase Ib: Dose intensity of capmatinib ^{[7][8]} |
|-----------------|--|

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 | Primary |
|----------------|---------|

End point timeframe:

From first dose of study medication up to last dose, with a maximum duration of 3.2 years

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis were planned for this primary endpoint.

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 10 | 11 | |
| Units: mg/day | | | | |
| median (full range (min-max)) | 391.2 (294 to 400) | 580.0 (390 to 600) | 755.6 (371 to 800) | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase Ib: Dose intensity of spartalizumab

| | |
|-----------------|--|
| End point title | Phase Ib: Dose intensity of spartalizumab ^{[9][10]} |
|-----------------|--|

End point description:

Dose intensity of spartalizumab was calculated as actual cumulative dose in milligrams divided by duration of exposure in weeks and then multiplied by 3 weeks (3W).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose of study medication up to last dose, with a maximum duration of 3.2 years

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis were planned for this primary endpoint.

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 10 | 11 | |
| Units: mg/3W | | | | |

| | | | | |
|-------------------------------|-------------------------|-------------------------|-------------------------|--|
| median (full range (min-max)) | 293.18 (235.7 to 300.0) | 300.00 (225.0 to 300.0) | 300.00 (272.7 to 300.0) | |
|-------------------------------|-------------------------|-------------------------|-------------------------|--|

Statistical analyses

No statistical analyses for this end point

Primary: Phase II: Overall Response Rate (ORR) per RECIST v1.1

| | |
|-----------------|---|
| End point title | Phase II: Overall Response Rate (ORR) per RECIST v1.1 ^[11] |
|-----------------|---|

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 treatment, assessed up to 2.2 years

Notes:

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

Justification: This endpoint is only applicable to Phase II arms.

| End point values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 30 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 9.4 (2.0 to 25.0) | 10.0 (2.1 to 26.5) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | combination vs. single agent |
|----------------------------|------------------------------|

Statistical analysis description:

Posterior probability of Odds ratio [ORR(spartalizumab+capmatinib) to ORR(spartalizumab)] was ≥ 1

| | |
|---|---|
| Comparison groups | Phase II: Spartalizumab 300 mg Q3W v Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Number of subjects included in analysis | 62 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Bayesian Logistic Regression Model |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.561 |

| | |
|---------------------|------------|
| Confidence interval | |
| level | Other: 0 % |
| sides | 1-sided |
| upper limit | 999 |

Secondary: Phase Ib and Phase II: Best Overall Response (BOR) per RECIST v1.1

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Best Overall Response (BOR) per RECIST v1.1 |
|-----------------|--|

End point description:

BOR is defined as the best response recorded from the start of the study treatment until disease progression/recurrence, based on local investigator assessment per RECIST v1.1.

For RECIST v1.1, R=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 diameters of all target lesions, taking as reference the baseline sum of diameters; PD= At least a 20% increase in the sum of diameters of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition, the sum must also demonstrate an absolute increase of at least 5 mm; SD= Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progression).

The number of participants in each response category is reported in the table.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From start of treatment until end of treatment, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: participants | | | | |
| Complete Response (CR) | 0 | 0 | 0 | 0 |
| Partial Response (PR) | 2 | 0 | 2 | 3 |
| Stable Disease (SD) | 1 | 7 | 2 | 12 |
| Progressive Disease (PD) | 3 | 2 | 7 | 13 |
| Unknown | 0 | 1 | 0 | 4 |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: participants | | | | |
| Complete Response (CR) | 0 | | | |
| Partial Response (PR) | 3 | | | |
| Stable Disease (SD) | 9 | | | |
| Progressive Disease (PD) | 15 | | | |

| | | | | |
|---------|---|--|--|--|
| Unknown | 3 | | | |
|---------|---|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Best Overall Response (BOR) per irRC

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Best Overall Response (BOR) per irRC |
|-----------------|---|

End point description:

BOR is defined as the best response recorded from the start of the study treatment until disease progression/recurrence, based on local investigator assessment per Immune-related Response Criteria (irRC).

For irRC, irCR=Disappearance of all non-nodal target lesions and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; irPR= At least a 30% decrease in the sum of diameters of all target lesions including new measurable lesions, taking as reference the baseline sum of diameters; irPD= At least a 20% increase in the sum of diameters of all measured target lesions including new measurable lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition, the sum must also demonstrate an absolute increase of at least 5 mm; irSD= Neither sufficient shrinkage to qualify for irPR or irCR nor an increase in lesions which would qualify for irPD).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From start of treatment until end of treatment, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: participants | | | | |
| Immune-related Complete Response (irCR) | 0 | 0 | 0 | 0 |
| Immune-related Partial Response (irPR) | 2 | 0 | 3 | 4 |
| Immune-related Stable Disease (irSD) | 1 | 7 | 3 | 15 |
| Immune-related Progressive Disease (irPD) | 3 | 2 | 5 | 10 |
| Unknown | 0 | 1 | 0 | 3 |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: participants | | | | |

| | | | | |
|---|----|--|--|--|
| Immune-related Complete Response (irCR) | 0 | | | |
| Immune-related Partial Response (irPR) | 3 | | | |
| Immune-related Stable Disease (irSD) | 9 | | | |
| Immune-related Progressive Disease (irPD) | 14 | | | |
| Unknown | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Overall Response Rate (ORR) per RECIST v1.1

| | |
|-----------------|---|
| End point title | Phase Ib: Overall Response Rate (ORR) per RECIST v1.1 ^[12] |
|-----------------|---|

End point description:

Tumor response was based on local investigator assessment as per 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 | Secondary |
|----------------|-----------|

End point timeframe:

From start of treatment until end of treatment, assessed up to 3.2 years

Notes:

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 10 | 11 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 33.3 (4.3 to 77.7) | 0 (0.0 to 30.8) | 18.2 (2.3 to 51.8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Overall Response Rate (ORR) per irRC

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Overall Response Rate (ORR) per irRC |
|-----------------|---|

End point description:

Tumor response was based on local investigator assessment as per irRC. ORR per irRC is defined as the percentage of participants with a best overall response of immune related Complete Response (irCR) or immune related Partial Response (irPR).

For irRC, irCR=Disappearance of all non-nodal target lesions and non-target lesions. In addition, any

pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; irPR= At least a 30% decrease in the sum of diameters of all target lesions including new measurable lesions, taking as reference the baseline sum of diameters.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From start of treatment until end of treatment, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II | |

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 33.3 (4.3 to 77.7) | 0 (0.0 to 30.8) | 27.3 (6.0 to 61.0) | 12.5 (3.5 to 29.0) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 10.0 (2.1 to 26.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Duration of Response (DOR) per RECIST v1.1

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Duration of Response (DOR) per RECIST v1.1 |
|-----------------|---|

End point description:

DOR only applies to patients for whom best overall response is complete response (CR) or partial response (PR) based on local investigator assessment of overall lesion response according to RECIST v1.1. DOR is defined as the time from the date of first documented response (confirmed CR or confirmed PR) to the date of first documented disease progression or death due to any cause. If a patient not had an event, duration was censored at the date of last adequate tumor assessment before the start of a new anticancer therapy, if any.

According to the statistical analysis plan (SAP), summary estimates of DOR using the Kaplan-Meier method were planned to be reported if there were at least 10 patients achieving a confirmed CR or PR in each treatment group/arm.

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 first documented response to first documented disease progression or death due to any cause, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 0 ^[13] | 2 | 3 |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | (to) | 999 (999 to 999) | 999 (999 to 999) |

Notes:

[13] - No patients with CR or PR

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Duration of Response (DOR) per irRC

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Duration of Response (DOR) per irRC |
|-----------------|--|

End point description:

DOR only applies to patients for whom best overall response is immune-related complete response (irCR) or immune-related partial response (irPR) based on local investigator assessment of overall lesion response according to irRC. DOR is defined as the time from the date of first documented response (confirmed irCR or confirmed irPR) to the date of first documented disease progression or death due to any cause. If a patient not had an event, duration was censored at the date of last adequate tumor assessment before the start of a new anticancer therapy, if any. According to the SAP, summary estimates of DOR using the Kaplan-Meier method were planned to be reported if there were at least 10 patients achieving confirmed irCR or irPR in each treatment group. 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 first documented response to first documented disease progression or death due to any cause, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 0 ^[14] | 3 | 4 |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | (to) | 999 (999 to 999) | 999 (999 to 999) |

Notes:

[14] - No patients with CR or PR

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Time to Response (TTR) per RECIST v1.1

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Time to Response (TTR) per RECIST v1.1 |
|-----------------|---|

End point description:

TTR is defined as the time from the date of start of treatment to the date of first documented response (CR or PR, which must be confirmed subsequently) for patients who achieved a confirmed CR or PR. Tumor response was based on local investigator assessment per RECIST v1.1. Patients who did not achieve a confirmed CR or PR were censored at the maximum follow-up time for patients who had a PFS event (i.e. either progressed or died due to any cause), or at the date of last adequate tumor assessment before the start of a new anticancer therapy (if any) otherwise. According to the SAP, summary estimates of TTR using the Kaplan-Meier method were planned to be reported if there were at least 10 patients achieving confirmed CR or PR in each treatment group. 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 first documented response, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Time to Response (TTR) per irRC

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Time to Response (TTR) per irRC |
|-----------------|--|

End point description:

TTR is defined as the time from the date of start of treatment to the date of first documented response (irCR or irPR, which must be confirmed subsequently) for patients who achieved confirmed irCR or irPR. Tumor response was based on local investigator assessment per irRC.

Patients who did not achieve confirmed irCR or irPR were censored at the maximum follow-up time for patients who had a PFS event (i.e. either progressed or died due to any cause), or at the date of last adequate tumor assessment before the start of a new anticancer therapy (if any) otherwise.

According to the SAP, summary estimates of TTR using the Kaplan-Meier method were planned to be reported if there were at least 10 patients achieving confirmed irCR or irPR in each treatment group.

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 first documented response, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Progression-Free Survival (PFS) per RECIST v1.1

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Progression-Free Survival (PFS) per RECIST v1.1 |
|-----------------|--|

End point description:

PFS is defined as the time from the date of start of treatment to the date of the first documented progression per RECIST v1.1 or death due to any cause. If a patient did not experience an event or started a new anticancer therapy, PFS was censored at the date of the last adequate tumor evaluation before the start of a new anticancer therapy, if any. Tumor response was based on local investigator assessment per RECIST v1.1.

PFS was estimated using the Kaplan-Meier Method.

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 first documented progression or death due to any cause, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |

| | | | | |
|----------------------------------|--------------------|--------------------|----------------------|---------------------|
| median (confidence interval 95%) | 3.42 (1.18 to 999) | 4.44 (1.25 to 999) | 1.35 (1.22 to 13.73) | 2.79 (2.60 to 3.88) |
|----------------------------------|--------------------|--------------------|----------------------|---------------------|

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 2.79 (1.45 to 4.07) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Progression-Free Survival (PFS) per irRC

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Progression-Free Survival (PFS) per irRC |
|-----------------|---|

End point description:

PFS is defined as the time from the date of start of treatment to the date of the first documented and confirmed progression per irRC or death due to any cause. If a patient did not experience an event or started a new anticancer therapy, PFS was censored at the date of the last adequate tumor evaluation before the start of a new anticancer therapy, if any. Tumor response was based on local investigator assessment per irRC.

PFS was estimated using the Kaplan-Meier Method.

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 first documented progression or death due to any cause, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |
| median (confidence interval 95%) | 3.42 (1.18 to 999) | 4.44 (1.68 to 999) | 5.55 (1.25 to 999) | 3.06 (2.63 to 4.17) |

| | | | | |
|-------------------------|----------------------------|--|--|--|
| End point values | Phase II: Spartalizumab | | | |
|-------------------------|----------------------------|--|--|--|

| | | | | |
|----------------------------------|---------------------|--|--|--|
| | 300 mg Q3W | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 2.79 (1.61 to 5.75) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Time to Progression (TTP) per RECIST v1.1

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Time to Progression (TTP) per RECIST v1.1 |
|-----------------|--|

End point description:

TTP is defined as the time from the date of start of treatment to the date of the first documented progression per RECIST v1.1 or death due to underlying cancer. If a patient did not experience an event or started a new anticancer therapy, TTP was censored at the date of the last adequate tumor evaluation before the start of a new anticancer therapy, if any. Tumor response was based on local investigator assessment per RECIST v1.1.

TTP was estimated using the Kaplan-Meier Method.

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 first documented progression or death due to underlying cancer, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |
| median (confidence interval 95%) | 3.42 (1.18 to 999) | 4.44 (1.25 to 999) | 1.35 (1.22 to 999) | 2.79 (2.60 to 3.88) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 2.79 (1.45 to 4.07) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Time to Progression (TTP) per irRC

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Time to Progression (TTP) per irRC |
|-----------------|---|

End point description:

TTP is defined as the time from the date of start of treatment to the date of the first documented and confirmed progression per irRC or death due to underlying cancer. If a patient did not experience an event or started a new anticancer therapy, TTP was censored at the date of the last adequate tumor evaluation before the start of a new anticancer therapy, if any. Tumor response was based on local investigator assessment per irRC.

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 first documented progression or death due to underlying cancer, assessed up to 3.2 years in Phase Ib and up to 2.2 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |
| median (confidence interval 95%) | 3.42 (1.18 to 999) | 4.44 (1.68 to 999) | 5.55 (1.25 to 999) | 3.06 (2.63 to 4.17) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 2.79 (1.61 to 5.75) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Overall Survival (OS)

| | |
|--|--|
| End point title | Phase Ib and Phase II: 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. If a patient was not known to have died, OS time was censored at the date of last contact. OS was estimated using the Kaplan-Meier Method. 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 death due to any cause, assessed up to 3.6 years in Phase Ib and up to 2.9 years in Phase II | |

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: months | | | | |
| median (confidence interval 95%) | 14.98 (2.37 to 999) | 12.11 (1.68 to 19.45) | 16.53 (2.83 to 999) | 14.88 (9.00 to 19.48) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9.78 (3.65 to 22.31) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period

| | |
|---|---|
| End point title | Phase II: Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period ^[15] |
| End point description: Number of participants with AEs and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. The on-treatment period is defined from the day of first administration of study treatment up to 30 days | |

after the date of its last administration.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. For CTCAE v4.03, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose of study medication up to 30 days after last dose, with a maximum duration of 2.3 years

Notes:

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

Justification: This endpoint is only applicable to Phase II arms.

| End point values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 30 | | |
| Units: participants | | | | |
| AEs | 32 | 30 | | |
| Treatment-related AEs | 30 | 18 | | |
| AEs with grade ≥ 3 | 25 | 15 | | |
| Treatment-related AEs with grade ≥ 3 | 18 | 3 | | |
| SAEs | 14 | 10 | | |
| Treatment-related SAEs | 7 | 1 | | |
| Fatal SAEs | 1 | 1 | | |
| AEs leading to discontinuation | 10 | 1 | | |
| Treatment-related AEs leading to discontinuation | 7 | 0 | | |
| AEs leading to dose adjustment/interruption | 22 | 11 | | |
| AEs requiring additional therapy | 30 | 29 | | |
| AE due to infusion reaction | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Number of participants with dose reductions and dose interruptions of capmatinib and spartalizumab

| | |
|-----------------|--|
| End point title | Phase II: Number of participants with dose reductions and dose interruptions of capmatinib and spartalizumab ^[16] |
|-----------------|--|

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.

No dose modifications (i.e. dose reduction) were allowed for spartalizumab.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose of study medication up to last dose, with a maximum duration of 2.2 years

Notes:

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

Justification: This endpoint is only applicable to Phase II arms.

| End point values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | | |
|---------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 30 | | |
| Units: participants | | | | |
| Capmatinib dose reduction | 18 | 999 | | |
| Capmatinib dose interruption | 22 | 999 | | |
| Spartalizumab dose reduction | 0 | 0 | | |
| Spartalizumab dose interruption | 12 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Dose intensity of capmatinib

| | |
|--|--|
| End point title | Phase II: Dose intensity of capmatinib ^[17] |
| 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 study medication up to last dose, with a maximum duration of 2.2 years | |

Notes:

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

Justification: This endpoint is only applicable to Phase II arms.

| End point values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 0 ^[18] | | |
| Units: mg/day | | | | |
| median (full range (min-max)) | 696.4 (167 to 800) | (to) | | |

Notes:

[18] - Patients did not receive capmatinib

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Dose intensity of spartalizumab

| | |
|---|---|
| End point title | Phase II: Dose intensity of spartalizumab ^[19] |
| End point description: Dose intensity of spartalizumab was calculated as actual cumulative dose in milligrams divided by duration of exposure in weeks and then multiplied by 3 weeks (3W). | |
| End point type | Secondary |
| End point timeframe: From first dose of study medication up to last dose, with a maximum duration of 2.2 years | |
| Notes: [19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable to Phase II arms. | |

| End point values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 30 | | |
| Units: mg/3W | | | | |
| median (full range (min-max)) | 300.00 (200.0 to 300.0) | 300.00 (166.7 to 300.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Maximum observed plasma concentration (Cmax) of capmatinib

| | |
|---|--|
| End point title | Phase Ib: Maximum observed plasma concentration (Cmax) of capmatinib ^[20] |
| 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, 0.5, 1, 2, 4 and 8 hours post capmatinib dose on Cycle 2 Day 1 (C2D1). The duration of one cycle was 21 days. | |
| Notes: [20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable to Phase 1b arms. | |

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 5 | 7 | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 1680 (\pm 64.0) | 3110 (\pm 61.2) | 4980 (\pm 23.0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib: Time to reach maximum plasma concentration (Tmax) of capmatinib

| | |
|-----------------|---|
| End point title | Phase Ib: Time to reach maximum plasma concentration (Tmax) of capmatinib ^[21] |
|-----------------|---|

End point description:

Pharmacokinetic (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, 0.5, 1, 2, 4 and 8 hours post capmatinib dose on Cycle 2 Day 1 (C2D1). The duration of one cycle was 21 days.

Notes:

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 5 | 7 | |
| Units: hours | | | | |
| median (full range (min-max)) | 0.959 (0.567 to 1.00) | 1.00 (1.00 to 2.05) | 1.00 (1.00 to 4.22) | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Phase Ib: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration |
|-----------------|--|

End point description:

Pharmacokinetic (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, 0.5, 1, 2, 4 and 8 hours post capmatinib dose on Cycle 2 Day 1 (C2D1). The duration of one cycle was 21 days.

Notes:

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

Justification: This endpoint is only applicable to Phase 1b arms.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 5 | 7 | |
| Units: hours*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 5740 (\pm 51.6) | 8570 (\pm 60.7) | 16000 (\pm 30.6) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Pre-dose plasma concentration of capmatinib

End point title

Phase II: Pre-dose plasma concentration of capmatinib^[23]

End point description:

Capmatinib plasma concentration was assessed in samples taken at pre-dose. Pre-dose samples were collected before the next dose administration.

End point type

Secondary

End point timeframe:

Pre-dose of capmatinib on Cycle 2 Day 1, Cycle 3 Day 1, Cycle 4 Day 1, Cycle 5 Day 1 and Cycle 6 Day 1. The duration of one cycle was 21 days.

Notes:

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

Justification: This endpoint is only applicable to Phase II arms.

| End point values | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Spartalizumab 300 mg Q3W | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 0 ^[24] | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 2 Day 1 (n=16,0) | 607 (\pm 99.4) | () | | |

| | | | | |
|------------------------|--------------|-----|--|--|
| Cycle 3 Day 1 (n=16,0) | 345 (± 110) | () | | |
| Cycle 4 Day 1 (n=16,0) | 410 (± 132) | () | | |
| Cycle 5 Day 1 (n=10,0) | 363 (± 68.6) | () | | |
| Cycle 6 Day 1 (n=11,0) | 275 (± 102) | () | | |

Notes:

[24] - Patients did not receive capmatinib

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Maximum observed serum concentration (Cmax) of spartalizumab

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: 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-dose, 1, 24, 48, 72, 168, 240, 336 and 504 hours after completion of spartalizumab infusion on Cycle 1 and Cycle 3. The duration of one cycle was 21 days.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 (n=6,9,11,32,30) | 75.7 (± 22.6) | 77.2 (± 20.9) | 84.7 (± 23.3) | 81.7 (± 30.1) |
| Cycle 3 (n=5,8,7,27,21) | 105 (± 35.8) | 101 (± 22.3) | 128 (± 20.9) | 115 (± 30.2) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|---|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 (n=6,9,11,32,30) | 72.8 (± 30.9) | | | |
| Cycle 3 (n=5,8,7,27,21) | 101 (± 42.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Time to reach maximum serum concentration (Tmax) of spartalizumab

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Time to reach maximum serum concentration (Tmax) of spartalizumab |
|-----------------|--|

End point description:

Pharmacokinetic (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-dose, 1, 24, 48, 72, 168, 240, 336 and 504 hours after completion of spartalizumab infusion on Cycle 1 and Cycle 3. The duration of one cycle was 21 days.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 (n=6,9,11,32,30) | 1.51 (1.42 to 1.77) | 1.50 (0.583 to 1.67) | 1.50 (1.18 to 1.73) | 1.64 (0.917 to 581) |
| Cycle 3 (n=5,8,7,27,21) | 1.53 (1.50 to 1.60) | 1.47 (1.42 to 22.6) | 1.52 (1.45 to 1.92) | 1.75 (0.00 to 24.2) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 (n=6,9,11,32,30) | 1.59 (0.633 to 22.9) | | | |
| Cycle 3 (n=5,8,7,27,21) | 1.58 (1.33 to 22.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab |
|-----------------|---|

End point description:

Pharmacokinetic (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-dose, 1, 24, 48, 72, 168, 240, 336 and 504 hours after completion of spartalizumab infusion on Cycle 1 and Cycle 3. The duration of one cycle was 21 days.

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 10 | 11 | 32 |
| Units: day*µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 (n=6,9,11,32,30) | 739 (± 24.7) | 726 (± 20.9) | 813 (± 19.4) | 805 (± 33.4) |
| Cycle 3 (n=5,8,7,27,21) | 1280 (± 39.2) | 1220 (± 25.5) | 1630 (± 23.2) | 1330 (± 41.6) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|---|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: day*µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 (n=6,9,11,32,30) | 693 (± 35.3) | | | |
| Cycle 3 (n=5,8,7,27,21) | 883 (± 79.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: Percent marker area for CD8 expression in tumor samples

| | |
|-----------------|--|
| End point title | Phase Ib and Phase II: Percent marker area for CD8 expression in tumor samples |
|-----------------|--|

End point description:

The expression of CD8 was measured in tumor samples by immunohistochemical methods. This record summarizes the percent marker area for CD8 expression in tumor samples.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (screening) and post-baseline (assessed throughout the treatment up to maximum 115 days).

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|--------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 9 | 8 | 22 |
| Units: CD8 percent marker area | | | | |
| median (full range (min-max)) | | | | |
| Baseline (n=4,7,7,19,19) | 0.6 (0 to 1) | 0.9 (0 to 37) | 0.4 (0 to 3) | 0.5 (0 to 5) |
| Post-baseline (n=1,8,3,10,12) | 3.0 (3 to 3) | 2.6 (0 to 14) | 1.0 (0 to 1) | 1.3 (0 to 7) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|--------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 23 | | | |
| Units: CD8 percent marker area | | | | |
| median (full range (min-max)) | | | | |
| Baseline (n=4,7,7,19,19) | 0.3 (0 to 27) | | | |
| Post-baseline (n=1,8,3,10,12) | 0.9 (0 to 21) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase Ib and Phase II: PD-L1 percent positive tumor

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: PD-L1 percent positive tumor |
|-----------------|---|

End point description:

The expression of programmed cell death-ligand 1 (PD-L1) was measured in tumor samples by immunohistochemical methods. This record summarizes the PD-L1 positivity percentage in tumor samples.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (screening) and post-baseline (assessed throughout the treatment up to maximum 115 days).

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 10 | 8 | 26 |
| Units: PD-L1 positivity percentage | | | | |
| median (full range (min-max)) | | | | |
| Baseline (n=4,8,7,21,22) | 0.0 (0 to 5) | 0.0 (0 to 90) | 0.0 (0 to 2) | 0.0 (0 to 7) |
| Post-baseline (n=2,8,3,10,10) | 12.5 (0 to 25) | 0.0 (0 to 100) | 0.0 (0 to 5) | 0.0 (0 to 3) |

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|------------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 24 | | | |
| Units: PD-L1 positivity percentage | | | | |
| median (full range (min-max)) | | | | |
| Baseline (n=4,8,7,21,22) | 0.0 (0 to 3) | | | |
| Post-baseline (n=2,8,3,10,10) | 0.0 (0 to 5) | | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Phase Ib and Phase II: All-Collected Deaths

| | |
|-----------------|---|
| End point title | Phase Ib and Phase II: All-Collected Deaths |
|-----------------|---|

End point description:

On-treatment and post-treatment safety follow-up deaths were collected from first dose of study medication to 150 days after the last dose of study medication, for a maximum duration of 3.6 years in Phase Ib and 2.6 years in Phase II.

Post-treatment survival follow-up deaths were collected from day 151 after last dose of study medication to end of study, up to 3.6 years in Phase Ib and 2.9 years in Phase II.

All deaths refer to the sum of on-treatment and post-treatment safety follow-up deaths plus post-

treatment survival follow-up deaths.

| | |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

On-treatment and post-treatment safety follow-up deaths: up to 3.6 years in Phase Ib and 2.6 years in Phase II. Post treatment survival follow-up deaths: up to 3.6 years in Phase Ib and 2.9 years in Phase II

| End point values | Phase Ib: Capmatinib 200 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 300 mg BID + Spartalizumab 300 mg Q3W | Phase Ib: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W | Phase II: Capmatinib 400 mg BID + Spartalizumab 300 mg Q3W |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 ^[25] | 10 ^[26] | 11 ^[27] | 32 ^[28] |
| Units: participants | | | | |
| On-treatment and post-treatment safety FU deaths | 3 | 3 | 4 | 8 |
| Post-treatment survival FU deaths | 3 | 5 | 4 | 15 |
| All deaths | 6 | 8 | 8 | 23 |

Notes:

[25] - n= 6 (on-treatment and safety FU), 3 (survival), 6 (all)

[26] - n= 10 (on-treatment and safety FU), 7 (survival), 10 (all)

[27] - n= 11 (on-treatment and safety FU), 7 (survival), 11 (all)

[28] - n= 32 (on-treatment and safety FU), 24 (survival), 32 (all)

| End point values | Phase II: Spartalizumab 300 mg Q3W | | | |
|---|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 ^[29] | | | |
| Units: participants | | | | |
| On-treatment and post-treatment safety FU deaths | 13 | | | |
| Post-treatment survival FU deaths | 10 | | | |
| All deaths | 23 | | | |

Notes:

[29] - n= 30 (on-treatment and safety FU), 17 (survival), 30 (all)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3.6 years in Phase Ib and 2.6 years in Phase II.

AEs were collected from first dose to 150 days after last dose (on-treatment and post-treatment safety FU).

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.

Deaths in the survival FU are not considered AEs.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Ib: Capmatinib 200mg BID + Spartalizumab 300mg Q3W-Safety FU |
|-----------------------|--|

Reporting group description:

AEs during on-treatment period and post-treatment safety follow-up (FU) (up to 150 days post-treatment)

| | |
|-----------------------|---------------------------------------|
| Reporting group title | II: Spartalizumab 300mg Q3W-Safety FU |
|-----------------------|---------------------------------------|

Reporting group description:

AEs during on-treatment period and post-treatment safety follow-up (FU) (up to 150 days post-treatment)

| | |
|-----------------------|--|
| Reporting group title | II: Capmatinib 400mg BID + Spartalizumab 300mg Q3W-Safety FU |
|-----------------------|--|

Reporting group description:

AEs during on-treatment period and post-treatment safety follow-up (up to 150 days post-treatment)

| | |
|-----------------------|--|
| Reporting group title | Ib: Capmatinib 300mg BID + Spartalizumab 300mg Q3W-Safety FU |
|-----------------------|--|

Reporting group description:

AEs during on-treatment period and post-treatment safety follow-up (up to 150 days post-treatment)

| | |
|-----------------------|--|
| Reporting group title | Ib: Capmatinib 400mg BID + Spartalizumab 300mg Q3W-Safety FU |
|-----------------------|--|

Reporting group description:

AEs during on-treatment period and post-treatment safety follow-up (up to 150 days post-treatment)

| Serious adverse events | Ib: Capmatinib 200mg BID + Spartalizumab 300mg Q3W-Safety FU | II: Spartalizumab 300mg Q3W-Safety FU | II: Capmatinib 400mg BID + Spartalizumab 300mg Q3W-Safety FU |
|--|--|---------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 12 / 30 (40.00%) | 14 / 32 (43.75%) |
| number of deaths (all causes) | 3 | 13 | 8 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|----------------|----------------|----------------|
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 30 (6.67%) | 3 / 32 (9.38%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| 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 | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 30 (6.67%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood corticotrophin decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test abnormal | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Injury, poisoning and procedural complications | | | |
| Post procedural fever | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 5 / 32 (15.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoperitoneum | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal varices haemorrhage | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Hepatobiliary disorders | | | |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Hepatorenal syndrome | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Renal and urinary disorders | | | |

| | | | |
|---|---------------|----------------|----------------|
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|----------------|----------------|
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (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 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Ib: Capmatinib 300mg BID + Spartalizumab 300mg Q3W-Safety FU | Ib: Capmatinib 400mg BID + Spartalizumab 300mg Q3W-Safety FU | |
|--|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 6 / 11 (54.55%) | |
| number of deaths (all causes) | 3 | 4 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood corticotrophin decreased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Post procedural fever | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Nervous system disorders | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoperitoneum | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatorenal syndrome | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertransaminaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |

| | | | |
|---|-----------------|-----------------|--|
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Ib: Capmatinib 200mg BID + Spartalizumab 300mg Q3W-Safety FU | II: Spartalizumab 300mg Q3W-Safety FU | II: Capmatinib 400mg BID + Spartalizumab 300mg Q3W-Safety FU |
|--|---|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 6 / 6 (100.00%) | 30 / 30 (100.00%) | 32 / 32 (100.00%) |
| Vascular disorders | | | |
| Hot flush subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematoma subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypertension subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypotension subjects affected / exposed | 2 / 6 (33.33%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 2 | 0 | 2 |
| General disorders and administration site conditions | | | |
| Chills subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 5 / 32 (15.63%) |
| occurrences (all) | 0 | 0 | 8 |
| Asthenia subjects affected / exposed | 2 / 6 (33.33%) | 10 / 30 (33.33%) | 14 / 32 (43.75%) |
| occurrences (all) | 2 | 11 | 30 |
| Fatigue subjects affected / exposed | 2 / 6 (33.33%) | 2 / 30 (6.67%) | 4 / 32 (12.50%) |
| occurrences (all) | 2 | 3 | 4 |
| Malaise subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 1 | 1 |

| | | | |
|---|----------------|-----------------|------------------|
| Nodule | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 6 / 30 (20.00%) | 15 / 32 (46.88%) |
| occurrences (all) | 7 | 7 | 26 |
| Oedema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 30 (6.67%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 2 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 5 / 30 (16.67%) | 14 / 32 (43.75%) |
| occurrences (all) | 4 | 6 | 28 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 30 (6.67%) | 5 / 32 (15.63%) |
| occurrences (all) | 0 | 8 | 7 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 4 / 32 (12.50%) |
| occurrences (all) | 0 | 2 | 5 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 0 | 1 |
| Oropharyngeal pain | | | |

| | | | |
|--------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 0 | 1 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 4 / 30 (13.33%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 4 | 5 |
| Irritability | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 6 / 30 (20.00%) | 4 / 32 (12.50%) |
| occurrences (all) | 3 | 7 | 5 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 4 / 32 (12.50%) |
| occurrences (all) | 0 | 2 | 4 |
| Aspartate aminotransferase increased | | | |

| | | | |
|--------------------------------------|----------------|------------------|-----------------|
| subjects affected / exposed | 3 / 6 (50.00%) | 10 / 30 (33.33%) | 7 / 32 (21.88%) |
| occurrences (all) | 3 | 11 | 9 |
| Bilirubin conjugated increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 3 | 6 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 4 / 30 (13.33%) | 3 / 32 (9.38%) |
| occurrences (all) | 2 | 6 | 3 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 4 / 30 (13.33%) | 8 / 32 (25.00%) |
| occurrences (all) | 2 | 5 | 9 |
| Creatinine renal clearance decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 0 / 30 (0.00%) | 5 / 32 (15.63%) |
| occurrences (all) | 4 | 0 | 8 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 6 / 32 (18.75%) |
| occurrences (all) | 0 | 1 | 7 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 2 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 2 / 32 (6.25%) |
| occurrences (all) | 1 | 1 | 2 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |

| | | | |
|---|--|---|---|
| subjects affected / exposed occurrences (all) | 2 / 6 (33.33%) 2 | 1 / 30 (3.33%) 1 | 2 / 32 (6.25%) 3 |
| Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 30 (10.00%) 3 | 1 / 32 (3.13%) 1 |
| Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all) Angina unstable subjects affected / exposed occurrences (all) Atrioventricular block first degree subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Cerebral ischaemia subjects affected / exposed occurrences (all) Dysaesthesia subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Neuralgia subjects affected / exposed occurrences (all) Serotonin syndrome | 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 3 / 30 (10.00%) 3 0 / 30 (0.00%) 0 | 3 / 32 (9.38%) 3 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 2 / 32 (6.25%) 2 5 / 32 (15.63%) 7 0 / 32 (0.00%) 0 |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 2 / 32 (6.25%) 3 |
| Blood and lymphatic system disorders | | | |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 3 / 30 (10.00%) 5 | 4 / 32 (12.50%) 4 |
| Neutropenia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 2 | 1 / 30 (3.33%) 1 | 2 / 32 (6.25%) 2 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 1 / 30 (3.33%) 2 | 3 / 32 (9.38%) 4 |
| Ear and labyrinth disorders | | | |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 32 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Dry eye subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Diplopia | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 2 / 32 (6.25%) 3 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 5 / 30 (16.67%) | 7 / 32 (21.88%) |
| occurrences (all) | 1 | 5 | 9 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 30 (10.00%) | 4 / 32 (12.50%) |
| occurrences (all) | 1 | 3 | 5 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 30 (10.00%) | 5 / 32 (15.63%) |
| occurrences (all) | 1 | 3 | 6 |
| Anal fissure | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aptyalism | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 5 / 30 (16.67%) | 7 / 32 (21.88%) |
| occurrences (all) | 1 | 5 | 9 |
| Chapped lips | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 30 (10.00%) | 4 / 32 (12.50%) |
| occurrences (all) | 1 | 4 | 5 |

| | | | |
|----------------------------------|----------------|-----------------|------------------|
| Dry mouth | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 6 / 30 (20.00%) | 10 / 32 (31.25%) |
| occurrences (all) | 2 | 10 | 25 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 4 / 30 (13.33%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 5 | 3 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 0 | 3 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 1 |
| Nausea | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 2 / 30 (6.67%) | 15 / 32 (46.88%) |
| occurrences (all) | 3 | 2 | 26 |
| Plicated tongue | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 30 (6.67%) | 2 / 32 (6.25%) |
| occurrences (all) | 1 | 2 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 30 (3.33%) | 9 / 32 (28.13%) |
| occurrences (all) | 3 | 1 | 17 |
| Toothache | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Liver injury | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blister | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Dry skin | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences (all) | 2 | 1 | 1 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lichen planus | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 3 / 6 (50.00%) 4 | 8 / 30 (26.67%) 9 | 4 / 32 (12.50%) 7 |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 2 | 4 / 30 (13.33%) 6 | 4 / 32 (12.50%) 5 |
| Psoriasis | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 2 / 30 (6.67%) 3 | 0 / 32 (0.00%) 0 |
| Rash erythematous | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 3 / 32 (9.38%) 3 |
| Rash pruritic | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 30 (3.33%) 2 | 2 / 32 (6.25%) 2 |
| Skin ulcer | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 32 (3.13%) 1 |
| Stasis dermatitis | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Lichenoid keratosis | | | |
| subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 32 (3.13%) 1 |
| Dysuria | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Pollakiuria | | | |
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 32 (0.00%) 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 1 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 30 (10.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 3 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 30 (10.00%) | 5 / 32 (15.63%) |
| occurrences (all) | 1 | 10 | 6 |
| Back pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 30 (10.00%) | 3 / 32 (9.38%) |
| occurrences (all) | 1 | 4 | 3 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 1 | 2 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 3 / 32 (9.38%) |
| occurrences (all) | 1 | 1 | 4 |
| Musculoskeletal pain | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 30 (6.67%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 2 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 0 | 1 |
| Infections and infestations | | | |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 1 | 2 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 1 | 3 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|------------------------------------|----------------|-----------------|------------------|
| Paronychia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 30 (10.00%) | 15 / 32 (46.88%) |
| occurrences (all) | 0 | 4 | 18 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 30 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 2 / 32 (6.25%) |
| occurrences (all) | 1 | 1 | 2 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 4 / 30 (13.33%) | 9 / 32 (28.13%) |
| occurrences (all) | 2 | 4 | 12 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 30 (6.67%) | 3 / 32 (9.38%) |
| occurrences (all) | 0 | 2 | 4 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 30 (3.33%) | 4 / 32 (12.50%) |
| occurrences (all) | 1 | 1 | 6 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 30 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 0 | 2 |
| Hypophosphataemia | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 30 (3.33%) | 2 / 32 (6.25%) |
| occurrences (all) | 0 | 1 | 2 |

| Non-serious adverse events | Ib: Capmatinib 300mg BID + Spartalizumab 300mg Q3W-Safety FU | Ib: Capmatinib 400mg BID + Spartalizumab 300mg Q3W-Safety FU | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | 10 / 11 (90.91%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 0 | 2 | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 0 | 2 | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 4 / 11 (36.36%) | |
| occurrences (all) | 3 | 4 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Influenza like illness | | | |

| | | | |
|--|-----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 0 / 11 (0.00%) 0 | |
| Nodule subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 11 (0.00%) 0 | |
| Non-cardiac chest pain subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 2 | 1 / 11 (9.09%) 1 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 6 / 10 (60.00%) 12 | 6 / 11 (54.55%) 7 | |
| Oedema subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Pain subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 11 (0.00%) 0 | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 4 / 11 (36.36%) 8 | |
| Immune system disorders Anaphylactic reaction subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 6 | |
| Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Cough subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 1 / 11 (9.09%) 2 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 3 / 11 (27.27%) 4 | |
| Dyspnoea exertional | | | |

| | | | |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 0 | 3 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 1 | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 2 | |
| Irritability | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 5 / 11 (45.45%) | |
| occurrences (all) | 3 | 6 | |
| Amylase increased | | | |

| | | |
|--------------------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 10 |
| Aspartate aminotransferase increased | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 4 | 3 |
| Bilirubin conjugated increased | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 |
| Blood alkaline phosphatase increased | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 |
| Blood bilirubin increased | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 3 | 2 |
| Creatinine renal clearance decreased | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 |
| Blood creatinine increased | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 3 | 8 |
| Electrocardiogram QT prolonged | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 |
| Lipase increased | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 12 |
| Lymphocyte count decreased | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 |
| Neutrophil count decreased | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 |
| Platelet count decreased | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 2 |

| | | | |
|---|----------------------|----------------------|--|
| Weight increased subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 0 / 11 (0.00%) 0 | |
| Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Angina unstable subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Atrioventricular block first degree subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 11 (18.18%) 2 | |
| Cerebral ischaemia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Dysaesthesia subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 11 (0.00%) 0 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 11 (18.18%) 3 | |
| Headache subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 0 / 11 (0.00%) 0 | |

| | | | |
|--------------------------------------|-----------------|----------------|--|
| Neuralgia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Serotonin syndrome | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Dry eye | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 1 | 5 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 0 | 2 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 3 | 2 | |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal tenderness | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Aphthous ulcer | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Aptyalism | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Ascites | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|----------------------------------|-----------------|-----------------|--|
| Constipation | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 4 | 15 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 0 | 2 | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 3 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 5 / 11 (45.45%) | |
| occurrences (all) | 3 | 9 | |
| Plicated tongue | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 4 / 10 (40.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 1 | 4 | |
| Toothache | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Liver injury | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Blister | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Erythema | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Eczema | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Lichen planus | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Palmar-plantar erythrodysesthesia syndrome | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 4 / 11 (36.36%) | |
| occurrences (all) | 3 | 5 | |
| Rash | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 3 | 4 | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 2 | |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 1 | |
| Stasis dermatitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lichenoid keratosis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|--|----------------------|---------------------|--|
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Endocrine disorders | | | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Adrenal insufficiency subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 2 | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 10 (30.00%) 3 | 0 / 11 (0.00%) 0 | |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 0 / 11 (0.00%) 0 | |
| Joint swelling subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 11 (9.09%) 1 | |
| Lumbar spinal stenosis subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 11 (0.00%) 0 | |
| Muscular weakness subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 11 (0.00%) 0 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 2 | 0 / 11 (0.00%) 0 | |
| Myalgia | | | |

| | | | |
|-----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 1 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 0 | 2 | |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 2 | |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 1 | |

| | | | |
|------------------------------------|-----------------|-----------------|--|
| Pneumonia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 11 (18.18%) | |
| occurrences (all) | 0 | 3 | |
| Paronychia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 3 | 3 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 3 / 11 (27.27%) | |
| occurrences (all) | 5 | 3 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Hyponatraemia | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 11 (9.09%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 27 June 2016 | <p>Based on Health Authority requests, the following changes were implemented:</p> <ul style="list-style-type: none">• Subjects who refused sorafenib treatment were excluded from the subject population to be enrolled in this study. To be eligible, subjects should have received prior systemic sorafenib treatment for HCC with documented progression during or after discontinuation of sorafenib treatment, or were intolerant to sorafenib (that led to sorafenib discontinuation).• A mandatory HIV test was introduced at screening. Considering the limited clinical experience with PD-1 inhibitors in HIV positive subjects, to reduce the potential risk of virus reactivation, HIV testing was mandated and HIV positive subjects were excluded from the study.• Thrombocytopenia CTCAE grade 3 with clinically significant bleeding was listed as DLT, as well as nausea/vomiting grade 4 (regardless of anti-emetic treatment) and diarrhea grade 4 (regardless of anti-diarrheal treatment).• Enrollment of subjects potentially eligible for any loco regional liver treatment (e.g. hepatic resection, hepatic arterial embolization, radiofrequency ablation) was not allowed.• History of organ transplant was added as an additional exclusion criterion. Limited data were reported for the efficacy and toxicity, such as organ rejection, of immune checkpoints including PD-1 inhibitors in subjects with organ transplant, therefore considering the risk, subjects with a history of organ transplant were excluded from the study. |
| 07 November 2017 | <p>The main purpose for this amendment was threefold. The first was to reduce the focus on the cMET high population; the second was to expand the eligible clinical population to include subjects with HCV, and subjects with mild ascites; and the third to introduce additional biomarker collections based on emerging PD data.</p> |
| 27 March 2018 | <p>The main purpose of this amendment was to update the exclusion criteria, the list of prohibited medications, the list of medications used with caution and the criteria for dose modifications based on the available capmatinib clinical data as per capmatinib Investigator's Brochure edition 8 with primary focus on pneumonitis/ILD events that were reported with capmatinib.</p> |
| 14 September 2018 | <p>The primary purpose of this amendment was to incorporate health authority-requested language requiring study treatment discontinuation in the event of Stevens-Johnson syndrome/ Toxic epidermal necrolysis (SJS/TEN). After the occurrence of a case of SJS in a study with spartalizumab in combination with another investigational agent, the dose modification guidelines for protocols using spartalizumab were updated to mandate permanent discontinuation of study treatment for subjects who experienced SJS or Lyell syndrome/TEN. This change was already implemented as part of an urgent safety measure released on 15-Jun-2018. This protocol amendment was now formalizing these changes in the dose modification section and corresponding table describing the criteria for dose reduction/interruption and re-initiation of treatment for adverse drug reactions. In addition, based on a health authority request, subjects with indolent malignancies that have never required therapy were no longer considered eligible for this study. Exclusion criterion 'Malignant disease, other than that being treated in this study. Exceptions to this exclusion included the following: malignancies that were treated curatively and have not recurred within 2 years prior to study treatment; completely resected basal cell and squamous cell skin cancers; any malignancy considered to be indolent and that has never required therapy; and completely resected carcinoma in situ of any type' was updated accordingly.</p> |

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| 14 February 2020 | <p>The primary purpose of this amendment was to incorporate dose modification and management guidelines for myocarditis, as well as the option for subjects to be transferred to another study or an alternative treatment option to continue study treatment at the time of end of this study.</p> <p>After the occurrence of a case of myocarditis, the dose modification guidelines for protocols using capmatinib in combination with spartalizumab were updated to mandate permanent discontinuation of study treatment in case of myocarditis grade ≥ 2 or other cardiac event grade ≥ 3. In addition, recommended clinical management guidelines in case of such an event were provided.</p> <p>This protocol amendment revised the definition of end of study to include the option for subjects still on study treatment and who, in the opinion of the Investigator, were still deriving clinical benefit at the time of end of study, to transfer to another study or to an alternative treatment option to continue providing study treatment to these subjects.</p> |
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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.

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| <p>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 for complete trial results.</p> |
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Notes: