# Clinical trial results:
# FORWARD 1: A Randomized, Open-label Phase 3 Study to Evaluate the Safety and Efficacy of Mirvetuximab Soravtansine (IMGN853) Versus Investigator's Choice of Chemotherapy in Women with Folate Receptor positive Advanced Epithelial Ovarian Cancer, Primary Peritoneal Cancer or Fallopian Tube Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2015-004060-11 |
| Trial protocol | ES GB BE PL BG IT |
| Global end of trial date | 21 January 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 February 2021 |
| First version publication date | 19 February 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | IMGN853-0403 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02631876 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | ImmunoGen, Inc. |
| Sponsor organisation address | 830 Winter Street, Waltham, United States, MA 02451 |
| Public contact | CMO, ImmunoGen, ImmunoGen, Inc., +1 781-895-0600, clinicaltrials@immunogen.com |
| Scientific contact | CMO, ImmunoGen, ImmunoGen, Inc., +1 781-895-0600, clinicaltrials@immunogen.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 | 21 January 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 21 January 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To compare the progression-free survival (PFS) of participants randomized to mirvetuximab soravtansine versus selected standard of care chemotherapy.

Protection of trial subjects:

This study was designed and monitored in accordance with sponsor requirements, which comply with the ethical principles of ICH E6 Good Clinical Practice as required by the country-specific health authorities, and in accordance with principles laid out in the Declaration of Helsinki. The protocol also complied with the laws and regulations, as well as any applicable guidelines, of the countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 02 March 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Spain: 57 |
| Country: Number of subjects enrolled | United Kingdom: 24 |
| Country: Number of subjects enrolled | Belgium: 11 |
| Country: Number of subjects enrolled | Czechia: 1 |
| Country: Number of subjects enrolled | France: 12 |
| Country: Number of subjects enrolled | Ireland: 13 |
| Country: Number of subjects enrolled | Canada: 48 |
| Country: Number of subjects enrolled | Italy: 73 |
| Country: Number of subjects enrolled | Russian Federation: 8 |
| Country: Number of subjects enrolled | Serbia: 3 |
| Country: Number of subjects enrolled | Ukraine: 4 |
| Country: Number of subjects enrolled | United States: 112 |
| Worldwide total number of subjects | 366 |
| EEA total number of subjects | 191 |

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) | 194 |
| From 65 to 84 years | 169 |
| 85 years and over | 3 |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted in participants with folate receptor alpha-positive, platinum-resistant epithelial ovarian cancer at 101 sites in 12 countries between 02 March 2016 and 21 January 2020. Participants who had received 1-3 prior systemic lines of anti-cancer therapy and who fulfilled the eligibility criteria were enrolled.

### Pre-assignment

Screening details:

A total of 366 participants were randomized in a ratio of 2:1 to receive either mirvetuximab soravtansine or the investigator's choice of chemotherapy.

### 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** | Mirvetuximab Soravtansine |

Arm description:

Participants received mirvetuximab soravtansine at 6 milligrams/kilogram (mg/kg) adjusted ideal body weight (AIBW) administered intravenously (IV) on Day 1 of a 3 week cycle. Participants continued to receive study drug until they experienced progressive disease (PD) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (as assessed by the blinded independent review committee [BIRC]), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Mirvetuximab soravtansine |
| Investigational medicinal product code | IMGN853 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Mirvetuximab Soravtansine was administered per dose and schedule specified in the arm description.

| | |
|---|---|
| **Arm title** | Investigator's Choice (IC) Chemotherapy |

Arm description:

Participants received a dose of IC chemotherapeutic agent calculated using body surface area (BSA). Paclitaxel administered at 80 milligrams/square meter (mg/m^2) as a 1-hour IV infusion on Days 1, 8, 15, and 22 of a 4-week cycle; or topotecan administered at 4 mg/m^2 over 30 minutes on Days 1, 8, and 15 of a 4-week cycle. Alternatively, topotecan could have been administered at 1.25 mg/m^2 over 30 minutes on Days 1 to 5 of a 3-week cycle; or pegylated liposomal doxorubicin (PLD) administered at 40 mg/m^2 as a 1 mg/minute IV infusion on Day 1 of a 4-week cycle. After Cycle 1, if tolerated, PLD could have been administered as a 1-hour infusion. Participants continued to receive study drug until they experienced PD per RECIST version 1.1 (as assessed by BIRC), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

| | |
|---|---|
| Dosage and administration details:<br>Paclitaxel was administered per dose and schedule specified in the arm description. | |
| Investigational medicinal product name | Pegylated liposomal doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details:<br>PLD was administered per dose and schedule specified in the arm description. | |
| Investigational medicinal product name | Topotecan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details:<br>Topotecan was administered per dose and schedule specified in the arm description. | |

| **Number of subjects in period 1** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy |
|---|---|---|
| Started | 248 | 118 |
| Safety Population | 243 | 109 |
| Completed | 129 | 55 |
| Not completed | 119 | 63 |
| Consent withdrawn by subject | 16 | 9 |
| Physician decision | 1 | - |
| Death | 96 | 50 |
| Other than specified | 4 | 4 |
| Lost to follow-up | 2 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Mirvetuximab Soravtansine |
| Reporting group description: | |
| Participants received mirvetuximab soravtansine at 6 milligrams/kilogram (mg/kg) adjusted ideal body weight (AIBW) administered intravenously (IV) on Day 1 of a 3 week cycle. Participants continued to receive study drug until they experienced progressive disease (PD) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (as assessed by the blinded independent review committee [BIRC]), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study. | |
| Reporting group title | Investigator's Choice (IC) Chemotherapy |
| Reporting group description: | |
| Participants received a dose of IC chemotherapeutic agent calculated using body surface area (BSA). Paclitaxel administered at 80 milligrams/square meter (mg/m^2) as a 1-hour IV infusion on Days 1, 8, 15, and 22 of a 4-week cycle; or topotecan administered at 4 mg/m^2 over 30 minutes on Days 1, 8, and 15 of a 4-week cycle. Alternatively, topotecan could have been administered at 1.25 mg/m^2 over 30 minutes on Days 1 to 5 of a 3-week cycle; or pegylated liposomal doxorubicin (PLD) administered at 40 mg/m^2 as a 1 mg/minute IV infusion on Day 1 of a 4-week cycle. After Cycle 1, if tolerated, PLD could have been administered as a 1-hour infusion. Participants continued to receive study drug until they experienced PD per RECIST version 1.1 (as assessed by BIRC), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study. | |

| **Reporting group values** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | Total |
|---|---|---|---|
| Number of subjects | 248 | 118 | 366 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 62.7 | 62.9 | |
| standard deviation | ± 10.29 | ± 10.51 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 248 | 118 | 366 |
| Male | 0 | 0 | 0 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 12 | 9 | 21 |
| Not Hispanic or Latino | 225 | 102 | 327 |
| Unknown or Not Reported | 11 | 7 | 18 |
| Race | | | |
| Units: Subjects | | | |

| | | | |
|---|---|---|---|
| American Indian or Alaska Native | 0 | 1 | 1 |
| Asian | 6 | 2 | 8 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 7 | 3 | 10 |
| White | 225 | 105 | 330 |
| Other | 2 | 2 | 4 |
| Unknown or Not Reported | 8 | 5 | 13 |

## End points

### End points reporting groups

| Reporting group title | Mirvetuximab Soravtansine |
|---|---|

Reporting group description:

Participants received mirvetuximab soravtansine at 6 milligrams/kilogram (mg/kg) adjusted ideal body weight (AIBW) administered intravenously (IV) on Day 1 of a 3 week cycle. Participants continued to receive study drug until they experienced progressive disease (PD) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (as assessed by the blinded independent review committee [BIRC]), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study.

| Reporting group title | Investigator's Choice (IC) Chemotherapy |
|---|---|

Reporting group description:

Participants received a dose of IC chemotherapeutic agent calculated using body surface area (BSA). Paclitaxel administered at 80 milligrams/square meter (mg/m^2) as a 1-hour IV infusion on Days 1, 8, 15, and 22 of a 4-week cycle; or topotecan administered at 4 mg/m^2 over 30 minutes on Days 1, 8, and 15 of a 4-week cycle. Alternatively, topotecan could have been administered at 1.25 mg/m^2 over 30 minutes on Days 1 to 5 of a 3-week cycle; or pegylated liposomal doxorubicin (PLD) administered at 40 mg/m^2 as a 1 mg/minute IV infusion on Day 1 of a 4-week cycle. After Cycle 1, if tolerated, PLD could have been administered as a 1-hour infusion. Participants continued to receive study drug until they experienced PD per RECIST version 1.1 (as assessed by BIRC), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study.

### Primary: PFS, as Assessed by BIRC Per RECIST Version 1.1 in All Participants Randomized to the Study

| End point title | PFS, as Assessed by BIRC Per RECIST Version 1.1 in All Participants Randomized to the Study[1] |
|---|---|

End point description:

PFS was defined as the time from randomization until PD or death from any cause, whichever occurred first, estimated using the Kaplan-Meier method. PD: At least a 20% increase in the sum of the longest diameters (SoD) of target lesions, taken as reference the smallest (nadir) SoD since and including baseline. In addition to the relative increase of 20%, the SoD must also demonstrate an absolute increase of at least 5 mm. Unequivocal progression of non-target lesions and appearance of new lesions. Unequivocal progression should not normally trump target lesion status. It must be representative of overall disease status change, not a single lesion increase. The intent-to-treat (ITT) population included all participants randomized in the study.

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

End point timeframe:

From the date of randomization until the time of death or PD (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

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 additional statistical analysis was pre-specified for this endpoint.

| End point values | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 248 | 118 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.14 (3.75 to 4.53) | 4.44 (2.83 to 5.59) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: PFS, as Assessed by BIRC Per RECIST Version 1.1 in Participants With High Folate Receptor Alpha Level (≥ 75% of Tumor Staining)

| End point title | PFS, as Assessed by BIRC Per RECIST Version 1.1 in Participants With High Folate Receptor Alpha Level (≥ 75% of Tumor Staining)[2] |
|---|---|

End point description:

PFS was defined as the time from randomization until PD or death from any cause, whichever occurred first, estimated using the Kaplan-Meier method. PD: At least a 20% increase in the SoD of target lesions, taken as reference the smallest (nadir) SoD since and including baseline. In addition to the relative increase of 20%, the SoD must also demonstrate an absolute increase of at least 5 mm. Unequivocal progression of non-target lesions and appearance of new lesions. Unequivocal progression should not normally trump target lesion status. It must be representative of overall disease status change, not a single lesion increase. The ITT population included all participants randomized in the study. Here, the 'number of subjects analysed' signifies participants with high folate receptor alpha level.

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

End point timeframe:

From the date of randomization until the time of death or PD (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No additional statistical analysis was pre-specified for this endpoint.

| **End point values** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 71 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.76 (4.11 to 5.68) | 3.25 (1.97 to 5.59) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR): Percentage of Participants With Objective Response, as Assessed by BIRC Per RECIST Version 1.1

| End point title | Objective Response Rate (ORR): Percentage of Participants With Objective Response, as Assessed by BIRC Per RECIST Version 1.1 |
|---|---|

End point description:

ORR was defined as percentage of participants with a best overall response (BOR) of complete response

(CR) or partial response (PR). CR: Disappearance of all target or non-target lesions. All pathological or non-pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<) 10 millimeters (mm). PR: At least 30 percent (%) decrease in the SoD of target lesions, taking as reference the baseline SoD. The ITT population included all participants randomized in the study.

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

End point timeframe:

From randomization until first BOR of CR or PR (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

| **End point values** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 248 | 118 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 22 (17.2 to 27.9) | 12 (6.6 to 19.1) | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Overall Survival (OS)**

| End point title | Overall Survival (OS) |
|---|---|

End point description:

OS was defined as the time from the date of randomization until the date of death from any cause. Participants who did not experience the event of death were censored at their last date known to be alive. OS was estimated using the Kaplan-Meier method. The ITT population included all participants randomized in the study.

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

End point timeframe:

From the date of randomization until the time of death (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

| **End point values** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 248 | 118 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 15.57 (12.85 to 18.04) | 13.93 (11.40 to 18.50) | | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Number of Participants Achieving at Least a 15% (≥ 15-Point) Absolute Improvement From Baseline on the EORTC QLQ-OV28 Abdominal/Gastrointestinal (AB/GI) Symptom Subscale at Week 8/9 Assessment

| End point title | Number of Participants Achieving at Least a 15% (≥ 15-Point) Absolute Improvement From Baseline on the EORTC QLQ-OV28 Abdominal/Gastrointestinal (AB/GI) Symptom Subscale at Week 8/9 Assessment |
|---|---|

End point description:

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer 28 (EORTC QLQ-OV28) is a 28-item ovarian cancer supplemental module. It comprises of 6 symptom scales (AB/GI symptoms, peripheral neuropathy, other chemotherapy side-effects, hormonal symptoms, body image, attitude to disease, treatment) and sexual functioning. Participants were asked to indicate extent to which they experienced AB/GI symptoms. Participants responded on a scale of 1-4 (1 = not at all, 2 = a little, 3 = quite a bit, 4 = very much) to following: Did you have abdominal pain? Did you have a bloated feeling in your abdomen? Did you have problems with your clothes feeling too tight? Did you experience any change in bowel habit as a result of your disease or treatment? Were you troubled by passing wind/gas/flatulence? Have you felt full too quickly after beginning to eat? Have you had indigestion/heartburn? Data were transformed to a scale from 0 - 100. ITT population.

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

End point timeframe:

Baseline, Week 8/9

| **End point values** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 50 | | |
| Units: Participants | 45 | 7 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) |
|---|---|

End point description:

Adverse event (AE): any untoward medical occurrence that develops or worsens in severity during the conduct of a clinical study and does not necessarily have a causal relationship to study drug. TEAEs: any AE that emerged on or after the first dose, and within 30 days of the last dose. A summary of serious and all other non-serious AEs regardless of causality is located in the AEs module. The safety population included all enrolled participants who received at least 1 dose of mirvetuximab soravtansine or IC chemotherapy.

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

End point timeframe:

From first dose of study drug up to 30 days after last dose of study drug (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

| End point values | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 243 | 109 | | |
| Units: Participants | 242 | 107 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Gynecologic Cancer Intergroup (GCIG) CA-125 Response Rate: Percentage of Participants With GCIG CA-125 Confirmed Clinical Responses

| End point title | Gynecologic Cancer Intergroup (GCIG) CA-125 Response Rate: Percentage of Participants With GCIG CA-125 Confirmed Clinical Responses |
|---|---|

End point description:

CA-125 Response rate was defined as the number of participants with a CA-125 confirmed response divided by the number of participants in the CA-125 response-evaluable population multiplied by 100. The CA-125-evaluable population included all randomized population whose pretreatment sample was ≥ 2.0 times the upper limit of normal, within 2 weeks prior to randomization, and who had at least 1 post-baseline CA-125 evaluation.

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

End point timeframe:

From first dose of study drug until CA-125 response (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

| End point values | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 203 | 82 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 51 (44.1 to 58.3) | 27 (17.6 to 37.8) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: PFS, as Assessed by Investigator Per RECIST Version 1.1

| End point title | PFS, as Assessed by Investigator Per RECIST Version 1.1 |
|---|---|

End point description:

PFS was defined as the time from randomization until PD or death whichever occurred first, estimated

using the Kaplan-Meier method. PD: At least a 20% increase in the SoD of target lesions, taken as reference the smallest (nadir) SoD since and including baseline. In addition to the relative increase of 20%, the SoD must also demonstrate an absolute increase of at least 5 mm. Unequivocal progression of non-target lesions and appearance of new lesions. Unequivocal progression should not normally trump target lesion status. It must be representative of overall disease status change, not a single lesion increase. The ITT population included all participants randomized in the study.

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

End point timeframe:

From the date of randomization until the time of death or PD (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

| **End point values** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 248 | 118 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.27 (4.11 to 5.06) | 4.24 (2.76 to 5.36) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR), as Assessed by BIRC Per RECIST Version 1.1

| End point title | Duration of Response (DOR), as Assessed by BIRC Per RECIST Version 1.1 |
|---|---|

End point description:

DOR was defined as the time from the date of the first response (CR or PR), whichever was recorded first, until the date of PD. PD: At least a 20% increase in the SoD of target lesions, taken as reference the smallest (nadir) SoD since and including baseline. In addition to the relative increase of 20%, the SoD must also demonstrate an absolute increase of at least 5 mm. Unequivocal progression of non-target lesions. Unequivocal progression should not normally trump target lesion status. It must be representative of overall disease status change, not a single lesion increase. DOR was only defined for participants who had a BOR of CR or PR using the method of Kaplan-Meier. The ITT population included all participants randomized in the study. Here, the 'number of subjects analysed' signifies participants evaluable for this outcome measure and values of '99999' = not calculable.

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

End point timeframe:

From the date of first response (CR or PR) until the date of PD (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

| End point values | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 14 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 5.65 (4.17 to 8.51) | 7.26 (4.14 to 99999) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Plasma Concentration-Versus Time Curve From Time of Dose Over All Time Measurements (AUClast) of Mirvetuximab Soravtansine, Total M9346A Antibody, DM4, and S-methyl DM4

| End point title | Area Under the Plasma Concentration-Versus Time Curve From Time of Dose Over All Time Measurements (AUClast) of Mirvetuximab Soravtansine, Total M9346A Antibody, DM4, and S-methyl DM4[3] |
|---|---|

End point description:

Pharmacokinetic (PK) parameters were calculated using standard non-compartmental methods. The PK population included all participants who received at least 1 infusion of mirvetuximab soravtansine, had evaluable PK data, and had samples collected with no major deviations related to administration of study drug. Here, the 'number of subjects analysed' signifies participants evaluable for this outcome measure and n = number of participants analyzed in each cycle.

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

End point timeframe:

Pre-dose and within 5 minutes after mirvetuximab soravtansine infusion on Day 1 of Cycles 1 and 3; single samples were taken on Days 8 and 15 of Cycles 1 and 3

Notes:

[3] - 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: Pharmacokinetic assessment was pre-specified for the Mirvetuximab Soravtansine arm only.

| End point values | Mirvetuximab Soravtansine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 235 | | | |
| Units: hours*milligrams/milliliter (hr*mg/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Mirvetuximab Soravtansine at Cycle 1 (n = 235) | 20.53 (± 10.31) | | | |
| Mirvetuximab Soravtansine at Cycle 3 (n = 146) | 22.40 (± 7.770) | | | |
| Total M9346A antibody at Cycle 1 (n = 235) | 23.23 (± 9.463) | | | |
| Total M9346A antibody at Cycle 3 (n = 146) | 31.20 (± 11.52) | | | |
| DM4 at Cycle 1 (n = 233) | 348.5 (± 265.7) | | | |
| DM4 at Cycle 3 (n = 142) | 347.4 (± 280.9) | | | |
| S-methyl DM4 at Cycle 1 (n = 234) | 1586 (± 1496) | | | |

| | | | | |
|---|---|---|---|---|
| S-methyl DM4 at Cycle 3 (n = 146) | 1512 (± 1278) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Anti-Drug Antibodies (ADA)

| End point title | Number of Participants With Anti-Drug Antibodies (ADA)[4] |
|---|---|

End point description:

An electrochemiluminescent method was used for the detection of anti–mirvetuximab soravtansine antibodies in plasma from samples collected in dipotassium ethylenediaminetetraacetic acid (K2EDTA) tubes. The qualitative assay was designed to detect anti–mirvetuximab soravtansine antibodies in human plasma. The immunogenicity population included all participants who received at least 1 infusion of mirvetuximab soravtansine and had evaluable immunogenicity data.

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

End point timeframe:

Pre-dose and within 5 minutes after mirvetuximab soravtansine infusion on Day 1 of Cycles 1, 2, and 4, and pre-dose on Day 1 of Cycle 6

Notes:

[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: Immunogenicity assessment was pre-specified for the Mirvetuximab Soravtansine arm only.

| **End point values** | Mirvetuximab Soravtansine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 230 | | | |
| Units: Participants | 13 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 30 days after last dose of study drug (maximum exposure: 86.9 weeks for mirvetuximab soravtansine arm and 62.9 weeks for IC chemotherapy arm)

Adverse event reporting additional description:

The safety population included all enrolled participants who received at least 1 dose of mirvetuximab soravtansine or IC chemotherapy.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Mirvetuximab Soravtansine |

Reporting group description:

Participants received mirvetuximab soravtansine at 6 mg/kg AIBW administered IV on Day 1 of a 3 week cycle. Participants continued to receive study drug until they experienced PD per RECIST version 1.1 (as assessed by the BIRC), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study.

| | |
|---|---|
| Reporting group title | Investigator’s Choice (IC) Chemotherapy |

Reporting group description:

Participants received a dose of IC chemotherapeutic agent calculated using BSA. Paclitaxel administered at 80 mg/m^2 as a 1-hour IV infusion on Days 1, 8, 15, and 22 of a 4-week cycle; or topotecan administered at 4 mg/m^2 over 30 minutes on Days 1, 8, and 15 of a 4-week cycle. Alternatively, topotecan could have been administered at 1.25 mg/m^2 over 30 minutes on Days 1 to 5 of a 3-week cycle; or PLD administered at 40 mg/m^2 as a 1 mg/minute IV infusion on Day 1 of a 4-week cycle. After Cycle 1, if tolerated, PLD could have been administered as a 1-hour infusion. Participants continued to receive study drug until they experienced PD per RECIST version 1.1 (as assessed by BIRC), experienced unacceptable toxicity, or withdrew consent, whichever came first, or until the sponsor terminated the study.

| Serious adverse events | Mirvetuximab Soravtansine | Investigator’s Choice (IC) Chemotherapy | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 67 / 243 (27.57%) | 31 / 109 (28.44%) | |
| number of deaths (all causes) | 96 | 50 | |
| number of deaths resulting from adverse events | 5 | 4 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant pleural effusion | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Embolism | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Complication associated with device | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 3 / 109 (2.75%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 243 (0.82%) | 2 / 109 (1.83%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 5 / 243 (2.06%) | 3 / 109 (2.75%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 7 / 243 (2.88%) | 2 / 109 (1.83%) | |
| occurrences causally related to treatment / all | 7 / 7 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 243 (1.23%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Mania | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Acetabulum fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 2 / 243 (0.82%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 2 / 243 (0.82%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Eye pain | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Keratopathy | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| Abdominal incarcerated hernia | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 243 (1.23%) | 2 / 109 (1.83%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 2 / 109 (1.83%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 4 / 243 (1.65%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 10 / 243 (4.12%) | 3 / 109 (2.75%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal perforation | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 4 / 243 (1.65%) | 2 / 109 (1.83%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 243 (0.82%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 5 / 243 (2.06%) | 4 / 109 (3.67%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 243 (0.82%) | 2 / 109 (1.83%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Influenza | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal infection | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 3 / 243 (1.23%) | 3 / 109 (2.75%) | |
| occurrences causally related to treatment / all | 0 / 4 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 3 | |
| Systemic infection | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 243 (0.82%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 243 (0.41%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vestibular neuronitis | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 243 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 4 / 243 (1.65%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Mirvetuximab Soravtansine | Investigator's Choice (IC) Chemotherapy | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 239 / 243 (98.35%) | 103 / 109 (94.50%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 16 / 243 (6.58%) | 4 / 109 (3.67%) | |
| occurrences (all) | 25 | 4 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 51 / 243 (20.99%) | 25 / 109 (22.94%) | |
| occurrences (all) | 90 | 73 | |
| Fatigue | | | |
| subjects affected / exposed | 83 / 243 (34.16%) | 38 / 109 (34.86%) | |
| occurrences (all) | 138 | 85 | |
| Influenza like illness | | | |
| subjects affected / exposed | 4 / 243 (1.65%) | 6 / 109 (5.50%) | |
| occurrences (all) | 4 | 7 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 2 / 243 (0.82%) | 6 / 109 (5.50%) | |
| occurrences (all) | 2 | 6 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 8 / 243 (3.29%) | 10 / 109 (9.17%) | |
| occurrences (all) | 9 | 11 | |
| Pyrexia | | | |
| subjects affected / exposed | 25 / 243 (10.29%) | 7 / 109 (6.42%) | |
| occurrences (all) | 29 | 7 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 39 / 243 (16.05%) | 15 / 109 (13.76%) | |
| occurrences (all) | 48 | 19 | |
| Dyspnoea | | | |
| subjects affected / exposed | 36 / 243 (14.81%) | 16 / 109 (14.68%) | |
| occurrences (all) | 49 | 24 | |

| | | | |
|---|---|---|---|
| Pneumonitis | | | |
| subjects affected / exposed | 13 / 243 (5.35%) | 1 / 109 (0.92%) | |
| occurrences (all) | 17 | 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 14 / 243 (5.76%) | 8 / 109 (7.34%) | |
| occurrences (all) | 20 | 9 | |
| Insomnia | | | |
| subjects affected / exposed | 23 / 243 (9.47%) | 16 / 109 (14.68%) | |
| occurrences (all) | 24 | 18 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 40 / 243 (16.46%) | 6 / 109 (5.50%) | |
| occurrences (all) | 80 | 6 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 43 / 243 (17.70%) | 8 / 109 (7.34%) | |
| occurrences (all) | 94 | 8 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 19 / 243 (7.82%) | 4 / 109 (3.67%) | |
| occurrences (all) | 27 | 4 | |
| Weight decreased | | | |
| subjects affected / exposed | 17 / 243 (7.00%) | 4 / 109 (3.67%) | |
| occurrences (all) | 24 | 5 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 16 / 243 (6.58%) | 3 / 109 (2.75%) | |
| occurrences (all) | 20 | 3 | |
| Dysgeusia | | | |
| subjects affected / exposed | 30 / 243 (12.35%) | 9 / 109 (8.26%) | |
| occurrences (all) | 33 | 11 | |
| Headache | | | |
| subjects affected / exposed | 57 / 243 (23.46%) | 14 / 109 (12.84%) | |
| occurrences (all) | 86 | 20 | |
| Neurotoxicity | | | |
| subjects affected / exposed | 9 / 243 (3.70%) | 6 / 109 (5.50%) | |
| occurrences (all) | 14 | 16 | |

| | | | |
|---|---|---|---|
| Peripheral neuropathy | | | |
| subjects affected / exposed | 86 / 243 (35.39%) | 21 / 109 (19.27%) | |
| occurrences (all) | 151 | 34 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 34 / 243 (13.99%) | 32 / 109 (29.36%) | |
| occurrences (all) | 54 | 91 | |
| Leukopenia | | | |
| subjects affected / exposed | 9 / 243 (3.70%) | 16 / 109 (14.68%) | |
| occurrences (all) | 24 | 38 | |
| Neutropenia | | | |
| subjects affected / exposed | 16 / 243 (6.58%) | 43 / 109 (39.45%) | |
| occurrences (all) | 36 | 119 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 27 / 243 (11.11%) | 17 / 109 (15.60%) | |
| occurrences (all) | 80 | 52 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 36 / 243 (14.81%) | 2 / 109 (1.83%) | |
| occurrences (all) | 52 | 2 | |
| Dry eye | | | |
| subjects affected / exposed | 68 / 243 (27.98%) | 2 / 109 (1.83%) | |
| occurrences (all) | 122 | 2 | |
| Eye pain | | | |
| subjects affected / exposed | 31 / 243 (12.76%) | 1 / 109 (0.92%) | |
| occurrences (all) | 50 | 1 | |
| Keratopathy | | | |
| subjects affected / exposed | 83 / 243 (34.16%) | 1 / 109 (0.92%) | |
| occurrences (all) | 185 | 1 | |
| Photophobia | | | |
| subjects affected / exposed | 34 / 243 (13.99%) | 2 / 109 (1.83%) | |
| occurrences (all) | 48 | 2 | |
| Vision blurred | | | |
| subjects affected / exposed | 104 / 243 (42.80%) | 6 / 109 (5.50%) | |
| occurrences (all) | 258 | 7 | |
| Visual acuity reduced | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 52 / 243 (21.40%) | 2 / 109 (1.83%) | |
| occurrences (all) | 78 | 3 | |
| Vitreous floaters | | | |
| subjects affected / exposed | 13 / 243 (5.35%) | 0 / 109 (0.00%) | |
| occurrences (all) | 13 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 26 / 243 (10.70%) | 11 / 109 (10.09%) | |
| occurrences (all) | 33 | 13 | |
| Abdominal pain | | | |
| subjects affected / exposed | 96 / 243 (39.51%) | 33 / 109 (30.28%) | |
| occurrences (all) | 156 | 49 | |
| Ascites | | | |
| subjects affected / exposed | 9 / 243 (3.70%) | 6 / 109 (5.50%) | |
| occurrences (all) | 12 | 6 | |
| Constipation | | | |
| subjects affected / exposed | 64 / 243 (26.34%) | 31 / 109 (28.44%) | |
| occurrences (all) | 89 | 38 | |
| Diarrhoea | | | |
| subjects affected / exposed | 107 / 243 (44.03%) | 18 / 109 (16.51%) | |
| occurrences (all) | 191 | 42 | |
| Dyspepsia | | | |
| subjects affected / exposed | 18 / 243 (7.41%) | 5 / 109 (4.59%) | |
| occurrences (all) | 26 | 5 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 14 / 243 (5.76%) | 5 / 109 (4.59%) | |
| occurrences (all) | 18 | 7 | |
| Nausea | | | |
| subjects affected / exposed | 131 / 243 (53.91%) | 46 / 109 (42.20%) | |
| occurrences (all) | 223 | 65 | |
| Stomatitis | | | |
| subjects affected / exposed | 10 / 243 (4.12%) | 23 / 109 (21.10%) | |
| occurrences (all) | 11 | 43 | |
| Vomiting | | | |
| subjects affected / exposed | 64 / 243 (26.34%) | 22 / 109 (20.18%) | |
| occurrences (all) | 108 | 32 | |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 7 / 243 (2.88%) | 14 / 109 (12.84%) | |
| occurrences (all) | 7 | 16 | |
| Dry skin | | | |
| subjects affected / exposed | 4 / 243 (1.65%) | 8 / 109 (7.34%) | |
| occurrences (all) | 4 | 8 | |
| Erythema | | | |
| subjects affected / exposed | 7 / 243 (2.88%) | 6 / 109 (5.50%) | |
| occurrences (all) | 7 | 11 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 1 / 243 (0.41%) | 16 / 109 (14.68%) | |
| occurrences (all) | 1 | 23 | |
| Pruritus | | | |
| subjects affected / exposed | 12 / 243 (4.94%) | 7 / 109 (6.42%) | |
| occurrences (all) | 15 | 9 | |
| Rash | | | |
| subjects affected / exposed | 10 / 243 (4.12%) | 12 / 109 (11.01%) | |
| occurrences (all) | 10 | 22 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 37 / 243 (15.23%) | 7 / 109 (6.42%) | |
| occurrences (all) | 49 | 7 | |
| Back pain | | | |
| subjects affected / exposed | 23 / 243 (9.47%) | 9 / 109 (8.26%) | |
| occurrences (all) | 29 | 10 | |
| Muscle spasms | | | |
| subjects affected / exposed | 25 / 243 (10.29%) | 4 / 109 (3.67%) | |
| occurrences (all) | 27 | 7 | |
| Myalgia | | | |
| subjects affected / exposed | 22 / 243 (9.05%) | 5 / 109 (4.59%) | |
| occurrences (all) | 32 | 5 | |
| Pain in extremity | | | |
| subjects affected / exposed | 15 / 243 (6.17%) | 7 / 109 (6.42%) | |
| occurrences (all) | 18 | 9 | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Urinary tract infection | | | |
| subjects affected / exposed | 28 / 243 (11.52%) | 11 / 109 (10.09%) | |
| occurrences (all) | 39 | 16 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 60 / 243 (24.69%) | 16 / 109 (14.68%) | |
| occurrences (all) | 86 | 22 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 14 / 243 (5.76%) | 3 / 109 (2.75%) | |
| occurrences (all) | 18 | 10 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 18 / 243 (7.41%) | 9 / 109 (8.26%) | |
| occurrences (all) | 25 | 15 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 40 / 243 (16.46%) | 10 / 109 (9.17%) | |
| occurrences (all) | 62 | 19 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 9 / 243 (3.70%) | 6 / 109 (5.50%) | |
| occurrences (all) | 14 | 8 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 September 2015 | The primary reasons for amending the protocol were to revise the secondary objectives for Stage 1, revise Exclusion Criterion 3 to avoid inclusion of patients with pre-existing ocular conditions, update the management of ocular AEs to align with mirvetuximab soravtansine program-level changes, and to improve clarity and consistency among sections. |
| 23 September 2015 | The primary reason for amending the protocol was to revise the table for management of potential infusion-related reactions. |
| 20 October 2015 | The primary reason for amending the protocol was to provide details on the rationale for the selection of dose levels and the dosing schedule for the chemotherapeutic agents in the IC arm of Stage 2, clarification around high-risk biopsies in Inclusion Criterion 2, modification of the CA-125 assessment schedule, and corrections for inconsistencies among sections. |
| 01 February 2016 | The primary reason for amending the protocol was to add an exclusion criterion for patients with known hypersensitivity to any of the standard of care drugs (gemcitabine, PLD, paclitaxel, or topotecan) and revise Inclusion Criterion 13 regarding the use of contraception methods. |
| 17 August 2016 | The primary reason for amending the protocol was to close enrollment to Stage 1 of the study and revise the study from a Phase 2 to a Phase 3 study. |
| 19 September 2016 | The primary reason for amending the protocol was to correct an important typographical error in Inclusion Criterion 2, which affected the definition of the patient population under study. In the previous version of the protocol, platinum-resistant ovarian cancer was defined as disease having progressed within 6 months of completing a minimum of 4 cycles of first-line platinum-containing therapy. The descriptor “first-line” for platinum therapy was a typographical error and has been deleted. |
| 04 November 2016 | The primary reason for amending the protocol was to remove the option for patients on IC chemotherapy to cross over. The study schema was updated to reflect this change. |
| 08 May 2017 | The primary reason for amending the protocol was to revise Inclusion Criterion 4 to include hormonal therapies and cancer vaccines as prior lines of anti-cancer therapy. |
| 05 December 2019 | The primary reason for amending the protocol was to allow patients who are receiving mirvetuximab soravtansine and experiencing clinical benefit the option to continue to receive mirvetuximab soravtansine after the closure of the study by the Sponsor. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported