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: 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: 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: 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
Physician decision	1	-
Consent withdrawn by subject	16	9
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