ImmunoGen, Inc.
Protocol #: 0402

A Phase 1b/2 Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Mirvetuximab Soravtansine (IMGN853) in Combination with Bevacizumab, Carboplatin, Pegylated Liposomal Doxorubicin, Pembrolizumab, or Bevacizumab + Carboplatin, in Adults with Folate Receptor Alpha Positive Advanced Epithelial Ovarian Cancer, Primary Peritoneal Cancer, or Fallopian Tube Cancer

Statistical Analysis Plan

Version 2.0

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Abbreviation or Specialist Term	Explanation
ADA	Anti-drug antibodies
AE	Adverse event
AIBW	Adjusted ideal body weight
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
AUC	Area under the time-concentration curve
BOR	Best Overall Response
BRCA	Breast cancer susceptibility gene
BSA	Body Surface Area
CA125	Cancer antigen 125
Cl	Clearance
CM	Concomitant medication
C_{max}	Maximum plasma concentration
CP	Concomitant procedure
CR	Complete response/remission
CRC	Cohort Review Committee
CT	Computed Tomography
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of Variation
DCR	Disease Control Rate
DLT	Dose limiting toxicity
DM4	N2'-[4-[(3-carboxypropyl)dithio]-4-methyl-1-oxo-2-sulfopentyl]-N2'-deacetylmaytansine
DM4-Me	Methylated N2'-[4-[(3-carboxypropyl)dithio]-4-methyl-1-oxo-2-sulfopentyl]-N2'-deacetylmaytansine
DOR	Duration of response
ECG	Electrocardiogram
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic case report form
EOC	Epithelial Ovarian Cancer

Abbreviation or Specialist Term	Explanation
FcγR	Fc gamma receptor
FIH	First in human
FRα	Folate receptor α
GCIG	Gynecologic Cancer Intergroup
IEC	Independent ethics committee
IHC	Immunohistochemistry
IMGN	ImmunoGen
IRB	Institutional review board
irRECIST	Immune-related Response Evaluation Criteria in Solid Tumors
MDR1	Multi-drug resistent gene
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum tolerated dose
MUGA scan	Multigated Acquisition scan
ORR	Objective Response Rate
OS	Overall Survival
PARP	Poly (ADP-ribose) polymerase
PD	Progressive Disease
PD-1	Programmed death receptor-1
PFS	Progression-free Survival
Pgp	P-Glycoprotein
PK	Pharmacokinetics
PR	Partial Response/remission
PT	Preferred Term (MedDRA terminology)
Q3W	Every 3 weeks
Q4W	Every 4 weeks
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	Recommended Phase 2 Dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SCP	Second Course Phase
SD	Stable Disease

Abbreviation or Specialist Term	**Explanation**
SOC	System Organ Classification (MedDRA terminology)
$t_{1/2(\beta)}$	Terminal Half-life
TBL	Total Bilirubin
TEAE	Treatment Emergent Adverse Events
T_{max}	Time to maximum plasma concentration
TTR	Time to Response
ULN	Upper Limit of Normal
V_{SS}	Volume of distribution at steady state
WCBP	Woman of childbearing potential
WHO-DD	World Health Organization –Drug Dictionary

1. INTRODUCTION

1.1. Background

In the first-in-human (FIH) Phase 1 study (Study IMGN853-0401) of single-agent mirvetuximab soravtansine, objective responses have been observed in patients with heavily pretreated FRα positive EOC and endometrial cancer. As of 29 April 2016, mirvetuximab soravtansine has a 26% confirmed overall response rate (95% CI 14%, 41%) and median PFS (mPFS) 4.8 months (95% CI 3.9, 5.7 months) in the 46 patients with platinum-resistant EOC in the patient expansion cohort in study IMGN853-0401 (Moore 2016). The confirmed overall response rate is 44% (95% CI 20%, 70%) and the median PFS (mPFS) is 6.7 months (95% CI 3.9, 11 months) in the subset of 16 patients with FRα−positive (medium/high expression) platinum-resistant EOC with one to three prior regimens treated as part of a 46 patient expansion cohort in study IMGN853-0401 (Moore 2016). Adverse events occurring in > 20% of patients in this cohort included diarrhea, blurred vision, fatigue, nausea, vomiting, and peripheral neuropathy, and were mostly low grade. Blurred vision is likely related to corneal keratopathy, transient microcysts that form on the cornea, causing temporary astigmatism.

Bevacizumab carboplatin and pegylated liposomal doxorubicin are currently in use for the treatment of EOC. Doublet combinations of mirvetuximab soravtansine with bevacizumab, carboplatin, and pegylated liposomal doxorubicin have all demonstrated additive activity in preclinical models. Pembrolizumab, an anti-programmed death receptor-1 (PD-1), monoclonal antibody is approved for the treatment of melanoma and non-small cell lung cancer and has shown preliminary anti-tumor activity as a single agent in EOC (Varga 2015).

The current study is designed to establish the maximum tolerated dose (MTD) and determine the recommended Phase 2 dose (RP2D) of mirvetuximab soravtansine when administered in combination with either bevacizumab, carboplatin, pegylated liposomal doxorubicin, or pembrolizumab. The study will also investigate activity signals, and safety and tolerability of a triplet dose regimen of mirvetuximab soravtansine + bevacizumab + carboplatin. All study treatments will be administered intravenously to adult patients with FRα positive ovarian cancer, primary peritoneal cancer, or fallopian tube cancer. The safety, tolerability, immunogenicity of mirvetuximab soravtansine, and preliminary anti-tumor activity of mirvetuximab soravtansine in combination with bevacizumab, carboplatin, pegylated liposomal doxorubicin, pembrolizumab, or bevacizumab + carboplatin will be characterized. The pharmacokinetics (PK) of mirvetuximab soravtansine, bevacizumab, carboplatin and pegylated liposomal doxorubicin will be characterized. PK profile of pembrolizumab may be characterized, if warranted, due to a safety signal.

The protocol for Study 0402 describes the general approach to analysis of data from the study. This analysis plan describes additional detail needed to complete such an analysis. Table, figure and listing shells will be supplied in an accompanying document.

This Statistical Analysis Plan (SAP) is based on Amendment 5 of Protocol IMGN853-0402.

A brief history of protocol amendments is presented in Table 1.

This SAP will govern the analysis of data from this study. The plan may be modified until time of database lock. Any deviations from the analysis plan will be documented as such in the study report.

Table 1: History of Protocol Amendments

Version	Approval Date	Salient Changes, if any*
Protocol	11 August 2015	
Amendment 1	23 September 2015	No changes that require accommodation in this analysis plan.
Amendment 1A	11 February 2016	No changes that require accommodation in this analysis plan.
Amendment 1B	13 May 2016	No changes that require accommodation in this analysis plan.
Amendment 2	21 June 2016	Regimen D was added to the protocol. This regimen is mirvetuximab soravtansine in combination with pembrolizumab. The entire protocol was updated to include this regimen. There is a dose escalation part and a dose expansion for Regimen D. The time period for reporting AEs and SAEs was updated. In this amendment, Aes and SAEs regardless of causality are recorded and reported from the time of informed consent until at least 30 days after the last dose of study medication. Adverse events of special interest were added.
Amendment 3	26 June 2017	The exploratory endpoint regarding BRCA testing was removed. The endpoint for analysis of tumor infiltrating cells by IHC was clarified. The secondary objective and endpoint sections were updated to specify that the objective response rate analysis is to be performed for the dose escalation cohorts for all regimens, plus the dose expansion cohort 3 for Regimen A. Hormonal therapy was added as a prior therapy. Prophylactic corticosteroid eye drops and lubricating eye drops were added as required pretreatments.
Amendment 4	14 November 2017	Regimen E was added to the protocol. This regimen is mirvetuximab soravtansine in combination with bevacizumab and carboplatin. The entire protocol was updated to include this regimen. Endometrial cancer cohort (Regimen A, Cohort 3) was removed. The entire protocol was updated to remove this cohort in the dose-expansion phase.

Table 1: History of Protocol Amendments (Continued)

Version	Approval Date	Salient Changes, if any*
Amendment 5	21 September 2018	Added an additional cohort (Cohort 3) to Regimen A, which will include patients with one to three prior therapies who may be either platinum resistant or platinum sensitive, and who may or may not have received prior therapy with bevacizumab. Changed the investigational product name from IMGN853 to the International Non-proprietary name of mirvetuximab soravtansine. Removed the alternative dosage schedule for Regimen A because it was not enrolled.

* Changes expected to require accommodation in analysis plan.

2. PROTOCOL OBJECTIVES

All objectives apply to all dosing regimens and all cohorts unless otherwise noted.

2.1. Primary Objectives

The protocol lists the following primary objectives:

2.1.1. Dose Escalation

Evaluate the safety and tolerability of mirvetuximab soravtansine when given in combination with bevacizumab, carboplatin, pegylated liposomal doxorubicin, or pembrolizumab (Regimens A, B, C, and D, respectively) in patients with EOC, primary peritoneal cancer, or fallopian tube cancer.

2.1.2. Dose Expansion (Regimens A and D) and Regimen E (Triplet)

Assess preliminary response-based anti-tumor activity of mirvetuximab soravtansine when administered in combination with bevacizumab (Regimen A) or pembrolizumab (Regimen D) and in combination with bevacizumab and carboplatin (Regimen E) in patients with EOC, primary peritoneal cancer, or fallopian tube cancer.

2.2. Secondary Objectives

The protocol lists the following secondary objectives:

- Evaluate the safety and tolerability of mirvetuximab soravtansine when administered in combination with bevacizumab or pembrolizumab (Dose Expansion, Regimens A and D, respectively) and in combination with bevacizumab and carboplatin (Regimen E [Triplet]) in patients with EOC, primary peritoneal cancer, or fallopian tube cancer
- Assess preliminary response-based anti-tumor activity of the combination Regimens (Dose Escalation, Regimens A through D)
- Assess PFS

- Measure duration of response (DOR): the time from first objective response (CR/PR) to the time of progressive disease (PD) among those who have achieved a PR or CR
- Assess Gynecologic Cancer Intergroup (GCIG) CA125 response rate of the combination regimens
- Characterize PK of mirvetuximab soravtansine when used in combination regimens
- Evaluate bevacizumab, carboplatin, and pegylated liposomal doxorubicin concentrations when administered in combination with mirvetuximab soravtansine
- Characterize immunogenicity of mirvetuximab soravtansine

2.3. Exploratory Objectives

The protocol lists the following exploratory objectives:

- Assess any association between FRα expression levels and clinical response
- Identify or evaluate potential biomarkers in blood and tumor tissue that might predict response to each of the four combinations
- Evaluate pembrolizumab concentrations if warranted by a safety signal (Regimen D only)
- Assess anti-tumor activity of the combination with pembrolizumab per immune-related RECIST (irRECIST) (Regimen D only)

3. STUDY ENDPOINTS

3.1. Primary Endpoints

The protocol lists the following primary endpoints:

3.1.1. Dose Escalation (Regimens A, B, C, and D)

- Treatment-emergent adverse events, laboratory test results, physical examination, electrocardiograms (ECGs), and vital signs.

3.1.2. Dose Expansion (Regimens A and D) and Regimen E (Triplet)

- Objective response rate, defined as percentage of patients with confirmed response (complete response/remission [CR] + partial response/remission [PR]) as assessed by Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1

3.2. Secondary Endpoints

The protocol lists the following as secondary endpoints:

- Treatment-emergent AEs, changes in laboratory test results, physical examination, ECGs, and vital signs (Dose Expansion [Regimens A and D] and Regimen E [Triplet])

- Objective response rate, defined as percentage of patients with confirmed response (CR + PR) as assessed by RECIST Version 1.1 (Dose Escalation, Regimens A through D)
- Progression-free survival, defined as the time from first dose to PD or death, whichever occurs first
- Duration of response, defined as the time from first objective response (CR/PR) to the time of PD among those who have achieved a PR or CR
- Number of patients with GCIG CA125 criteria clinical responses
- Mirvetuximab soravtansine PK parameters for intact ADC, total antibody, DM4, and S-methyl DM4 include, but are not limited to, Cycle 1 and Cycle 3 maximum plasma concentration (Cmax), area under the time-concentration curve (AUC), terminal halflife (t½), clearance (CL), volume of distribution at steady state (Vss), and time that Cmax occurs (tmax)
- Concentration data of bevacizumab, carboplatin, and pegylated liposomal doxorubicin will be measured before and after bevacizumab, carboplatin, and pegylated liposomal doxorubicin infusions (Cycle 1 through Cycle 6)
- Immunogenicity: presence of anti-drug antibodies (ADA) to mirvetuximab soravtansine

3.3. Exploratory Endpoints

The protocol lists the following exploratory endpoints.

- Correlation of FRα expression, by IHC (protein), quantitative reverse transcriptasepolymerasechain reaction (mRNA), or other quantitative methods, to clinical endpoints
- Measure biomarkers in blood and tumor tissue including, but not limited to, mutational and genomic alterations of tumor samples; expression and activation of oncogenic genes and pathways in tumor samples; expression and polymorphism of drug transporters such as multidrug resistance protein-1 (p-glycoprotein [PgP]); the genotype of FcγR; expression and of immune-related genes and gene signatures (Regimen D only), and infiltration of tumor-related immune cells (Regimen D only)
- Concentration data for pembrolizumab if warranted by a safety signal (Regimen D only)
- Evaluate efficacy endpoints per irRECIST (Appendix I) (Regimen D only)
  - Progression-free survival, ORR, and DOR per irRECIST are defined as specified for the respective endpoints using RECIST Version 1.1 above, except that a confirmation assessment of PD (at least 4 weeks after the initial PD assessment) is required for patients who remain on treatment after documented PD per RECIST Version 1.1. Patients who discontinue treatment after documented PD assessment per RECIST Version 1.1 will be counted as having PD on the date of the documented PD assessment.

Note: Unless specifically warranted by relevance to safety or efficacy endpoints, the exploratory endpoints will not be reported in the clinical study report.

4. STUDY DESIGN

4.1. Design Overview

This is an open label, Phase 1b/2, non-randomized combination study of mirvetuximab soravtansine with bevacizumab, carboplatin, pegylated liposomal doxorubicin, pembrolizumab, or bevacizumab + carboplatin in adult patients with FRα−positive advanced EOC, primary peritoneal cancer, or fallopian tube cancer.

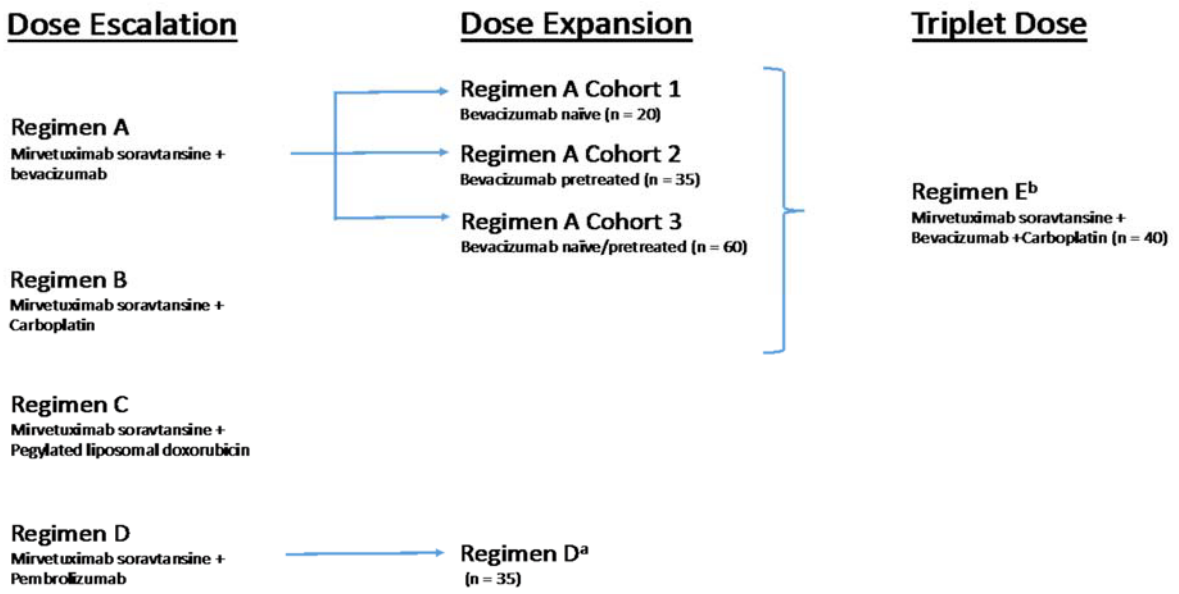
This Phase 1b/2 study comprises a dose escalation phase followed by an MTD expansion phase to further characterize the safety profile and confirm the MTD as the RP2D (Figure 1). A triplet Regimen (Regimen E: mirvetuximab soravtansine + bevacizumab + carboplatin) will be opened to evaluate the safety and toleratiblity and to assess any early signs of activity in patients dosed with the combination regimen.

The dose escalation phase will follow a standard 3+3 cohort design. The MTD will be determined from the assessment of Dose Limiting Toxicities (DLTs) during the first treatment cycle (see Protocol Table 5). A dose expansion phase is planned for Regimen A (mirvetuximab soravtansine + bevacizumab) and Regimen D (mirvetuximab soravtansine + pembrolizumab) and will open pending sponsor decision; patients enrolled in the dose expansion phase will receive study treatment at the MTD or RP2D determined during the dose escalation (Figure 1). For Regimen A, patients in the dose expansion phase may be enrolled according to prior exposure to bevacizumab and disease diagnosis into three dose expansion cohorts as follows: 1) Dose Expansion Cohort 1: bevacizumab naïve; 2) Dose Expansion Cohort 2: bevacizumab pretreated; and 3) Dose Expansion Cohort 3: one to three prior treatments, one of which could have been bevacizumab (Figure 1). Regimen E (Triplet Cohort) will be opened because enrollment and safety from Regimen A and B have been established, and Regimen A (Dose Expansion Cohorts) enrollment is currently ongoing. The planned doses for patients receiving the triplet dose (Regimen E) were derived from all available data in Regimens A and B. Regimen E may enroll approximately 40 patients, with a plan to be dosed at the maximum dose level determined to be safe.

Safety and tolerability will be assessed on an ongoing basis, and patients will be enrolled initially in a stepwise manner.

The period of observation extends from the time the patient receives the first dose of study treatment (mirvetuximab soravtansine and/or combination agent) until the final follow-up study visit. Patients will continue to receive mirvetuximab soravtansine and/or the combination agent until progressive disease (PD); unacceptable toxicity or withdrawal of consent, whichever comes first; or until the Sponsor terminates the study. Patients who experience PD, as defined by RECIST, while on study may remain on study, provided there is evidence of clinical benefit and no unacceptable toxicity, as agreed upon by the Investigator and the Medical Monitor. Pembrolizumab (Regimen D) will be continued for up to 2 years. Patients who discontinue study treatment for reasons other than PD will be followed until PD; start of new anti-cancer therapy; or death, whichever occurs first.

Figure 1: Study Design Schema



[a] Enrolled 46 patients to ensure 35 patients with medium and high FRα expression and 11 patients with low FRα expression
[b] Enroll approximately 50 patients to evaluate 40 patients at the MTD.

4.1.1. Cohort Review Committee

The Cohort Review Committee (CRC) is comprised of the ImmunoGen Medical Monitor and Investigators from participating sites. Once the last patient in a given cohort has completed a cycle of study treatment, a CRC meeting will be convened to review all safety data and decide whether to continue or halt dose escalation, further expand individual dose levels to gain additional safety data, or explore lower or intermediate dose levels. In addition to meeting to review safety data at the end of each dose level, the CRC will convene to review safety data for ongoing patients and patients in follow-up as per the cohort management plan.

4.1.2. Dose Escalation Phase

The primary aim of the dose escalation phase for each Regimen is to evaluate the safety and tolerability of mirvetuximab soravtansine in combination with bevacizumab, carboplatin, pegylated liposomal doxorubicin or pembrolizumab, to identify the MTD and RP2D, and to characterize the PK profile of mirvetuximab soravtansine, bevacizumab, carboplatin and pegylated liposomal doxorubicin. The PK profile of pembrolizumab may be characterized if warranted due to a safety signal.

Patients will be enrolled in cohorts of 3 to 6 patients until the MTD for each of the four regimens is defined. If a patient is eligible for more than one combination regimen, the investigator will assign the patient to the most appropriate combination regimen, taking into consideration the patient's disease history, treatment history, and/or preferences. Approximately 16 (Regimen A), 22 (Regimen B), 22 (Regimen C) and 16 (Regimen D) patients will be enrolled in each regimen, plus additional 10 patients in each arm to define the MTD.

The starting dose of mirvetuximab soravtansine will be 5 mg/kg, with the dose calculated using adjusted ideal body weight (AIBW). The four regimens will be evaluated in parallel and independently.

The treatment regimens and planned dose levels for the dose escalation phase of the study are outlined below and in Table 2, Table 3, Table 4, and Table 5.

Intermediate or lower dose levels of pegylated liposomal doxorubicin, bevacizumab, or carboplatin may be explored if DLTs can be attributed to their mechanism of action. Higher doses of pegylated liposomal doxorubicin (up to 50 mg/m^2) and carboplatin (AUC 6) may also be considered.

Regimen A: Mirvetuximab soravtansine +bevacizumab administered on day 1 of each 21-day cycle; alternatively, mirvetuximab soravtansine administered on day 1 and bevacizumab administered on days 1 and 15 of each 28-day cycle

Regimen B: Mirvetuximab soravtansine + carboplatin administered on day 1 of each 21-day cycle

Regimen C: Mirvetuximab soravtansine + pegylated liposomal doxorubicin administered on day 1 of each 28-day cycle

Regimen D: Mirvetuximab soravtansine + pembrolizumab administered on day 1 of each 21-day cycle

Table 2: Planned Dose Levels (Dose Escalation) for Regimen A (Mirvetuximab Soravtansine + Bevacizumab)

Cohort	Regimen A	
	Mirvetuximab Soravtansine[a] (mg/kg, D1q3W)[b]	**Bevacizumab[c] (mg/kg, D1q3W)**
-1	4	15
1	5	15
2	6	15

[a] Mirvetuximab soravtansine dose calculated using adjusted ideal body weight (AIBW). Maximum allowable dose is 6 mg/kg AIBW.
[b] Day 1, every 3 weeks.
[c] Maximum allowable dose of bevacizumab is 15 mg/kg.

Table 3: Planned Dose Levels (Dose Escalation) for Regimen B (Mirvetuximab Soravtansine + Carboplatin)

Cohort	Regimen B	
	Mirvetuximab Soravtansine[a] (mg/kg, D1q3W)[b]	**Carboplatin[c] (AUC, D1q3W)**
-1	4	AUC4
1	5	AUC4
2	5	AUC5
3	6	AUC5

[a] Mirvetuximab soravtansine dose calculated using adjusted ideal body weight (AIBW). Maximum allowable dose is 6 mg/kg AIBW.
[b] Day 1, every 3 weeks.
[c] Maximum allowable dose of carboplatin is AUC6, subject to CRC review.

Table 4: Planned Dose Levels (Dose Escalation) for Regimen C (Mirvetuximab Soravtansine + Pegylated Liposomal Doxorubicin)

Cohort	Regimen C	
	Mirvetuximab Soravtansine[a] (mg/kg, D1q3W)[b]	**Pegylated Liposomal Doxorubicin[c] (mg/m^2, D1q4W)**
-1	4	30
1	5	30
2	5	40
3	6	40

[a] Mirvetuximab soravtansine dose calculated using adjusted ideal body weight (AIBW). Maximum allowable dose is 6 mg/kg AIBW.
[b] Day 1, every 3 weeks.
[c] The approved dose of pegylated liposomal doxorubicin for ovarian cancer is 50 mg/m^2; however, a decrease in the incidence of hand-foot syndrome was observed at a dose of 40 mg/m^2 without a significant change in efficacy. Maximum allowable dose is 50 mg/m^2, subject to CRC review.

Table 5: Planned Dose Levels (Dose Escalation) for Regimen D (Mirvetuximab Soravtansine + Pembrolizumab)

Cohort	Regimen D	
	Mirvetuximab Soravtansine[a] (mg/kg, D1q3W)[b]	Pembrolizumab[c] (mg, D1q3W)
-1	4	200
1	5	200
2	6	200

[a] Mirvetuximab soravtansine dose calculated using adjusted ideal body weight (AIBW). Maximum allowable dose is 6 mg/kg AIBW.
[b] Day 1, every 3 weeks.
[c] Maximum allowable dose of pembrolizumab is 200 mg.

The dose escalation phase will follow a standard 3+3 cohort design. No intra-patient dose-escalation will be allowed. The MTD will be determined from the assessment of DLTs during the first treatment cycle. See Protocol Section 4.1.3.2 for further dose escalation rules, and Protocol Section 4.1.4 for definition of DLT.

To better characterize safety, 10 patients may receive mirvetuximab soravtansine and the assigned combination agent at the MTD level established for each combination regimen.

4.1.3. Dose Expansion Phase

Once the CRC determines the MTD, the CRC will determine the dose and schedule to be administered in the dose expansion phase. The dose expansion phase will commence enrollment pending sponsor decision. The primary aims of the dose expansion phase are to further evaluate safety and tolerability and to assess preliminary anti-tumor activity of mirvetuximab soravtansine in combination with bevacizumab or mirvetuximab soravtansine in combination with pembrolizumab. Data obtained in the dose expansion phase will help define the RP2D.

Regimen A (Mirvetuximab Soravtansine + Bevacizumab)

Patients enrolled in the dose expansion phase may be assigned to one of two dose expansion cohorts according to previous exposure to bevacizumab as follows:

1. Dose Expansion Cohort 1: bevacizumab naïve; will enroll approximately 20 patients
2. Dose Expansion Cohort 2: bevacizumab pretreated; may enroll 35 patients
3. Dose Expansion Cohort 3: patients with at least one but no more than three prior systemic treatment regimens, where prior regimens may have included bevacizumab; may enroll approximately 60 patients

Regimen D (Mirvetuximab Soravtansine + Pembrolizumab)

The dose expansion phase will enroll sufficient patients to ensure 35 patients have medium or high FRα expression.

Dose expansion is planned for Regimen A and D, pending sponsor decision; however, based on emerging safety and preliminary anti-tumor activity data, the CRC may make the decision to

expand Regimens B and/or C to collect additional safety information. If expanded, Regimens B and C will each enroll a maximum of 20 patients who will be treated at the MTD established for the corresponding regimen.

Safety will be evaluated continuously, separately, and in aggregate in the expansion cohorts. If at any time ≥ 33% of at least 3 patients treated in an expansion cohort experiences a Cycle 1 DLT, further enrollment to that cohort will stop and a CRC will be convened. The CRC will review all available safety data to determine how further dosing should proceed. If it is decided that a new dose should be investigated, enrollment to the cohort will begin anew.

4.1.4. Triplet Dose Cohort (Regimen E)

Following evaluation of the safety, tolerability, and activity data from patients receiving Regimens A and B (dose escalation and dose expansion) in this study, a triplet dose cohort (Regimen E) will be opened. The planned doses for patients receiving the triplet dose are derived from all available data from Regimens A and B. Regimen E may enroll approximately 50 patients, as exploration of alternative doses is required to enroll approximately 40 planned patients to be dosed at the maximum dose level determined to be safe.

The MTD will be determined from the assessment of DLTs during the first treatment cycle.

Initially, six patients will be dosed at the target triplet dose defined in Table 6. If there are <2 Cycle 1 DLTs (total), a further 6 patients will be dosed. If there are <4 Cycle 1 DLTs (total) in all 12 patients, the remaining 28 patients will be enrolled. See Protocol Section 4.1.5 for further dosing rules, and Protocol Section 4.1.4 for definition of DLT.

Table 6: Planned Doses Triplet Cohort Regimen E (Mirvetuximab Soravtansine + Bevacizumab + Carboplatin)

Dose Level	Regimen E		
	Mirvetuximab soravtansine[a] (mg/kg, D1q3W)[b]	Bevacizumab (mg/kg, D1q3W)	Carboplatin[c] (AUC, D1q3W)
-2	5	15	4
-1[d]	6	15	4
-1[e]	5	15	5
1	6	15	5

[a] Mirvetuximab soravtansine dose calculated using adjusted ideal body weight (AIBW).
[b] Day 1, every 3 weeks.
[c] Carboplatin dose may be reduced to AUC4 if safety data from the first 6 or 12 patients suggest the triplet dose is not being tolerated.
[d] Dose reduction of Carboplatin due to Carboplatin associated toxicity.
[e] Dose reduction of mirvetuximab soravtansine due to mirvetuximab soravtansine associated toxicity.

4.1.5. Second Course Phase for Regimen D (Mirvetuximab Soravtansine + Pembrolizumab)

Patients on Regimen D (mirvetuximab soravtansine + pembrolizumab) who stop mirvetuximab soravtansine and pembrolizumab with CR per Protocol Section 5.10.6.4.1 may be eligible for up

to 1 year of additional treatment with pembrolizumab in combination with mirvetuximab soravtansine or as monotherapy if they progress after stopping study treatment. This Second Course Phase of this study is available only if the study remains open and the patient meets the following conditions:

- Stopped initial treatment with mirvetuximab soravtansine and pembrolizumab after attaining an investigator-determined confirmed CR according to RECIST Version 1.1.
  - Was treated for at least 24 weeks with mirvetuximab soravtansine and pembrolizumab before discontinuing therapy.
  - Received at least two treatments with mirvetuximab soravtansine and pembrolizumab beyond the date when the initial CR was declared.

AND

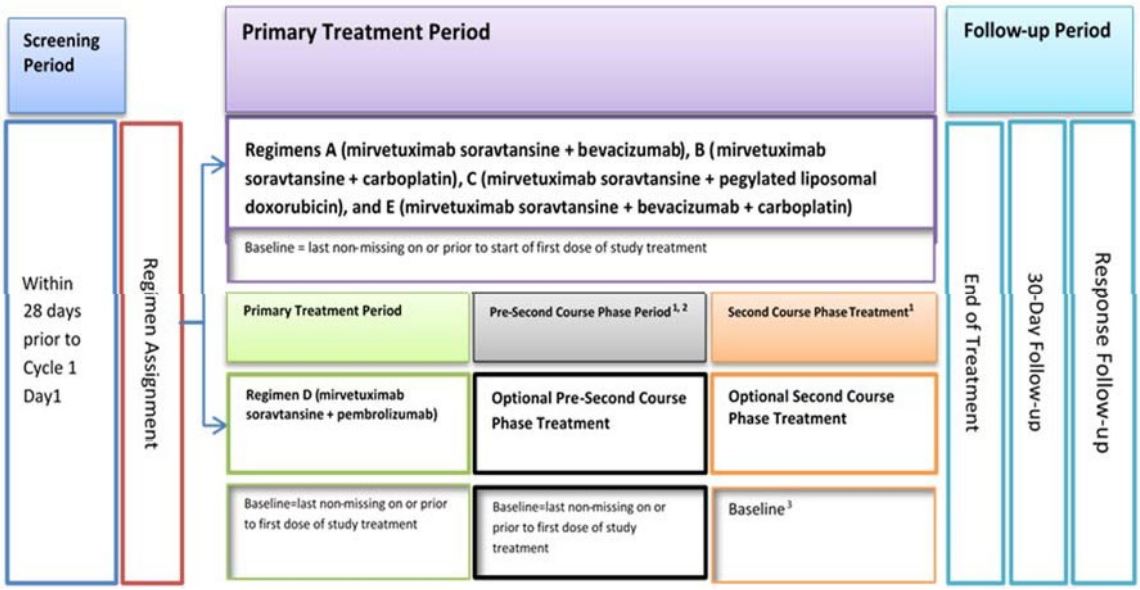
- Experienced Investigator-determined confirmed radiologic PD after stopping their initial treatment with mirvetuximab soravtansine and pembrolizumab.
- Did not receive any anti-cancer treatment since the last dose of mirvetuximab soravtansine and pembrolizumab.
- Has a performance status of 0 or 1 on the ECOG PS.
- Demonstrates adequate organ function as detailed in the inclusion criteria (Protocol Section 3.1).
- If WCBP, defined as a sexually mature woman who has not undergone surgical sterilization or who has not been naturally postmenopausal for at least 12 consecutive months (ie, who has had menses any time in the preceding 12 consecutive months): has a negative serum or urine pregnancy test within 72 hours before receiving retreatment with study medication.
- If WCBP: agrees to use effective contraceptive methods (examples include oral, parenteral, or implantable hormonal contraceptive, intra-uterine device, or vasectomy) while on study treatment and for at least 12 weeks after the last dose of mirvetuximab soravtansine and for at least 4 months after the last dose of pembrolizumab.
- Does not have a history or current evidence of any condition, therapy, or laboratory abnormality that a) might interfere with the patient's participation for the full duration of the study, or b) makes it not in the best interest of the patient to participate, in the opinion of the treating Investigator.

Patients who restart treatment will be retreated at the same dose frequency as when they last received pembrolizumab and mirvetuximab soravtansine. Treatment will be administered for up to 1 additional year. Patients will follow the Schedule of Clinical Assessments in Protocol Appendix C.

4.2. Study Period Schema

Figure 2 below illustrates the Study Periods for each Regimen. The periods are defined by regimen and will be the same for the Dose Escalation and Dose Expansion phases of the trial.

Figure 2: Study Period Schema



[1] Discontinuation of treatment may be considered for patients who have attained a confirmed complete response (CR) that have been treated for at least 24 weeks with mirvetuximab soravtansine+pembrolizumab and had at least 2 cycles with mirvetuximab soravtansine+pembrolizumab beyond the date when the initial CR was declared. Retreatment with pembrolizumab in combination with mirvetuximab soravtansine or as monotherapy may be considered if the patient has a CR and meets the criteria in the protocol.

[2] This is the period of time between the discontinuation of pembrolizumab or mirvetuximab soravtansine+pembrolizumab, and the start of the second course phase treatment.

[3] Second Course Phase Treatment has separate baselines for efficacy and safety analyses. For safety analyses, the baseline is the same as the baseline for the Primary Treatment period (i.e. the last non-missing value on or prior to the first dose of study treatment). For efficacy analyses, the baseline is the last non-missing value on or prior to the first SCP treatment.

4.3. Study Population

See Protocol Section 3.1 for a complete list of the inclusion/exclusion criteria.

4.3.1. Enrolled Patient and Screen Failure Definitions

Patients who have signed an IRB/IEC approved informed consent form the study and who have received at least one dose of study treatment will be considered enrolled. Patients who are issued a patient number, but who do not successfully complete the screening process and who do not receive a dose of mirvetuximab soravtansine and/or combination drug will be considered a screen failure. Patient numbers for patients who screen fail will not be re-issued.

4.4. Sample Size Predictions

4.4.1. Dose Escalation

Ascending doses of mirvetuximab soravtansine and bevacizumab, carboplatin, pegylated liposomal doxorubicin or pembrolizumab are to be evaluated to identify the MTD for each of the four combination regimens. The actual number of patients accrued during the dose escalation phase will be determined largely by the findings observed during the course of their treatment. Regimen A (mirvetuximab soravtansine + bevacizumab) is expected to enroll 16 patients whereas Regimens B (mirvetuximab soravtansine + carboplatin) and C (mirvetuximab soravtansine + pegylated liposomal doxorubicin) are expected to enroll 22 patients. Regimen D (mirvetuximab soravtansine + pembrolizumab) is expected to enroll 16 patients.

For all four regimens, 10 patients may be treated at the MTD.

Overall, the dose escalation phase of the study is expected to enroll approximately 76-120 patients.

4.4.2. Dose Expansion

Following MTD determination, there will be an expansion phase for Regimen A (mirvetuximab soravtansine + bevacizumab) and Regimen D (mirvetuximab soravtansine + pembrolizumab). Overall, the dose expansion phase is expected to enroll up to 130 patients.

Regimen A (Mirvetuximab Soravtansine + Bevacizumab)

Patients enrolled in the dose expansion phase will be allocated to three Dose Expansion Cohorts according to prior exposure to bevacizumab and disease diagnosis as follows: 1) Dose expansion Cohort 1: bevacizumabnaïve; 2) Dose expansion Cohort 2: bevacizumab pretreated; and 3) Dose expansion cohort 3: patients with at least one but no more than three prior systemic treatment regimens, where prior regimens may have included bevacizumab.

For the bevacizumab naïve cohort (Cohort 1), assuming a response rate of 55%, there is a 94.2% probability of detecting at least 8 responders if 20 patients are recruited. The response rate assumption is based on an ORR of 53% observed with the standard of care therapy of paclitaxel in combination with bevacizumab in patients with platinum-resistant EOC (Bevacizumab [package insert] 2014).

For the bevacizumab pretreated cohort (Cohort 2), assuming a response rate of 50%, there is a 91.2% probability of detecting at least 14 responders if 35 patients are recruited.

For the bevacizumab expansion cohort 3, assuming a response rate of 50%, there is a 95.4% probability of detecting at least 24 response if 60 patients are recruited. In addition, the 90% confidence interval for true ORR is given in Table 7 below if the observed number of responders is between 20 and 40 of 60 patients.

Table 7: Confidence Interval (90%) for True ORR with Sample Size = 60

Responses Observed, 60 patients	90% Exact Confidence Interval for True ORR
20/60 (33%)	(23%, 45%)
21/60 (35%)	(25%, 46%)
22/60 (37%)	(26%, 48%)
23/60 (38%)	(28%, 50%)
24/60 (40%)	(29%, 51%)
25/60 (42%)	(31%, 53%)
26/60 (43%)	(32%, 55%)
27/60 (45%)	(34%, 56%)
28/60 (47%)	(36%, 58%)
29/60 (48%)	(37%, 60%)
30/60 (50%)	(39%, 61%)
31/60 (52%)	(40%, 63%)
32/60 (53%)	(42%, 64%)
33/60 (55%)	(44%, 66%)
34/60 (57%)	(45%, 68%)
35/60 (58%)	(47%, 69%)
36/60 (60%)	(49%, 71%)
37/60 (62%)	(50%, 72%)
38/60 (63%)	(52%, 74%)
39/60 (65%)	(54%, 75%)
40/60 (67%)	(55%, 77%)

Regimen D (Mirvetuximab Soravtansine+ Pembrolizumab):

In the dose expansion phase for Regimen D, a total of 35 patients will be enrolled with medium or high FRα expression and 11 patients with a low FRα expression. Assuming a response rate of 50%, there is a 91.2% probability of detecting at least 14 responders if 35 patients are recruited. In addition, the 90% confidence interval for true ORR is given in Table 8 below if the observed number of responders is 12-18 out of 35 patients.

Table 8: Confidence Interval (90%) for True ORR with Sample Size = 35

Responses observed out of 35 patients	90% exact confidence interval for true ORR rate
12/35 (34%)	(21%, 50%)
13/35 (37%)	(24%, 52%)
14/35 (40%)	(26%, 55%)
15/35 (43%)	(29%, 58%)
16/35 (46%)	(31%, 61%)
17/35 (49%)	(34%, 64%)
18/35 (51%)	(36%, 66%)

Regimen E (Mirvetuximab Soravtansine + Bevacizumab + Carboplatin):

In Regimen E (triplet), approximately 50 patients will be enrolled to ensure 40 patients will be treated at the MTD. Assuming a response rate of 60%, there is a 92.6% probability of detecting at least 20 responders if 40 patients are recruited. In addition, the 90% confidence interval for true ORR is given in Table 9 if the observed number of responders is 20-26 out of 40 patients.

Table 9: Confidence Interval (90%) for True ORR with Sample Size = 40

Responses observed out of 40 patients	90% exact confidence interval for true ORR rate
20/40 (50.0%)	(36%, 64%)
21/40 (52.5%)	(38%, 66%)
22/40 (55.0%)	(41%, 69%)
23/40 (57.5%)	(43%, 71%)
24/40 (60.0%)	(46%, 73%)
25/40 (62.5%)	(48%, 75%)
26/40 (65.0%)	(51%, 77%)

4.4.3. Overall

Overall, the dose escalation phase of the study is expected to enroll approximately 76-120 patients and the dose expansion phase is expected to enroll up to 211 patients. Assuming that approximately 90% of enrolled patients will be evaluable, the trial is projected to accrue approximately 311-355 patients.

4.5. Treatment Randomization

No randomization will be performed in this study.

4.6. Assessment Schedule

See Protocol Appendices A-D for the study schedule of assessments.

5. INTERVENTIONS

5.1. Clinical Trial Material

For all regimens, the total dose of mirvetuximab soravtansine will be calculated according to AIBW. Mirvetuximab soravtansine should be administered first, followed by the assigned combination drug (bevacizumab, carboplatin, pegylated liposomal doxorubicin or pembrolizumab).

For Regimen A (Mirvetuximab Soravtansine + Bevacizumab):

Mirvetuximab soravtansine and bevacizumab will be administered on day 1 of each 21-day cycle.

For Regimen B (Mirvetuximab Soravtansine + Carboplatin):

Mirvetuximab soravtansine and carboplatin will be administered on day 1 of each 21-day cycle.

For Regimen C (Mirvetuximab Soravtansine + Pegylated Liposomal Doxorubicin):

Mirvetuximab soravtansine and pegylated liposomal doxorubicin will be administered on day 1 of each 28-day cycle.

For Regimen D (Mirvetuximab Soravtansine + Pembrolizumab):

Mirvetuximab soravtansine and pembrolizumab will be administered on day 1 of each 21-day cycle.

For Regimen E (Mirvetuximab Soravtansine + Bevacizumab + Carboplatin):

Mirvetuximab soravtansine, followed by bevacizumab and then carboplatin will be administered on day 1 of each 21-day cycle.

Protocol Section 5 provides additional details.

6. GENERAL ANALYTICAL CONSIDERATIONS

6.1. Data Sources

Data are recorded on electronic case report forms (eCRFs). Central laboratory data will be provided via electronic data transfers. Protocol Section 12 provides additional details regarding data recording and handling.

6.2. Definition of Baseline

Study Day 1 will be designated as the first day a patient receives study drug (i.e. Cycle 1 Day 1). The baseline value for the Primary Treatment period is defined as the last non-missing value on or prior to the first dose of study treatment. Patients in Regimen D who experience a CR may withdraw from treatment and enter the optional Pre-Second Course Phase period. The baseline for the Pre-Second Course Phase period will be the same as the baseline for the Primary Treatment period (i.e. the last non-missing value on or prior to the first dose of study treatment). For patients in Regimen D who enter the optional Second Course Phase Treatment period, the baseline for the Second Course Phase for efficacy analyses will be the last non-missing

assessment following the last mirvetuximab soravtansine+pembrolizumab treatment in the Primary Treatment period, and on or prior to the first mirvetuximab soravtansine+pembrolizumab or pembrolizumab treatment in the Second Course Phase treatment period. The baseline for the Second Course Phase for safety analyses will be the last non-missing value on or prior to the first dose of study treatment (note: this is the same as the baseline definition for the primary treatment period). For ECG assessments, this may be the average of replicate readings.

6.3. Missing Data

Partial dates are allowed on the CRF for Adverse Event (AE) onset and resolution dates, Concomitant Medication (CM) start and stop dates, and Concomitant Procedure (CP) procedure dates. An entry for the year is required in the eCRF system for each of these dates. Only the month and day may be entered as unknown. Dates from these forms will be reported in listings as collected. Every effort will be made to query missing dates.

For records with a missing AE onset date, the following procedure will be employed for use in determining whether the AE is treatment-emergent:

- AE onset dates with missing day and non-missing month will be assumed to occur on the first day of the non-missing month, except for AEs occurring in the first month of dosing, in which case the date will be the first day of dosing.
- AE onset dates with missing month will be assumed to occur on the first day of the non-missing year (i.e. January 1), except for AEs occurring in the first year of dosing, in which case the date will be the first day of dosing.

For records with a missing medication start and/or stop date, the following procedure will be employed for use in determining whether the medication is prior or concomitant:

- Medication start dates with a missing day and non-missing month will be assumed to occur on the *first* day of the non-missing month, except for medications occurring in the first month of dosing, in which case the date will be the first day of dosing.
- Medication start dates with missing month will be assumed to occur on the *first* day of the non-missing year (i.e. January 1), except for medications occurring in the first year of dosing, in which case the date will be the first day of dosing.
- Medications that are *not* ongoing, and have a medication stop date with a missing day and non-missing month will be assumed to occur on the *last* day of the non-missing month.
- Medications that are *not* ongoing, and have a medication stop date with a missing month will be assumed to occur on the *last* day of the non-missing year (i.e. December 31).

For records with a missing procedure date, the following procedure will be employed for use in determining whether the procedure is prior or concomitant:

- Procedure dates with a missing day and non-missing month will be assumed to occur on the first day of the non-missing month, except for procedures occurring in the first month of dosing, in which case the date will be the first day of dosing.

- Procedure dates with missing month will be assumed to occur on the first day of the non-missing year (i.e. January 1), except for procedures occurring in the first year of dosing, in which case the date will be the first day of dosing.

All other data will be reported as they are collected. No imputation methods will be used to replace missing data unless otherwise stated in this document.

6.4. Multiple Assessments for the Same Assessment Time Point

In the case of multiple observations at a specific visit, the first non-missing measurement will be used for analysis, unless multiple study assessments are expected (e.g. pre-dose vs. post-dose). When multiple study assessments are expected, the first non-missing measurement for the visit and assessment time point will be used for analysis. The exception to this rule will be for triplicate ECGs, for which the average of the three triplicates will be used for analysis.

6.5. Multiple Study Centers

No adjustment for study center is planned.

6.6. Covariate Adjustment in Primary Analysis

No covariate adjustments are planned.

6.7. Sample Size Reassessment

Not applicable.

6.8. Interim Analyses or Timing of Analyses

No formal interim analysis is planned for this study. However, a review of safety data will be conducted by the CRC upon completion of each dose escalation cohort, and at least every 4 weeks during MTD Dose Expansion. Results from this data review could enable selection of dose for additional studies with mirvetuximab soravtansine, before full completion of this study.

6.9. Test Sizes

No formal statistical hypothesis tests are planned. 95% confidence intervals will be provided where specified. Any tested hypotheses will be tested against two-sided alternatives, using procedures that provide an expected probability of Type I error (α) of 0.05.

6.10. Multiple Comparisons

No control for the effect of multiple comparisons is planned.

6.11. Analysis Populations

Four analysis populations will be defined for use with various analyses. The following table illustrates the relationship between each population and the analyses for which the data from the population will be used.

Analysis Population	Analysis			
	Baseline	Patient Disposition	Efficacy	Safety
Safety	X	X		X
Response- Evaluable			X	
CA125 Evaluable			X	

6.11.1 Screened

The Screened population includes all patients entered into the eCRF system who have signed an informed consent.

6.11.2 Safety Population

All patients who received at least one dose of study treatment (mirvetuximab soravtansine, bevacizumab, carboplatin, pegylated liposomal doxorubicin or pembrolizumab) will be included in the Safety population.

6.11.3 Response-Evaluable Population

To meet the definition of response-evaluable, patients must have undergone radiographic assessment at baseline, received at least one dose of combination treatment (i.e. mirvetuximab soravtansine with bevacizumab, carboplatin, pegylated liposomal doxorubicin or pembrolizumab), and must have had at least one post-dose radiographic tumor assessment or have died with 105 days of first dose.

6.11.4 CA125 Evaluable Population

The CA125 evaluable population is defined as all patients whose pretreatment sample is ≥ 2.0 times the ULN, within 2 weeks prior to the first dose of combination treatment, and who have at least one post-baseline CA125 evaluation.

6.12. Data Display Characteristics

Data displays produced for this study will include three types—summary tables, data listings, and figures. Unless stated otherwise, data listings will be produced for all recorded data. Summary tables will be produced as specified in the following sections. Additional data listings will be produced for outcome measures that involve extensive procedures to derive the analyzed outcomes. Figures will be produced when specified in sections to follow.

Unless otherwise specified, tables and figures will be presented separately for the Dose Escalation and Dose Expansion phases of the study. Data listings will display data from both phases of the study.

Data listings will simply list the data recorded on the eCRF or derived for each patient. They will be ordered by study phase (Dose Escalation followed by Dose Expansion), treatment, site, patient number, and date/time of assessment. When expedient, additional levels of ordering hierarchy may reflect subsets of assessments within patient. Data listings will not display patient initials.

Summary tables will display summary statistics calculated for each regimen and cohort. Separate tables will be generated for each regimen, and the presentation of cohorts will depend on the type of analysis, as described in the following sections.

Summaries of demographics, disposition, and baseline characteristics will be presented by escalation cohort for Regimens B and C, and will include a total column summarizing all escalation cohorts. For Regimens A and D, summaries will be presented by escalation and expansion cohort, and will include a total column summarizing all escalation and expansion patients who receive a full dose of mirvetuximab soravtansine**.** All patients enrolled in Regimen E will be summarized in one column. Each regimen will be presented on a separate page.

Summaries of safety data will be presented by dose cohort for Regimens B and C and will not include a total column. For Regimens A and D, summaries will be presented by dose cohort, combining patients who receive a full dose of mirvetuximab soravtansine. All patients enrolled in Regimen E will be summarized in one column. Each regimen will be presented on a separate page.

Summaries of efficacy data will be presented for all dosed patients by escalation cohort for Regimens B and C and by escalation and expansion cohort for Regimens A and D. A total column will be included. For Regimen E, efficacy endpoints will be summarized in one column.

The summary statistics displayed will be a function of the type of data associated with the summarized assessment. Unless stated otherwise in relevant sections to follow, continuous data will be summarized with the number of non-missing values, mean, standard deviation, minimum, median, and maximum. Categorical data will be summarized with the number of non-missing values and the numbers of values equal to each of the possible values. Percentages of patients with each of the possible values will be calculated from the number of patients in the corresponding analysis population, unless stated otherwise. Some continuous variables may also be grouped into categorical levels and evaluated in frequency tables.

7. PATIENT ACCOUNTABILITY

7.1. Patient Characteristics

Patient characteristics will be summarized for the Safety population using the treatment actually received (i.e. the actual treatment arm variable(s) in SDTM/ADaM).

Demography. Data collected about the following patient characteristics at the screening visit will be summarized:

- Age. Age is collected in the eCRF system. As this is a global study, there are certain regions where local regulations prohibit the collection of a complete date of birth. Therefore, age will not be recalculated for analysis purposes. The collected age will be used for summarization.
- Sex and childbearing potential yes/no
- Ethnicity
- Race

All demography data including informed consent date will be listed.

Height, Baseline Weight, Baseline AIBW and Baseline BSA. Height, baseline weight, baseline AIBW and baseline body surface area (BSA) will be summarized by treatment group and presented in a listing. Note that BSA is collected depending on the treatment group (i.e. combination agent) to which a patient is assigned. Thus, baseline BSA will only be summarized for the treatment groups for which these data are available.

Medical History. Medical history will be coded using MedDRA (version 21.0 or later), associating lower-level terms with preferred terms and system organ classes by the primary hierarchy. Medical Histories will be summarized as the numbers and percentages of patients who reported at least one medical history event, numbers and percentages of patients who reported at least one medical history event in each system organ class. Within each system organ class, the tables will display the counts and percentages of patients reporting at least one medical history event as designated by the preferred terms. All medical history information will also be listed.

Disease Characteristics, Prior Therapy, and Gene Mutations. Listings of all collected data related to disease characteristics and prior therapy will be provided. A summary of the following elements will also be provided:

- Primary diagnosis (epithelial ovarian, fallopian tube, primary peritoneal, other)
- Folate receptor alpha status
  - low
  - medium
  - high
- BRCA mutation status
- Histology
- Stage at initial diagnosis
- Histologic grade
- Prior radiotherapy (yes/no)
- Prior systemic therapy (yes/no, number of prior therapies)
  - The number of prior systemic therapies is defined as the number of distinct regimens.
    - Adjuvant±Neoadjuvant will be considered as one regimen
    - Maintenance therapy will be considered to be part of the preceding regimen
    - PARP inhibitor therapy will be considered as a prior treatment
- Prior surgery (yes/no)
- Baseline ECOG performance status

- Platinum free interval, definded as time from last dose of prior platinum therapy to disease progression or relapse following last line of prior platinum therapy (<=6 months, > 6 months) (Regimen A only)

7.2. Patient Disposition

7.2.1 Screened Patients

For patients who failed screening, the number and percentage of patients will be summarized in a table by the reasons for screen failure. The reasons for screen failure will also be provided in a listing.

7.2.2 Safety Population

Disposition will be summarized for the Safety population using the treatment actually received (i.e. the actual treatment arm variable(s) in SDTM/ADaM).

Safety Disposition. A summary of patient disposition will summarize, for the Safety population, the numbers of patients who received study treatment and the reasons for treatment and study discontinuation. For Regimen D, the number of patients who continued into the Pre-Second Course Phase and Second Course Phase of treatment and the reasons for Second Course treatment discontinuation will be provided.

Percentages of patients who withdrew for each of the reasons on the End of Treatment and End of Study forms will be calculated using all members of the Safety population in the relevant treatment group for the denominator. For Regimen D, Second Course Phase of treatment summary, percentages of patients who withdrew for each of the reasons on the Second Course End of Treatment form will be calculated using the number of patients who entered the Second Course Phase of treatment as the denominator.

A listing of the End of Treatment and End of Study information will be provided for the Safety population.

Deaths. A summary table and listing of all reported deaths will be provided.

7.3. Protocol Deviations and Population Inclusions

Protocol deviations will be summarized for the Safety population using the treatment actually received (i.e. the actual treatment arm variable(s) in SDTM/ADaM).

Protocol deviations will be captured in a protocol deviation log. A summary of the number of patients with any protocol deviation by treatment group will be provided.

Protocol deviations will also be summarized by the following categories:

- Those who entered the study even though they did not satisfy the entry criteria
- Those who developed withdrawal criteria during the study but were not withdrawn
- Those who received the wrong treatment or incorrect dose
- Those who received an excluded concomitant treatment

The summary will be grouped first by deviation categories and then by site within each deviation category.

A listing from the protocol deviation log will be provided for patients who were enrolled even though they did not meet one or more eligibility criteria and patients who met withdrawal criteria discernible from recorded data during the study but were not withdrawn.

A hierarchical table of the populations in which Screened patients were included will summarize the relationship of the analysis populations. The number of screened patients will be provided in the Total column. Given population definitions, the Safety population will be treated as the starting, parent population. The numbers and percentages of Safety patients included in the Response-Evaluable population, and the CA125 Evaluable population will be presented for each treatment group.

8. EFFICACY ANALYSES

All efficacy analyses for RECIST-related variables will use data from the Response-Evaluable population. CA125 response analyses will use the CA125 Evaluable population. Patients will be analyzed by the treatment they actually received (i.e. the actual treatment arm variable(s) in SDTM/ADaM).

8.1. Efficacy Outcomes

CA125 Response. A CA125 response is defined as a ≥ 50% reduction in CA125 levels from baseline. The response must be confirmed and maintained for at least 28 days. The CA125 response will be analyzed using the CA125 Evaluable population. The date of response corresponds to the date when the CA125 level is first reduced by 50% or more. The summary table for CA125 will include a summarization of the n (%) of patients in the CA125 Evaluable population, and that n will then be used as the denominator for CA125 response rate.

RECIST and Immune-Related RECIST (irRECIST) Related Endpoints. Tumor response will be measured by RECIST v1.1 for Regimens A, B, C, D, and E. Immune-related RECIST (irRECIST) will be used to evaluate tumor response for Regimen D. All endpoints described below will use RECIST or irRECIST based on the regimen. PFS, ORR and DOR per irRECIST are defined as specified for the respective endpoints using RECIST 1.1 below, with the exception that a confirmation assessment of PD (at least 4 weeks after the initial PD assessment) is required for patients who remain on treatment following a documented PD per RECIST 1.1. Patients who discontinue treatment following a documented PD assessment per RECIST 1.1 will be counted as having disease progression on the date of the documented PD assessment. See Protocol Appendix I for further details.

Best Overall Response (BOR). Best overall response for a patient is the best response designation as assessed by the investigator, recorded between the date of the first dose of study treatment and the date of objectively documented progression per RECIST v1.1 or the date of treatment discontinuation, whichever occurs first. Patients with an overall response of CR or PR must have a repeat tumor assessment performed no less than 4 weeks (28 days) after the criteria for response are first met. Patients with an overall response of SD must have a minimum duration of 35 days (6 weeks – 1 week window = 35 days; with 6 weeks being the most frequent

scheduled radiographic tumor assessment for the study). The confirmatory scan is valid following treatment discontinuation as long as the patient has not started a new anti-cancer therapy.

Objective Response Rate (ORR). The ORR will be calculated as the number of patients with a BOR of CR or PR divided by the number of patients in the analysis population. Patients without at least one post-baseline RECIST assessment will be treated as non-responders. That is, these patients will contribute to the denominator, but not the numerator. Response or progression in the Second Course Phase for Regimen D patients will not count towards the ORR of the primary endpoint in this trial.

Progression Free Survival (PFS). PFS is defined as the time from the date of the first dose of study drug until the date of progressive disease (PD) or death from any cause, whichever occurs first. PFS is defined based on radiological assessments and determined by the investigator. Clinical progression is not considered a progression endpoint.

Table 10 provides a summary of the rules to be used for PFS. When an analysis cutoff date is implemented, only data (deaths and radiological assessments) occurring on or prior to the cutoff date will be used for analysis.

Table 10: PFS Definitions (includes investigator assessed radiographic progression only)

Situation	Date of PFS Event or Censoring	Outcome
No baseline tumor assessments or post-baseline radiological assessments and patient did not die within 105 days of Day 1	Date of first dose of study drug	Censored
No baseline tumor assessments or post-baseline radiological assessments and patient died within 105 days of Day 1	Date of death	Death
Death	Date of death	Death
Radiological Progression	Date of first radiological assessment indicating progression (i.e Overall Response = Progressive Disease on RECIST Response CRF).	Progression
New anti-cancer therapy prior to PD or death (including palliative radiotherapy during study treatment)	Date of last radiological assessment prior to the start of the new anticancer therapy	Censored
No death or progression	Date of last radiological assessment	Censored
PD or death after missing two or more consecutive radiological assessments (PD or death date – last radiological assessment date +1 >=105 days)	Date of last adequate radiological assessment showing no PD	Censored

Duration of Response (DOR). DOR is defined as the time from the date of the first response (CR or PR), whichever is recorded first, to the date of progressive disease (PD) or death from any

cause, whichever occurs first. Duration of response is only defined for patients who have a best overall response of CR or PR.

Per the BOR definition, patients with an overall response of CR or PR must have a repeat tumor assessment performed no less than 4 weeks after the criteria for response are first met. The first date at which a CR or PR response was noted will be used to calculate DOR, not the date of the confirmatory tumor assessment.

Patients who started a new anti-cancer therapy prior to documented PD or death will be censored at the last radiological assessment prior to initiation of new anti-cancer therapy. Patients who did not have PD or death will be censored at the date of their last radiological assessment. Patients who had PD or death after missing two or more consecutive radiological assessments (PD or death date – last radiological assessment date +1 >=105 days) will be censored at the date of their last radiological assessment. When an analysis cutoff date is implemented, only data (deaths or radiological assessments) occurring on or prior to the cutoff date will be used for analysis.

Overall Survival (OS). OS is defined as the time from the date of the first dose of study treatment until the date of death from any cause.

Patients who are alive or lost to follow-up at the analysis are censored at the last known date at which they were known to be alive. When an analysis cutoff date is implemented, only deaths occurring on or prior to the cutoff date are counted as OS events. Patients whose date of death or last date at which the patient was known to be alive is after the data cutoff date will be censored at the analysis cutoff date.

Table 11 provides a summary of the efficacy analyses planned for the study. These analyses are further described in Section 8.2, Section 8.3, and Section 8.4 below.

Table 11: Summary of Efficacy Analysis

Efficacy Analysis		**Regimen**						
		A		**B**	**C**	**D**		**E**
		Esc	**Exp**	**Esc**	**Esc**	**Esc**	**Exp**	
Primary	Number of Patients with RECIST 1.1 Clinical Responses Objective Response Rate		X				X	X
Secondary	Number of Patients with RECIST 1.1 Clinical Responses Objective Response Rate	X		X	X	X		
	RECIST 1.1 Progression-Free Survival	X	X	X	X	X	X	X
	RECIST 1.1 Duration of Response	X	X	X	X	X	X	X
	Number of Patients with Gynecologic Cancer Intergroup (GCIG) CA125 Criteria Clinical Responses	X	X	X	X	X	X	X

Efficacy Analysis		Regimen						
		A		B	C	D		E
		Esc	Exp	Esc	Esc	Esc	Exp	
	CA125 Response Rate							
	Overall Survival	X	X	X	X	X	X	X
Exploratory	Number of Patients with irRECIST Clinical Response Objective Response Rate Progression Free Survival Duration of Response					X	X	

8.2. Primary Efficacy Outcome Analysis

There is no primary efficacy endpoint for the Dose Escalation phase of the study.

The protocol specifies the following primary efficacy endpoints for the Dose Expansion phase of the study:

Regimen A and Regimen D (Dose Expansion cohorts) and Regimen E

- Number of patients with RECIST 1.1 criteria clinical responses
- RECIST 1.1 objective response rate (ORR)
- Note: Response or progression in the Second Course Phase for Regimen D patients will not count towards the ORR of the primary endpoint in this trial.

8.3. Secondary Efficacy Analyses

The protocol describes the following secondary efficacy endpoints:

Regimens A through D (Dose Escalation cohorts)

- Number of patients with RECIST 1.1 criteria clinical responses
- RECIST 1.1 objective response rate (ORR)

Regimens A through D (Dose Escalation and Dose Expansion cohorts) and Regimen E

- RECIST 1.1 progression-free survival (PFS)
- RECIST 1.1 duration of response (DOR)
- Number of patients with GCIG CA125 criteria clinical responses
- GCIG CA125 Response Rate
- Overall Survival (OS)

The distribution of time-to-event variables (PFS, DOR, and OS) will be summarized using the Kaplan-Meier method. Median times will be estimated for each treatment group from the 50th percentile of the corresponding Kaplan-Meier estimates. The 6 month rates will be estimated for

each treatment group from the corresponding Kaplan-Meier estimates at the 6 month time point. The 95% confidence intervals will also be provided.

8.4. Exploratory Efficacy Analyses

The protocol describes the following exploratory efficacy endpoints for Regimen D only:

Regimen D (Dose Escalation and Dose Expansion cohorts)

- Number of patients with irRECIST 1.1 criteria clinical responses
- irRECIST 1.1 objective response rate (ORR)
- irRECIST 1.1 duration of response (DOR)
- irRECIST 1.1 progression-free survival (PFS)

The distribution of time-to-event variables (PFS, DOR) will be summarized using the Kaplan-Meier method. Median time will be estimated for each treatment group from the 50^{th} percentile of the corresponding Kaplan-Meier estimates. The 6 month rate will be estimated for each treatment group from the corresponding Kaplan-Meier estimates at the 6 month time point. The 95% confidence interval will also be provided.

8.5. Efficacy Analysis on Subgroups of Patients

Efficacy analysis on the following subgroups of patients will be conducted for Regimens A, D and E for patients receiving full dosing of mirvetuximab soravtansine (6 mg/kg) in either escalation or expansion cohorts.

- Folate receptor alpha status (FRα)
  - Low (Regimens A and D only)
  - medium
  - high
- Number of prior lines of therapy
  - 1
  - 2-3
  - ≥4 (Regimens A and D only)
- Platinum free interval (Regimen A only)
  - ≤ 6 months
  - > 6 months
- Prior exposure to bevacizumab (Regimen A only)
  - Yes
  - No

8.6. Sensitivity Analyses

No formal sensitivity analyses are planned.

8.7. Other Efficacy-related Summaries

Listings of efficacy-related data will include:

- All lesion assessments (target lesion, non-target lesion, new lesion)
- Investigator's RECIST assessments
- CA125 results
- Derived parameters for CA125 response, BOR, PFS, DOR, and OS
- Censoring for time-to-event variables

9. SAFETY ANALYSES

Safety analyses will use data from the Safety population. Patients will be analyzed according to the actual study treatment received (i.e. the actual treatment arm variable(s) in SDTM/ADaM).

9.1. Exposure

Exposure to mirvetuximab soravtansine, bevacizumab, carboplatin, pegylated liposomal doxorubicin, and pembrolizumab will be summarized with descriptive statistics for the number of doses received, the number of cycles received, duration of dosing (weeks), total cumulative dose (AUC for carboplatin, mg for remaining investigational products), and total volume infused (mL). Absolute dose intensity and relative dose intensity will also be calculated and summarized for each investigational product, as shown in the following table.

Investigational Product		**Absolute Dose Intensity[1]**	**Relative Dose Intensity**
Mirvetuximab Soravtansine	Units	mg/kg/dose	%
	Calculation	Total Cumulative Dose (mg)/ Expected Number of Doses/AIBW (kg)	[Absolute Dose Intensity/6] x 100%
Bevacizumab	Units	mg/kg/dose	%
	Calculation	Total Cumulative Dose (mg)/ Expected Number of Doses/ Body Weight at C1D1 (kg)	[Absolute Dose Intensity/15] x 100%
Carboplatin	Units	mg/m^2/week	N/A
	Calculation	Total Cumulative Dose (mg)/ BSA (m^2) / Duration of dosing (weeks)	N/A
Pegylated Liposomal Doxorubicin	Units	mg/m^2/dose	%
	Calculation	Total Cumulative Dose (mg)/ Expected Number of Doses/BSA (m$^{2)}$	[Absolute Dose Intensity/40] x 100%
Pembrolizumab	Units	mg/dose	%
	Calculation	Total Cumulative Dose (mg)/ Expected Number of Doses	[Absolute Dose Intensity/200] x 100%

[1] For investigational products administered Q3W (mirvetuximab soravtansine, bevacizumab, carboplatin, pembrolizumab), the expected number of doses is defined as the duration of dosing in weeks / 3, where duration of dosing is defined as (date of last dose – date of first dose + 21) / 7. For investigational products administered Q4W (pegylated liposomal doxorubicin), the expected number of doses is defined as the duration of dosing in weeks / 4, where duration of dosing is defined as (date of last dose – date of first dose + 28) / 7.

The number of infusions with dose decreased, infusions interrupted, and dose delayed will also be summarized by regimen and study drug. The number of infusions with the rate of infusion decreased will also be summarized for the mirvetuximab soravtansine infusions.

Listings will be provided with the information from all of the study drug administration eCRFs (including mirvetuximab soravtansine administration, bevacizumab administration, carboplatin administration, carboplatin desensitization, pegylated liposomal doxorubicin administration, and pembrolizumab administration).

9.2. Adverse Events

Adverse events (AEs), will be documented on the AE eCRF and monitored continuously throughout the study from the time of the first dose of study treatment until 30 days after the patient's last study treatment or until the event has resolved, stabilized or an outcome has been reached, whichever comes first. AEs attributed to study procedures, including those events that occur prior to the first dose, should also be documented on the AE eCRF. Any other change in

medical condition, which occurs during the interval between consent and first dose, will be documented on the medical history eCRF.

For patients who discontinue study treatment due to a study-related AE, the reporting time-period may be extended. These patients must be followed at least once a week for four weeks, and subsequently at 4-week intervals until resolution or stabilization of the adverse event or laboratory abnormality, whichever comes first.

Adverse event (AE) data are available to ImmunoGen from two sources, the eCRFs and the SAE forms. While reconciliation will be performed, the production of data summaries and listings will be based on the data collected on the eCRF.

Pre-treatment AEs are defined as AEs with an onset date prior to the first dose of study drug. Treatment-emergent adverse events (TEAEs) are defined as adverse events with an onset date on or after the first dose of study drug, and within 30 days of the last dose of study drug (inclusive of all treatment periods, primary and SCP treatment if applicable). Medical history conditions that exist before the initiation of study treatment but worsen in severity during the study will also be recorded on the AE eCRF as an AE, and will be included as treatment-emergent in the summary tables and listings.

The adverse events will be coded using MedDRA (version 21.0 or later), associating lower-level terms with preferred terms and system organ classes by the primary hierarchy. The tables will display the counts and percentages of patients who reported at least one TEAE in each system organ class represented in the AE data. Within each system organ class, the tables will display the counts and percentages of patients reporting at least one TEAE as designated by the preferred terms.

AEs are graded using Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03. AE summaries may include summaries for all AEs and by the maximum CTCAE grade for the item being summarized (i.e., SOC or PT). In these cases, the outputs will include a row for All Grades as well as rows for the 5 potential CTCAE grades: Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe), Grade 4 (Life threatening or disabling), or Grade 5 (Death). AEs missing a severity grade will not be included in the Grade 1-5 rows of the tables. An AE reported by a patient more than once will be represented in the most severe category.

The following AE summaries will be produced:

- An Overall Summary of Safety will summarize the numbers of patients with TEAEs of each grade and the number of patients who died during the study or within 30 days of last dose.
- All TEAEs
- Serious TEAEs
- Non-Serious TEAEs (i.e. TEAEs excluding SAEs)
- Grade 3 or higher TEAEs
- TEAEs leading to drug withdrawal. This subset includes TEAEs with an Action Taken of “Drug Permanently Discontinued.”

- TEAEs related to study drug. This table will include TEAEs with a drug relationship of "Possibly Related," "Probably Related," "Definitely Related." It will also include TEAEs with missing drug relationships. An AE reported by a patient more than once will be included in this table if at least one of the drug association grades is one of the grades listed here.
- Serious, Related TEAEs. This subset includes all serious TEAEs with a drug relationship of "Possibly Related," "Probably Related," "Definitely Related." It will also include serious TEAEs with missing drug relationships. An AE reported by a patient more than once will be included in this table if at least one of the drug association grades is one of the grades listed here.
- TEAEs leading to dose reduction and/or delay
- Related TEAEs leading to dose reduction and/or delay
- Deaths on Study or within 30 Days of the Last Dose

The following AE listings will be produced:

- All pre-treatment AEs will be listed.
- All AEs, sorted chronologically within patient. This listing includes system organ class, preferred term, onset and end dates, and other relevant information.
- Serious TEAEs, sorted chronologically within patient.
- TEAEs leading to drug withdrawal. This subset includes TEAEs with an Action Taken of "Drug Permanently Discontinued."
- TEAEs related to study drug. This listing will include TEAEs with a drug relationship of "Possibly Related," "Probably Related," "Definitely Related." It will also include TEAEs with missing drug relationships.
- Serious TEAEs related to study drug. This listing will include serious TEAEs with a drug relationship of "Possibly Related," "Probably Related," "Definitely Related." It will also include serious TEAEs with missing drug relationships.
- TEAEs resulting in death. This listing includes TEAEs with a CTCAE Grade of "Grade 5 (Death)" or TEAEs with an outcome of "Fatal".

The following groupings of TEAEs will be generated as part of the focused analysis of safety:

- Ocular TEAEs
- A list of preferred terms for ocular AE will be provided and finalized by the Sponsor before the final database lock.
- Peripheral Neuropathy TEAEs
- A list of preferred terms meeting the criteria for peripheral neuropathy will be provided and finalized by the Sponsor before the final database lock.
- Pneumonitis

For each of the focused safety analysis groups, the following summary tables will be produced:

- TEAEs by SOC, PT, and maximum CTCAE grade.
- Related TEAEs by SOC, PT, and maximum CTCAE grade.
- Serious TEAEs by SOC, PT, and maximum CTCAE grade.
- Related serious TEAEs by SOC, PT, and maximum CTCAE grade.

Additionally, a table will be produced which contains the following for each of the focused safety analysis groups:

- The number of patients with at least 1 TEAE in each group, presented by treatment arm.
- Time to first onset of each group of TEAEs.
- Action taken with study drug with respect to each group of TEAEs.

For the focused safety analysis, the following listings will be produced:

- Ocular TEAEs.
- Peripheral neuropathy TEAEs.
- Pneumonitits TEAE.

9.3. Dose Limiting Toxicities (DLTs)

DLTs will be defined as a TEAE or abnormal laboratory value related to study treatment (i.e. assessed as unrelated to disease, intercurrent illness, or concomitant medications), including those TEAEs and abnormal laboratory values that result in a failure to meet the criteria for retreatment. DLTs will be considered related to the study treatment unless there is clear evidence of an alternative explanation and this attribution is agreed to by the CRC.

For the purposes of dose escalation and determination of the MTD, only DLTs that occur during the first cycle will be necessarily considered for decisions regarding dose escalation. Clinically significant toxicities or treatment-emergent adverse events that meet the definition of dose limiting but occurring after Cycle 1 (dose modifying events) may be considered when determining the MTD.

A listing of DLTs will be provided.

9.4. Clinical Laboratory Results

Laboratory test results (including hematology, coagulation, serum chemistry, thyroid panel and urinalysis) and abnormal laboratory values will be presented in data listings. Common Toxicity Criteria (CTCAE) version 4.03 lab grades will also be presented. CTCAE grades will be derived based on laboratory results, and will not factor in clinical evaluations.

Shift tables summarizing the changes from baseline in severity of lab grades will be provided for lab parameters that are graded according to the CTCAE v4.03. Summaries of actual values and changes from baseline will be presented by treatment group for each assessment time point, beginning with the first post-baseline assessment. Grade 3 or above lab values will also be summarized based on the worst grade observed on study.

Clinically significant values in liver function tests will be summarized by the following categories using the maximum value while on treatment. The denominator for the summaries will be the number of patients who had at least one non-missing value during treatment. Note the categories for each test are not mutually exclusive:

- Aspartate Aminotransferase (AST)
  - > 3xULN
  - > 5xULN
  - > 10xULN
  - > 20xULN
- Alanine Aminotransferase (ALT)
  - > 3xULN
  - > 5xULN
  - > 10xULN
  - > 20xULN
- AST or ALT
  - > 3xULN
  - > 5xULN
  - > 10xULN
  - > 20xULN
- Total Bilirubin (TBL)
  - > ULN
  - > 2xULN
- Alkaline Phosphatase (ALP)
  - > 1.5xULN
- (AST or ALT) and TBL
  - AST or ALT > 3xULN and TBL > 1.5xULN
  - AST or ALT > 3xULN and TBL > 2xULN
- (AST or ALT) and ALP and TBL
  - AST or ALT > 3xULN and ALP < 2xULN and TBL ≥ 2xULN

Results from pregnancy tests will be provided in data listings.

9.5. Vital Signs

Vital signs (including temperature, pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate and weight) will be presented in data listings.

9.6. Electrocardiograms (ECGs)

ECG results (Rhythm, Heart Rate, PR Interval, RR Interval, QRS Interval, QT Interval, QTcF Interval, and classification of Within Normal Limits, Abnormal, Not Clinically Significant, and Abnormal, Clinically Significant will be presented in data listings. If a different correction for QT is captured in the eCRF, that QTc will also be reported in the listing for that patient along with QTcF.

The number and percent of patients in the following non-mutually exclusive categories will be summarized by visit:

- QTc > 450 ms
- QTc > 480 ms
- QTc > 500 ms
- QTc change from baseline > 30 ms
- QTc change from baseline > 60 ms

This summary of QTc will be based on QTcF derived from QT and RR interval, not the QTcF value reported in eCRF.

For numeric results, summaries of actual values and changes from baseline will be presented by treatment group for each assessment time point, beginning with Cycle 1 Day 1 End of Infusion time point. Note that dosing ECGs are collected in triplicate and analyses for numeric results will be based on the average of the triplicate results.

For the overall ECG result (Within Normal Limits, Abnormal, Not Clinically Significant, and Abnormal, Clinically Significant) summaries will be provided for baseline and each post-baseline assessment time point. Note that dosing ECGs are collected in triplicate and analyses for the overall ECG result will be based on the worst-case result (i.e. if any one of the triplicate results is Abnormal, Clinically Significant then the value for the time point will be Abnormal, Clinically Significant). The hierarchy for the worst-case assessment is: Abnormal, Clinically Significant will be considered the worst value, with Abnormal, Not Clinically Significant being considered worse than Within Normal Limits.

9.7. Concomitant Medications (CMs)

All medications and supportive therapy taken within four weeks prior to Cycle 1, Day 1 and through 30 days after last study treatment must be recorded on the appropriate electronic case report form (eCRF). The identity of all medications, dosage, and route of administration, frequency, duration of administration, and indication for use will be recorded in the appropriate sections of the eCRF.

Prior medications are defined as medications with a stop date prior to the first dose of study treatment. Concomitant medications are defined as medications which are taken during the

course of study treatment and within 30 days of the last dose of study treatment (inclusive of all treatment periods, primary and SCP treatment if applicable). That is, medications started after the first dose of study treatment and within 30 days of the last dose of study treatment are considered as concomitant medications. Additionally, medications started prior to the first dose of study treatment, but with a stop date after the first dose of study treatment and within 30 days of the last dose of study treatment will be considered concomitant medications.

Prior and concomitant medications will be coded using the September 2015 or later version of World Health Organization drug dictionary (WHO Drug). Separate summary tables will be provided for prior and concomitant medications. Summary tables will be organized to display the anatomical main class of each coded medication (ATC level 1 term) and, within that, the pharmacological subgroup (ATC level 3 term) of the coded medication. The summary table will display counts and percentages of patients who reported using at least 1 medication in each represented pharmacological subgroup. If a patient has more than one medication in the subgroup, they will be counted only once.

A complete listing will be generated as well. The listing will contain both prior and concomitant medications with an indication of whether the medication is a prior or concomitant medication. The listing will display entries from the Concomitant Medications form, ordered within patient by the "Start Date." The listing will display the recorded term from the CRF and, adjacent to that, the WHO Drug anatomical main class (ATC level 1 term) and the pharmacological subgroup (ATC level 3 term) that appears in the tables.

9.8. Concomitant Procedures

All procedures within four weeks of Cycle 1, Day 1 and through 30 days after last study treatment must be recorded on the appropriate electronic case report form (eCRF).

Prior procedures are defined as procedures with a procedure date that is prior to the first dose of study drug. Concomitant procedures are defined as procedures with a procedure date on or after the first dose of study drug, and within 30 days of the last dose of study drug (inclusive of all treatment periods, primary and SCP treatment if applicable).

Prior and concomitant procedures will be coded using MedDRA (version 21.0 or later), associating lower-level terms with preferred terms and system organ classes by the primary hierarchy.

A complete listing will be generated. The listing will contain both prior and concomitant procedures with an indication of whether the procedure is a prior or concomitant procedure. The listing will display entries from the Concomitant Procedures form, ordered within patient by the "Date of Procedure." The listing will display the recorded term from the CRF and, adjacent to that, the system organ class and the preferred term that appears in the tables.

9.9. Ophthalmic Examinations

Ophthalmic Examinations are collected at the Screening, End of Treatment and 30-Day Follow-up Visits. Results of the Ophthalmic Examinations will be presented in data listings.

9.10. Ocular Symptom Assessments

Results of the Ocular Assessments will be presented in data listings.

9.11. Corticosteroid and Lubricating Eye Drop Compliance

All compliance information collected on the eCRF will be presented in data listings.

9.12. Transfusions

All Transfusions recorded on the eCRF will be presented in data listings.

9.13. Physical Examination

Physical Examination results will be presented in data listings.

9.14. Pulmonary Function Tests

Pulmonary Function Text results will be presented in data listings.

9.15. Pulse Oximetry

Pulse Oximetry will be presented in data listings.

9.16. Eastern Cooperative Oncology Group Performance Status (ECOG PS)

Eastern Cooperative Oncology Group performance status (ECOG PS) results will be presented in data listings. ECOG PS at baseline will be presented in summary table of baseline disease characteristics.

9.17. ECHO/MUGA

ECHO/MUGA scans are taken on for patients receiving pegylated liposomal doxorubicin. All ECHO/MUGA results will be presented in data listings.

9.18. 24 Hour Urine Protein

All 24 hour urine protein results will be presented in data listings.

10. IMMUNOGENICITY

The potential immunogenicity against mirvetuximab soravtansine will be assessed at various timepoints in Cycles 1 through 6, as outlined in Protocol Section 6.2 and Protocol Appendix F. Exploratory analyses will be completed to evaluate the potential impact of immunogenicity on PK, safety, and efficacy.

The anti-drug antibody (ADA) analyses, including the impact of immunogenicity on PK, will be covered by a separate, independent analysis plan (Section 12).

Impact of immunogenicity on safety and efficacy will be explored. A by patient TEAE listing for those patients determined seropositive for IMGN853 antibodies will be produced. Summary of TEAEs experienced within 1 and 3 days of ADA+ will be generated for those patients who sero-convert following the first dose of mirvetuximab soravtansine. Efficacy will be analysed by seroconversion status for patients treated with IMGN853, as appropriate.

11. BIOMARKERS

The biomarker analyses for this study will be covered by a separate, independent analysis plan.

12. PHARMACOKINETICS

Pharmacokinetic analyses for this study will be covered by a separate, independent analysis plan.

REFERENCES

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Varga A, Piha-Paul SA, Ott PA, et al. Antitumor activity and safety of pembrolizumab in patients (pts) with PD-L1 positive advanced ovarian cancer: Interim results from a phase Ib study. *J Clin Oncol* 33, (suppl; abstr 5510) 2015.

APPENDIX 1: TEMPLATE SAS® CODE

This appendix provides template SAS® code (version 9.3 or higher) that will be used for analysis.

Template code for the ORR, DCR, and GCIG CA125 response estimates along with the 95% confidence intervals:

```
proc freq data=AD_RESP;
    by TRTP;
    tables AVAL / binomial alpha=0.05;
run;
```

Template code for median time-to-event estimates along with 95% confidence intervals:

```
proc lifetest data=AD_TTE;
    time AVAL*CNSR(1);
    strata TRTP;
run;
```

where:

- AD_RESP is the name of the ADaM dataset used for response analysis
- AD_TTE is the name of the ADaM dataset used for time-to-event analysis
- TRTP is a variable containing the treatment used for analysis.
- AVAL is a variable containing the value for analysis (e.g. objective response or time to death)
- CNSR is a variable indicating whether the AVAL is censored (1=censored, 0=non-censored)