CLINICAL STUDY PROTOCOL

Study Title:	Open-label Rollover Study to Evaluate Long-Term Safety in Subjects with Metastatic Solid Tumors that are Benefiting from Continuation of Therapy with Sacituzumab Govitecan
Sponsor:	Gilead Sciences, Inc. (Immunomedics, Inc. is now part of the Gilead group of companies) 333 Lakeside Drive Foster City, CA 94404 USA
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Indication:	Metastatic solid tumors
Protocol ID:	IMMU-132-14
Contact Information:	The medical monitor name and contact information will be provided on the Key Study Team Contact List.
Protocol Version/Date:	Original: 16 December 2019 Amendment 1: 27 August 2021

This study will be conducted under United States Food and Drug Administration investigational new drug application regulations (21 Code of Federal Regulations Part 312); however, sites located in the European Economic Area, the United Kingdom, and Switzerland are not included under the investigational new drug application and are not considered to be investigational new drug application sites.

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PROTOCOL SYNOPSIS

Gilead Sciences, Inc.
(Immunomedics, Inc. is now part of the Gilead group of companies)
333 Lakeside Drive
Foster City, CA 94404

Name of Sponsor/Company: Gilead Sciences, Inc. (Immunomedics, Inc. is now part of the Gilead group of companies)		
Name of Investigational Product: Sacituzumab govitecan		
Name of Active Ingredient: Sacituzumab govitecan is an antibody-drug conjugate composed of hRS7, a humanized IgG1κ monoclonal antibody (mAb) that binds to trophoblast cell-surface antigen-2 (Trop-2); SN-38, a camptothecin analog that inhibits topoisomerase I; and CL2A, a pH-sensitive linker that couples SN-38 to hRS7.		
Protocol Number: IMMU-132-14	**Rollover Study**	**Country:** United States (US), Europe, and rest of the world countries
Title of Study: Open-label Rollover Study to Evaluate Long-Term Safety in Subjects with Metastatic Solid Tumors That are Benefiting from Continuation of Therapy with Sacituzumab Govitecan		
Primary Objective: Evaluate long-term safety in subjects with metastatic solid tumors that are benefiting from continuation of therapy with sacituzumab govitecan **Study Design:** This is a Phase 4, open-label, longitudinal cohort, rollover study designed to evaluate long-term safety in subjects with metastatic solid tumors that are benefiting from continuation of therapy with sacituzumab govitecan. Only subjects who continue to receive clinical benefit from continuation of sacituzumab govitecan therapy and are tolerating therapy at the time of enrollment are eligible for this study. Subjects enrolled may continue to receive sacituzumab govitecan at the dose that they were receiving in the Gilead (previously Immunomedics)-sponsored parent study at the time of consenting to participate in this rollover study. No dose escalation beyond the dose the subject was receiving in the parent study at the time of consenting to participate in this rollover study is permitted. Subjects who continued to receive sacituzumab govitecan in a parent study after disease progression (PD) may continue to receive sacituzumab govitecan in this rollover study. No subject will receive more than 10 mg/kg dose of sacituzumab govitecan in this rollover study. Subjects may continue to receive sacituzumab govitecan until they experience toxicity, disease progression with no evidence of clinical benefit, loss of clinical benefit, withdrawal of consent, lost to follow-up, or sponsor termination of the study is documented. Subjects of childbearing potential will be followed for Safety Follow-up after study drug discontinuation. Subjects with ongoing adverse events (AEs) or serious adverse events (SAEs) will be followed for Safety Follow-up after EOT.		

Number of subjects (planned): Up to approximately 200

Diagnosis and main criteria for inclusion:

Subjects meeting all the following inclusion criteria at Screening/Day -1 of treatment will be eligible for participation in the study.

1) Female or male subjects, ≥18 years of age, able to understand and give written informed consent
2) Receiving ongoing treatment with sacituzumab govitecan in a Gilead (previously Immunomedics)-sponsored parent study
3) Continuing to receive clinical benefit from sacituzumab govitecan therapy
4) Creatinine clearance ≥ 30 mL/min as assessed by the Cockcroft-Gault equation
5) Male subjects and female subjects of childbearing potential who engage in heterosexual intercourse must agree to use protocol-specified method(s) of contraception as described in Appendix 4.

Main criteria for exclusion:

Subjects meeting any of the following exclusion criteria at Screening/Day -1 of treatment will not be enrolled in the study.

1) Women who are pregnant or lactating (Appendix 4)
2) Initiated therapy with another cancer therapeutic agent (investigational or standard of care) since receiving the last dose of the study drug on the parent study in which they participated
3) Experienced a toxicity from sacituzumab govitecan that resulted in permanent discontinuation of therapy
4) Have an active serious infection requiring IV antibiotics (Contact medical monitor for clarification)
5) Have other concurrent medical or psychiatric conditions that, in the Investigator's opinion, may be likely to confound study interpretation or prevent completion of study procedures and follow-up examinations

Investigational product, dosage and mode of administration: Sacituzumab govitecan will be administered at the dose that the subject was receiving in the parent study at the time of consenting to participate in this rollover study. No dose escalation beyond the dose the subject was receiving in the parent study at the time of consenting to participate in this rollover study is permitted. No subject will receive more than 10 mg/kg dose of sacituzumab govitecan. Sacituzumab govitecan will be administered as an intravenous (IV) infusion on Days 1 and 8 of a 21-day cycle.

Duration of treatment: Sacituzumab govitecan will be administered as an IV infusion on Days 1 and 8 of a 21-day cycle until PD, toxicity or withdrawal of consent, lost to follow-up or loss of clinical benefit, or sponsor termination of the study is documented. Treatment beyond PD is permitted if there is evidence of clinical benefit per treating physician's assessment.

Criteria for evaluation:

Efficacy: Efficacy will not be assessed in this study.

Safety: Long-term safety will be evaluated based on AEs and SAEs noted with continued therapy.

Statistical methods:

Long-term safety will be evaluated based on AEs and SAEs noted with continued therapy, standard safety laboratories, study drug exposure, and concomitant medications. Descriptive analyses of the safety data will be performed.

These analyses will be presented by cancer type and histology when deemed appropriate and by the overall study population.CCI [redacted]

This study will be conducted in accordance with the guidelines of Good Clinical Practice, including archiving of essential documents.

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

The following abbreviations are used in this study protocol.

AE	adverse event
ANC	absolute neutrophil count
BUN	blood urea nitrogen
CFR	Code of Federal Regulation
CTCAE	Common Terminology Criteria for Adverse Events
eCRF	electronic case report form
EOS	end of study
EOT	end of treatment
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
hRS7	humanized RS7 anti-Trop-2 immunoglobulin G
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	independent ethics committee
IMMU-132	company code for sacituzumab govitecan
IMP	investigational medicinal product
IND	investigational new drug
IRB	institutional review board
IRR	infusion-related reaction
IWRS	interactive web response system
mAb	monoclonal antibody
MTD	maximum tolerated dose
mTNBC	metastatic triple-negative breast cancer
NCI	National Cancer Institute
NSCLC	non–small-cell lung cancer
PD	progressive disease/disease progression
SAE	serious adverse event
TNBC	triple-negative breast cancer
Trop-2	trophoblastic cell-surface antigen 2
UGT1A1	uridine diphosphate glucuronosyltransferase 1A1
US	United States (of America)

1. INTRODUCTION

1.1. Mechanism of Action of Sacituzumab Govitecan

Sacituzumab govitecan (company code: IMMU-132) is a trophoblast cell-surface antigen-2 (Trop-2)-directed antibody-drug conjugate that comprises SN-38, a topoisomerase I inhibitor and active metabolite of irinotecan, coupled by a linker (CL2A) to the humanized monoclonal antibody (mAb) hRS7 immunoglobulin G1 (IgG1)κ, which binds to Trop-2. Trop-2 is a transmembrane calcium signal transducer glycoprotein of the Tumor Associated Calcium Signal Transducer 2 (TACSTD2) gene family. Pharmacology data suggest that sacituzumab govitecan binds to Trop-2-expressing cancer cells and is internalized with the subsequent release of SN-38 via hydrolysis of the linker. SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single strand breaks. The resulting DNA damage leads to apoptosis and cell death. The hydrolysable linker may permit release of SN-38 in the acidic microenvironment of the tumor without Trop-2 binding.

1.2. Nonclinical Experience

1.2.1. Pharmacology

Sacituzumab govitecan has been evaluated for in vitro cytotoxicity and in vivo efficacy in a variety of human solid tumor types, including prostate, non–small-cell lung cancer (NSCLC), colon, pancreatic, squamous cell lung, gastric, and triple-negative breast cancer (TNBC) {Cardillo 2015, Cardillo 2011, Cardillo 2017, Goldenberg 2015}. In general, IC_{50} values ranged from 1 to 83 nM across various disease indications {Cardillo 2011, Cardillo 2017, Goldenberg 2015}. In vivo, significant anti-tumor effects mediated by sacituzumab govitecan therapy were noted in tumor xenograft disease models of TNBC, NSCLC, colon, pancreatic, gastric, and squamous cell lung.

Additional information regarding nonclinical pharmacology of sacituzumab govitecan can be found in the current edition of the investigator's brochure.

1.2.2. Toxicology

In acute toxicity studies in Swiss-Webster Mice, sacituzumab govitecan at doses of up to 750 mg/kg/dose (ie, cumulative doses of up to 1500 mg/kg) caused minimal loss (<10%) in body weight. There was no evidence of hematological toxicity and no abnormal histology findings. Transient increases in hepatic transaminases were observed that returned to normal by the end of the study.

In cynomolgus monkeys, sacituzumab govitecan administered 50 mg/kg/dose (human equivalent dose [HED] = 16 mg/kg/dose) for four treatment cycles (Days 1 and 8 of a 21-day cycle) was considered a no observed adverse effect level (NOAEL) and 120 mg/kg/dose administered 3 days apart was associated with lethality. In general, the observed toxicities were dose dependent and considered reversible. Target organs included the female reproductive tract, skin

(hair loss, pigmentation), kidney (periarteritis), lymphoid organs (lymphoid depletion), bone marrow (reduced cellularity) with concomitant reductions in red cells, white cells and platelets and the gastrointestinal tract (necrosis, erosions, inflammation, fibrosis, hemorrhage, edema).

SN-38 was negative for mutagenicity in a bacterial reverse mutation test and was found to be clastogenic in an in vitro mammalian cell micronucleus test. Neither the carcinogenicity, nor effects of sacituzumab govitecan on fertility, early embryonic development or pre- and post-natal development have been assessed. However, SN- 38 is a camptothecin and hence is likely carcinogenic. Furthermore, SN-38 is a known developmental toxicant.

Additional information regarding nonclinical toxicology of sacituzumab govitecan can be found in the current edition of the investigator's brochure.

1.3. Clinical Experience

Sacituzumab govitecan received accelerated approval in the US for use in metastatic TNBC (mTNBC) based on results from the Phase 1/2 Study IMMU-132-01, and subsequently received full approval based on results from the Phase 3 confirmatory Study IMMU-132-05. Sacituzumab govitecan received accelerated approval for use in metastatic urothelial cancer (mUC) based on results from the Phase 2 Study IMMU-132-06 and is currently being studied in subjects with mUC in the confirmatory Study IMMU-132-13. Sacituzumab govitecan is also currently being studied in metastatic breast cancer (IMMU-132-09) and various epithelial cancers (IMMU-132-11).

The largest experience to date is a Phase 1/2 study (IMMU-132-01) titled "Phase 1/2 Study of IMMU-132 (hRS7-SN38 Antibody Drug Conjugate) in Epithelial Cancers." Five hundred twenty subjects were enrolled in this study regardless of Trop-2 expression and were treated with sacituzumab govitecan monotherapy. Doses of 8 to 18 mg/kg were tested with the 10-mg/kg dose selected for further investigation.

Additional information regarding clinical studies can be found in the current edition of the investigator's brochure.

1.3.1. Pharmacokinetics

1.3.1.1. Pharmacokinetics

The serum pharmacokinetics (PK) of sacituzumab govitecan and free SN-38 were evaluated in a Phase 3 Study IMMU-132-05 in a population of mTNBC subjects who received sacituzumab govitecan as a single agent at a dose of 10 mg/kg. Sacituzumab govitecan and free SN-38 had a C_{max} percentage coefficient of variation (%CV) of 240,000 ng/mL (22.2%) and 90.6 ng/mL (65%) respectively, and AUC_{0-168} (%CV) of 5,340,000 h□ng/mL (23.7%) and 2,730 h□ng/mL (41.1%), respectively.

Additional information regarding PK parameters of sacituzumab govitecan can be found in the current edition of the investigator's brochure.

1.3.1.2. Distribution

Based on population PK analysis, central volume of distribution of sacituzumab govitecan is 2.96 L.

1.3.1.3. Elimination

The mean half-life of sacituzumab govitecan and free SN-38 was 15.3 and 19.7 hours, respectively. Based on population PK analysis, the clearance of the sacituzumab govitecan is 0.14 L/h.

1.3.1.4. Metabolism

No metabolism studies with sacituzumab govitecan have been conducted. SN-38 (the small molecule moiety of sacituzumab govitecan) is metabolized via uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1). SN-38 glucuronide (SN-38G) was detectable in the serum of subjects.

1.3.1.5. Excretion

SN-38 and SN-38G have been reported to be mainly eliminated via biliary excretion.

1.3.2. Immunogenicity

As with all therapeutic proteins, there is potential for an immune response to sacituzumab govitecan. None of the subjects with treatment-emergent adverse events (TEAEs) and subjects who were confirmed antidrug antibody (ADA) positive had infusion reactions or adverse events (AEs) suggestive of immunogenicity.

1.3.3. Rationale for Dose Regimen

The total body clearance (CL) of sacituzumab govitecan is mediated by both catabolism of the antibody and metabolism of the released payload, SN-38. The distribution and CL of the antibody portion of sacituzumab govitecan are likely to be similar to those other IgG1 antibodies and are influenced by target (Trop-2)-mediated uptake on antigen-expressing cells, pinocytosis, and neonatal Fc receptor negative-mediated CL mechanisms in vivo. SN-38 is primarily eliminated from the body via the hepatic route.

In the Phase 1 part of Study IMMU-132-01, dose escalation was performed with doses ranging from 8 to 18 mg/kg. A sacituzumab govitecan dose of 12 mg/kg was formally identified as the maximum tolerated dose (MTD) but was associated with dose delays and reductions in several subjects. A sacituzumab govitecan dose of 10 mg/kg was found to be safe and efficacious and is the recommended starting dose for subjects with normal hepatic function and mild hepatic impairment. Additional information regarding the safety and efficacy of sacituzumab govitecan can be found in the investigator's brochure.

In this study, sacituzumab govitecan will be administered at the dose the subject was receiving in the Gilead (previously Immunomedics)-sponsored parent study at the time of consenting to participate in this rollover study. No dose escalation beyond the dose the subject was receiving in the parent study at the time of consenting to participate in this rollover study is permitted. Sacituzumab govitecan will be administered as an IV infusion on Days 1 and 8 of a 21-day cycle until PD, toxicity or withdrawal of consent, lost to follow-up, loss of clinical benefit, or sponsor termination of the study is documented. Treatment beyond PD is permitted if there is evidence of clinical benefit per treating physician's assessment. This rollover study will provide these subjects an opportunity for continuation of therapy.

1.3.4. Summary of Sacituzumab Govitecan Safety

The safety profile for sacituzumab govitecan was similar in the treatment of mTNBC and mUC. The most common AEs were nausea, diarrhea, neutropenia, fatigue, alopecia, anemia, vomiting, and constipation. The most clinically relevant Grade 3 or Grade 4 AEs with sacituzumab govitecan were neutropenia and diarrhea. The most frequent AEs that led to treatment modification were neutropenia and diarrhea. The frequent AEs leading to permanent discontinuation of sacituzumab govitecan were fatigue, diarrhea, pneumonia, and neutropenia.

Neutropenia occurred in the first cycle of treatment and resolved within approximately 1 week of onset. Most cases of neutropenia were not febrile, were nonserious, and could be managed with granulocyte colony-stimulating factor (G-CSF) administration and/or dose reduction after Cycle 1.

Diarrhea with sacituzumab govitecan occurred within the first treatment cycle (median time of 12 days to first event) and resolved within approximately 1 week of onset. Most of the cases of diarrhea were nonsevere, nonserious, and did not lead to either a treatment interruption or dose reduction.

Higher incidences of neutropenia, febrile neutropenia, and anemia were seen in subjects who were homozygous for the UGT1A1*28 allele compared with subjects who were heterozygous for the UGT1A1*28 allele and subjects who were homozygous for the wild-type allele.

For further information on sacituzumab govitecan, refer to the current investigator's brochure.

2. STUDY OBJECTIVES AND PURPOSE

2.1. Primary Objective

Evaluate long-term safety in subjects with metastatic solid tumors that are benefiting from continuation of therapy with sacituzumab govitecan.

3. INVESTIGATIONAL PLAN

3.1. Overall Study Design

This is a Phase 4, open-label, longitudinal cohort, rollover study designed to evaluate long-term safety in subjects with metastatic solid tumors that are benefiting from continuation of therapy with sacituzumab govitecan. Only subjects who continue to receive clinical benefit from continuation of sacituzumab govitecan therapy and are tolerating therapy at the time of enrollment are eligible for this study. Subjects enrolled may continue to receive sacituzumab govitecan at the dose that they were receiving in the parent study at the time of consenting to participate in this rollover study. No dose escalation beyond the dose the subject was receiving in the parent study at the time of consenting to participate in this rollover study is permitted. Subjects who continued to receive sacituzumab govitecan in a parent study after disease progression (PD) may continue to receive sacituzumab govitecan in this rollover study. No subject will receive more than 10 mg/kg dose of sacituzumab govitecan in this rollover study. Subjects may continue to receive sacituzumab govitecan until they experience toxicity, disease progression with no evidence of clinical benefit, loss of clinical benefit, withdrawal of consent, lost to follow-up, or sponsor termination of the study is documented. Subjects of childbearing potential will be followed for Safety Follow-up after study drug discontinuation. Subjects with ongoing adverse events (AEs) or serious adverse events (SAEs) will be followed for Safety Follow-up after EOT.

3.2. Number of Subjects

Up to approximately 200 subjects may be enrolled. Only subjects currently receiving sacituzumab govitecan in a parent study are permitted.

3.3. Treatment Assignment

This is a non-randomized, open-label, longitudinal cohort, rollover study.

3.4. End of Treatment

After discontinuation of treatment (See Section 5.3), all subjects must complete an end of treatment (EOT) visit approximately 30 days after the last dose of the study drug. Data should be entered into the EOT electronic case report form (eCRF).

3.5. Safety Follow-Up

After the EOT visit, subjects of childbearing potential and subjects who have ongoing AEs or SAEs will be followed in Safety Follow-up according to the Schedule of Assessments (Table 1), unless the subject explicitly indicates their desire to forego Safety Follow-up in writing to their study investigator. The Safety Follow-up visits may be completed by telephone unless a confirmatory serum pregnancy test is required as outlined in the Schedule of Assessments (Table 1).

3.6. End of Study

The end of the study will be the date of the last visit/contact/follow-up in the study. An End of Study (EOS) visit must be performed and entered into the EOS eCRF if the criteria cited in Section 5.4 have been met. The EOS visit can be performed by telephone.

4. PROCEDURES

4.1. Informed Consent

No study-specific procedure or alteration of subject care will be undertaken until informed consent has been obtained from the subject or legal representative. The Investigator will explain the nature and scope of the study, potential risks and benefits of participation and answer all questions for the subject and/or legally authorized representative. Subjects must be informed of available alternative treatment options prior to consenting to participate in this study.

If the subject agrees to participate, the informed consent form must be signed, dated, and witnessed, with a copy given to the subject. The consenting process must be well documented by each investigational site.

4.2. Screening

Subjects must complete all screening procedures after signing the informed consent form. Absolutely no waivers for subject eligibility will be offered or permitted.

Subjects are permitted to rescreen only once for the study.

4.2.1. Screen Failures

Subjects who are consented to participate in the clinical study, and who do not meet one or more criteria required for participation in the study during the screening visit, are considered screen failures. All subjects who have signed informed consent and were deemed ineligible will be recorded with the reason for ineligibility on the appropriate eCRF. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, informed consent date, screen failure details, eligibility criteria, study discontinuation date, adverse events and any SAE.

4.3. Study Procedures

Enrollment occurs upon completion of all screening procedures. Enrollment will be performed centrally by an interactive web response system (IWRS). Clear documentation as to the reason the subject was not dosed should be provided on the relevant eCRF. Unless otherwise specified, collection windows for laboratory assessments prior to dosing may be obtained up to 3 days prior to dosing. Treatment (dosing) may be permitted either 1 day before or within 7 days after scheduled visits.

An infectious disease pandemic may pose additional risks to study drug availability, the study visit schedule, and adherence to protocol-specified safety monitoring or laboratory assessments. Refer to Appendix 2 for further details on the risks and risk mitigation strategy.

For safety parameters, please refer to Section 10.1.

Table 1. Schedule of Assessments

Phase	Pre-Treatment	Treatment					
Period	Screening	Treatment Cycle 1 through Last Cycle (21-day cycle)		Unscheduled Visit	End of Treatment[a]	Safety Follow-up[b]	End of Study[a]
Day	Days −21 to 1	Day 1 (includes baseline C1D1)	Day 8				
Informed consent	X						
Inclusion and exclusion criteria	X						
Prior sacituzumab govitecan parent study	X						
Weight		X					
Hematology[c]		X	X	X	X		
Serum chemistry[d]		X	X	X	X		
Urine pregnancy test[e]	X	X		X	X	X	X
FSH[f]	X						
Sacituzumab govitecan administration		X	X				
Concomitant medications		Throughout Study					
SAEs[g]		Throughout Study					
AEs[g]		Throughout Study					

AE = adverse event; C1D1= Cycle 1 Day 1; FSH = follicle-stimulating hormone; SAE = serious adverse event

a End of treatment (EOT) visit approximately 30 days of the last dose of the study drug. For the definition of End of Study (EOS), refer to Section 3.6.

b For subjects of childbearing potential, the Safety Follow-up visits will be every 28 days for 6 months after study drug discontinuation. For subjects of non-childbearing potential who have ongoing AEs or SAEs at EOT, the Safety Follow-up visits will be every 6 weeks for up to 6 months after study drug discontinuation or until the criteria for EOS (Section 3.6) have been met. Subjects of non-childbearing potential who do not have ongoing AEs or SAEs at EOT will be considered as having reached EOS.

c Hemoglobin, white blood cell (WBC) count and differential (with absolute neutrophil count [ANC]), and platelet count for all subjects is required at Day 1 and Day 8 of every Cycle, and EOT visit. ANC levels must be confirmed prior to each dose. May be obtained more frequently at the discretion of the managing physician if abnormal results warrant follow-up. Results of unscheduled tests should be documented. Refer to Section 6.3.2.3 for guidance regarding when sacituzumab govitecan should be administered based on ANC.

d Serum chemistries include total protein, albumin, total bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (estimated glomerular filtration rate [GFR] using a validated model, refer to Appendix 3), blood urea nitrogen (BUN) or urea, glucose, sodium, potassium, magnesium, chloride, bicarbonate, calcium, phosphorus. Serum chemistries are required in all subjects at Day 1 and Day 8 of every cycle, and the EOT visit. Prior to administration of sacituzumab govitecan at C1D1, subjects are required to have creatinine clearance ≥ 30 mL/min.

e The Cycle 1 Day 1 urine pregnancy test does not need to be conducted if the screening pregnancy test was performed within 72 hours before study treatment administration. Urine pregnancy testing will continue every 28 days up to 6 months after the last dose of study drug as discussed in Appendix 4. Testing during the Safety Follow-Up period may be performed at home and the result self-reported by the subject. If a urine pregnancy test is positive or equivocal, a confirmatory serum pregnancy test is required.

f Conduct as needed per Appendix 4 for determination of childbearing potential.

g Ongoing AEs and SAEs at EOT will be followed until resolution or stabilization in Safety Follow-up. For information on AEs beginning after EOT, please refer to Section 10.2.

NOTE: Unless otherwise specified, visit windows are within -1 and +7 days of the Treatment visits. Labs may be collected up to 3 days prior to dosing.

5. SELECTION AND WITHDRAWAL OF SUBJECTS

5.1. Subject Inclusion Criteria

Subjects meeting all the following inclusion criteria at Screening/Day -1 will be eligible for participation in the study.

1) Female or male subjects, ≥ 18 years of age, able to understand and give written informed consent

2) Receiving ongoing treatment with sacituzumab govitecan in a Gilead (previously Immunomedics)-sponsored parent study

3) Continuing to receive clinical benefit from sacituzumab govitecan therapy

4) Creatinine clearance ≥ 30 mL/min as assessed by the Cockcroft-Gault equation.

5) Male subjects and female subjects of childbearing potential who engage in heterosexual intercourse must agree to use protocol-specified method(s) of contraception as described in Appendix 4.

5.2. Subject Exclusion Criteria

Subjects meeting any of the following exclusion criteria at Screening/Day -1 of treatment will not be enrolled in the study.

1) Women who are pregnant or lactating (Appendix 4)

2) Initiated therapy with another cancer therapeutic agent (investigational or standard of care) since receiving the last dose of the study drug on the parent study in which they participated

3) Experienced a toxicity from sacituzumab govitecan that resulted in permanent discontinuation of therapy

4) Have an active serious infection requiring IV antibiotics (Contact medical monitor for clarification)

5) Have other concurrent medical or psychiatric conditions that, in the Investigator's opinion, may be likely to confound study interpretation or prevent completion of study procedures and follow-up examinations

5.3. Criteria for Treatment Discontinuation

Subjects will discontinue the treatment under any of the following conditions:

1) Withdrawal of consent from further treatment with study drug

2) Lost to follow-up. Subjects will be considered lost to follow up when there is no response to two attempts one month apart by phone and a registered letter. After these 3 failed attempts, lost to follow-up will be documented

3) An adverse event (AE) that, in the opinion of the Investigator or the sponsor, contraindicates further dosing

4) Initiation of alternative anti-tumor therapy, including any investigational agent

5) Pregnancy

6) Disease progression with no evidence of clinical benefit

7) Loss of clinical benefit

8) Subject non-compliance

9) Sponsor terminates the study

5.4. Criteria for Study Discontinuation

Subjects will discontinue the study under any of the following conditions:

1) Death

2) Withdrawal of consent from study

3) Lost to follow-up. Subjects will be considered lost to follow up when there is no response to two attempts one month apart by phone and a registered letter. After these 3 failed attempts, lost to follow-up will be documented.

4) End of treatment, with documentation of resolution or stabilization of AEs (if applicable)

5) Sponsor terminates the study

6. TREATMENT OF SUBJECTS

6.1. Description of Study Drug

Sacituzumab govitecan is a humanized mAb with a hydrolysable linker through which SN-38 is conjugated to the humanized mAb hRS7 IgG1κ to enhance the delivery of SN-38 to Trop-2-expressing tumors, while reducing systemic toxicity. SN-38 is the active metabolite of irinotecan.

6.2. Investigational Medicinal Product, Dosage and Mode of Administration

Sacituzumab govitecan will be administered at the dose that the subject was receiving in the parent study at the time of consenting to participate in this rollover study. No dose escalation beyond the dose the subject was receiving in the parent study at the time of consenting to participate in this rollover study is permitted. No subject will receive more than 10 mg/kg dose of sacituzumab govitecan. Sacituzumab govitecan will be administered as an intravenous (IV) infusion on Days 1 and 8 of a 21-day cycle.

6.3. Treatment of Sacituzumab Govitecan-Associated Toxicities

Instructions for the infusion of sacituzumab govitecan are provided in Section 7.5. The following sections provide guidance for sacituzumab govitecan administration and management of treatment-related toxicities, including modification of dosing and treatment discontinuation. Toxicities should be managed in accordance with standard institutional practices and accepted treatment guidelines.

6.3.1. Preventative Medications

Infusion-Related Reactions: Premedication for prevention of infusion-related reactions (IRRs) with antipyretics and H1 and H2 blockers should be administered before each sacituzumab govitecan infusion. Corticosteroids (hydrocortisone 50 mg or equivalent orally [PO] or IV) may be administered prior to subsequent infusions. Additional details of recommended treatment of IRRs are described in Section 6.3.2.1.

Nausea, Vomiting: Sacituzumab govitecan is considered to be moderately emetogenic. Premedication with a 2-drug antiemetic regimen is recommended. If nausea and vomiting are persistent, a 3-drug regimen may be used, including a 5-HT3 inhibitor (ondansetron or palonosetron, or other agents according to local practices), an NK1-receptor antagonist (fosaprepitant or aprepitant), and dexamethasone (10 mg PO or IV). Anticipatory nausea can be treated with olanzapine. The recommended treatment of delayed nausea and vomiting is described in Section 6.3.2.2.

6.3.2. Management of Sacituzumab Govitecan Toxicities

NCI CTCAE v5.0 is used to grade the severity of all AEs. The guidelines for management of toxicities associated with sacituzumab govitecan are based on the assessment of severity according to these criteria. Toxicities should be managed in accordance with standard medical practice and treatment guidelines. All clinically appropriate imaging or laboratory testing should be utilized to fully assess a toxicity to determine the appropriate treatment. Appropriate follow-up-studies should be utilized to follow all toxicities to resolution. Subjects with known UGT1A1 *28 polymorphisms may have a higher risk of developing treatment-related toxicities. Additional monitoring may be required in those subjects. Subjects suspected of having underlying UGT1A1 *28 polymorphisms due to increased episodes of diarrhea or neutropenia, may have their polymorphism assessed per Investigator's discretion. Instructions for sacituzumab govitecan dose reduction for treatment-related toxicities are provided in Section 6.3.2.5.

6.3.2.1. Infusion-Related Reactions

Infusion-related reactions are defined as symptoms that occur during and within the first 6 hours after the infusion of sacituzumab govitecan and can occur at any cycle. Symptoms can include: fever, chills, rigors, arthralgias, myalgias, urticaria, pruritus, rash, diaphoresis, hypotension, dizziness, syncope, hypertension, dyspnea, cough, and wheezing, as well as severe hypersensitivity reactions including anaphylactic reactions. Infusion-related reactions should be treated in accordance with best clinical practices and standard institutional guidelines. Because of the potential for life-threatening IRRs, sacituzumab govitecan should only be administered in a setting in which appropriately trained medical staff, emergency equipment, and medications are available in the event that resuscitation is required. NCI CTCAE v5.0 is used to grade the severity of all infusion-related AEs. Premedication for the prevention of IRRs is described in Section 6.3.1.

Grade 4 Events

Grade 4 reactions include potentially life-threatening reactions, requiring urgent intervention. If Grade 4 IRRs occur, sacituzumab govitecan should be permanently discontinued (Table 2).

Grade 2 and Grade 3 Events

Grade 2 IRRs are defined as those that require infusion interruption and respond to symptomatic treatment; prophylactic medications are indicated for ≤ 24 hours. For Grade 2 IRRs, the infusion should be interrupted until symptoms resolve. After symptoms resolve, the infusion should be resumed at a slower infusion rate determined appropriate by the managing physician. Recommended infusion rates are provided in the Pharmacy Manual. Grade 3 IRRs are defined as those that are prolonged and do not improve with symptomatic treatment and/or brief interruption of treatment, reactions that recur following treatment, and reactions that require hospitalization. For recurrent Grade 2 or Grade 3 IRRs despite optimal management, sacituzumab govitecan should be permanently discontinued (Table 2).

6.3.2.2. Gastrointestinal Toxicities

Nausea, vomiting, and diarrhea are frequent sacituzumab govitecan-associated toxicities. Appropriate treatment, including, as needed, fluid and electrolyte replacement, is required to minimize the risk of serious consequences such as dehydration. Instructions for sacituzumab govitecan dose reduction for treatment-related gastrointestinal toxicities are provided in Section 6.3.2.5.

Nausea and Vomiting

Instructions for the use of premedications for prophylactic treatment of nausea and vomiting and anticipatory nausea are provided in Section 6.3.1. Withhold sacituzumab govitecan for Grade 3 nausea or Grade 3 or 4 vomiting at the time of scheduled treatment administration and resume with additional supportive measures when resolved to Grade ≤ 1. Manage this toxicity per standard institutional guidelines.

Diarrhea

Dietary modification should be recommended for the management of diarrhea, including adequate fluid intake to maintain hydration. Loperamide can be administered at the onset of treatment-related Grade 1 or Grade 2 diarrhea, at an initial dose of 4 mg, followed by 2 mg with every episode of diarrhea to a maximum dose of 16 mg/day. If diarrhea is not resolved after 24 hours, consider adding diphenoxylate/atropine and/or opium tincture, as clinically indicated.

Add octreotide 100-150 µg subcutaneous (SC) three times per day (tid) if diarrhea persists. Withhold sacituzumab govitecan for Grade 3 or 4 diarrhea at the time of scheduled treatment administration and resume when resolved to Grade ≤ 1. For Grade 3 or Grade 4 diarrhea, consider hospitalization, and treat with IV fluids, and octreotide. Antibiotics can be administered as clinically indicated.

Subjects who exhibit an excessive cholinergic response to treatment with sacituzumab govitecan (eg, abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (eg, atropine) for subsequent treatments.

6.3.2.3. Neutropenia

Complete blood counts (CBC) must be obtained prior to each sacituzumab govitecan infusion. Sacituzumab govitecan should be administered only if absolute neutrophil counts (ANC) meet the following criteria:

- Day 1: ANC $\geq$1500/mm^3
- Day 8: ANC $\geq$1000/mm^3

Sacituzumab govitecan should not be administered in cases of neutropenic fever.

The routine prophylactic use of growth factors is not required; however, prophylactic administration may be considered and should comply with American Society of Clinical Oncology (ASCO) guidelines for use of growth factors. They may be used in subjects who have experienced febrile neutropenia or Grade 3 or Grade 4 neutropenia following previous infusions. Growth factors may also be administered in the setting of neutropenia in subjects at high risk of poor clinical outcomes, including those with prolonged neutropenia, ANC <1000/mm^3, febrile neutropenia, and serious infections.

6.3.2.4. Overdose

Overdose is defined as administration of a dose that is 10% higher than the calculated dose. In the event of an overdose, closely monitor the subject per standard institutional guidelines. Any AE resulting from overdose should be reported as described in Section 10.2.2.

6.3.2.5. Sacituzumab Govitecan Dose Modification Guidelines

Dose Delays

Sacituzumab govitecan is to be administered in 21-day cycles on Day 1 and Day 8; the next cycle should start a minimum 14 days after the Day 8 dose (ie, the Day 8 infusion will be counted as the first day of that 14-day period). Dosing 1 day prior to and 7 days after the scheduled infusion are permitted. The scheduled Day 1 and Day 8 infusions may be delayed for up to one week for treatment-related toxicities.

Instructions for dose delays and dose reductions for specific toxicities are summarized below. For toxicities not specifically addressed in the toxicity management table (Table 2), dosing may be delayed for > Grade 2 toxicities for a maximum of one week. If the toxicity has improved to ≤ Grade 2, the dose should be administered at that time. For a toxicity that delays Day 8 dosing, if the toxicity has not resolved to ≤ Grade 2 within one week, dosing should resume with the next scheduled cycle, ie, the next dose will be Day 1 of the following cycle. Regardless of whether the Day 8 dose is delayed for toxicity, there should be a minimum of 14 days between the Day 8 infusion and the Day 1 infusion of the next cycle (day of delay is counted as day 1 of this 14-day period).

Dose Reductions and Discontinuation

The major toxicities of sacituzumab govitecan are expected to be gastrointestinal symptoms and hematologic suppression. All subjects will be closely monitored over the course of their treatment and aggressively medically managed, including dose reduction and interruption, in order to prevent the need for treatment discontinuation and serious complications of these toxicities. All efforts to avoid dose reduction should be taken to address toxicity prior to institution of dose reduction. Sacituzumab govitecan dose reductions and interruptions will be managed based on toxicity severity, as assessed by NCI CTCAE v5.0. Leukopenia or lymphopenia in the absence of neutropenia will not require dose delay or dose modification. The dose of sacituzumab govitecan **must not** be re-escalated following a dose reduction. Table 2 summarizes recommendations for sacituzumab govitecan dose reductions and discontinuations for treatment-related toxicities.

Table 2. Recommended Dose Modification Schedule for Sacituzumab Govitecan

Adverse Reaction	Occurrence	Dose Modification or Action
Severe neutropenia		
Grade 4 neutropenia ≥ 7 days, OR Grade 3-4 febrile neutropenia, OR At time of scheduled treatment, Grade 3 or 4 neutropenia that delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1	First	25% dose reduction and administer G-CSF
	Second	50% dose reduction
	Third	Discontinue treatment
At time of scheduled treatment, Grade 3 or 4 neutropenia that delays dosing beyond 3 weeks for recovery to ≤ Grade 1	First	Discontinue treatment
Severe nonneutropenic toxicity		
Grade 4 nonhematologic toxicity of any duration, OR Any Grade 3 or 4 nausea, vomiting, or diarrhea due to treatment that is not controlled with antiemetics and antidiarrheal agents OR Other Grade 3 or 4 nonhematologic toxicity persisting > 48 hours despite optimal medical management, OR At time of scheduled treatment, Grade 3 or 4 nonneutropenic hematologic or nonhematologic toxicity that delays dose by 2 or 3 weeks for recovery to ≤ Grade 1	First	25% dose reduction
	Second	50% dose reduction
	Third	Discontinue treatment
In the event of Grade 3 or 4 nonneutropenic hematologic or nonhematologic toxicity that does not recover to ≤ Grade 1 within 3 weeks	First	Discontinue treatment
Infusion-Related Toxicities		
Grade 2 or Grade 3 infusion-related reaction despite optimal management	Recurrent	Discontinue treatment
Grade 4 infusion-related reaction	First	Discontinue treatment

G-CSF = granulocyte colony-stimulating factor; NCI-CTCAE = National Cancer Institute-Common Terminology Criteria for Adverse Events
Refer to Section 10.2.2.6 for the NCI-CTCAE severity grading details.

6.4. Concomitant Medications

Medications initiated prior to the first dose of study drug will be recorded as prior medications with medications initiated following receipt of the first dose of study drug until 30 days after treatment discontinuation will be captured as concomitant medications. Medication information will be entered in the appropriate eCRF with information regarding dose, indication, route of administration and dates of administration. Medications used for prophylaxis of anticipated study drug adverse events as outlined in the protocol should be documented with rationale for prophylactic intent.

Subjects must avoid the use of osteopathic traditional medicine and any other traditional medicine during the study.

No anti-cancer therapies, aside from the study drug are permitted during this study. However, palliative and/or supportive medications, such as pain medications, bone modifying-medications (bisphosphonates or denosumab), anti-emetics or anti-diarrheal medications, transfusions and growth factor support are allowed at the investigator's discretion. Palliative radiotherapy is permitted.

Treatment may be continued after completion of palliative radiotherapy. In this case, sacituzumab govitecan administration should be interrupted one week before the procedure and reinstated no earlier than two weeks after the procedure. In the event that a subject requires surgery, sacituzumab govitecan should be interrupted one week before the procedure if clinically feasible and dosing should be held for 2 weeks after the procedure. Dosing may resume thereafter if the subject is clinically stable. Extensive surgical procedures such as abdominal, cranial surgeries for example, may require suspension of dosing for 4 weeks before dosing may resume to allow for an adequate period for healing.

The study medical monitor must approve continuation of therapy with sacituzumab govitecan prior to resumption of dosing.

Subjects are allowed to receive the COVID-19 vaccine to reduce the risk and complications of COVID-19 infection. Details on the risk assessment and mitigation plan for concurrent administration of the COVID-19 vaccine are provided in Appendix 2.

6.5. Drug Interactions

No formal drug-drug interaction studies with sacituzumab govitecan have been conducted. SN-38 (the active metabolite of sacituzumab govitecan) is metabolized via human UGT1A1. Concomitant administration of inhibitors or inducers of UGT1A1 with sacituzumab govitecan should be avoided due to the potential to either increase (inhibitors) or decrease (inducers) the exposure to SN-38, unless there are no therapeutic alternatives.

6.5.1. UGT1A1 Inhibitors

Co-administration of sacituzumab govitecan with inhibitors of UGT1A1 (eg, atazanavir, gemfibrozil, indinavir) may increase systemic exposure to the active metabolite, SN-38. Do not administer UGT1A1 inhibitors with sacituzumab govitecan unless there are no therapeutic alternatives. A list of example UGT1A1 inhibitors is provided in Appendix 5.

6.5.2. UGT1A1 Inducers

Exposure to SN-38 may be substantially reduced in subjects concomitantly receiving UGT1A1 enzyme inducers. Do not administer UGT1A1 inducers with sacituzumab govitecan unless there are no therapeutic alternatives. A list of example UGT1A1 inducers is provided in Appendix 5.

6.6. Treatment Compliance

Sacituzumab govitecan will be administered at scheduled study centers under the supervision of the Investigator or sub-Investigator(s). The pharmacist will maintain records of study drug receipt, preparation, and dispensing, including the applicable lot numbers, subject's weight, and total drug administered in milligrams. Any discrepancy between the calculated dose and dose administered and the reason for the discrepancy must be recorded in the source documents.

7. STUDY DRUG MATERIALS AND MANAGEMENT

7.1. Study Drug

The Investigational Medicinal Product (IMP) is supplied as a sterile, off-white to yellowish lyophilized powder in single-dose glass vials. It is formulated in 2-(N-morpholino)ethane sulfonic acid (MES) buffer containing trehalose and polysorbate 80 and contains no preservatives. Following reconstitution, the concentration of the IMP is 10 mg/mL. The pH of the reconstituted solution is approximately 6.5.

7.2. Study Drug Packaging and Labeling

Vials are intended for clinical use only and the label includes the study name or code, name of the IMP, lot number, strength and expiration date, as applicable. Sacituzumab govitecan will be supplied in cartons, each containing 1 vial.

7.3. Study Drug Storage

The IMP is photosensitive and should be protected from light during storage, transport, and administration.

All vials of IMP must be stored under refrigeration (2 °C to 8 °C) and protected from light in a locked location that can be accessed only by the study Pharmacist, the Principal Investigator, or other duly authorized persons until administered to the subject. Additional information regarding study drug storage is presented in the Pharmacy Manual.

7.4. Study Drug Preparation

Dose preparation must be documented according to institutional guidelines and all records must be kept in the study file.

The Pharmacist is required to follow the appropriate steps regarding the reconstitution and dilution of the study drug per the Pharmacy Manual.

7.5. Administration

Sacituzumab govitecan is a cytotoxic drug. Follow applicable special handling and disposal procedures.

- Administer IMP as an IV infusion
- Infusions may be administered over 1 to 2 hours if previous infusions were well tolerated.
- Protect the infusion bag from light.
- An infusion pump may be used.

- Compatibility with polypropylene infusion bags has been confirmed.
- Compatibility with in-line filters and other ancillary infusion equipment has not been studied.
- Do not mix IMP, or administer as an infusion, with other medicinal products.
- Upon completion of the infusion, flush the IV line with 20 mL 0.9% Sodium Chloride Injection, United States Pharmacopeia (USP).

7.6. Study Drug Accountability

The IMP must be stored in a locked location that can be accessed only by the Study Pharmacist, the Principal Investigator, or another duly authorized study/site personnel.

The IMP must not be used outside of the context of this protocol. Under no circumstances should the Investigator or other site personnel supply IMP to other Investigators, subjects, or clinics, or allow supplies to be used other than as directed by this protocol without prior written authorization from the sponsor.

Records documenting receipt, use, return, loss, or other disposition of the IMP must be kept. A complete drug accountability record should be maintained. In all cases, information describing study medication supplies and their disposition, subject-by-subject, must be provided and signed by the Investigator (or the pharmacist or other person who dispensed the drug) and collected by the study sponsor or designee. Requisite data include relevant dates, quantities, batches or code numbers, and subject identification for subjects who received IMP.

7.7. Study Drug Handling and Disposal

7.7.1. Study Drug Shipment

The IMP will be shipped at refrigerated temperature in an insulated shipper, protected from light and with a temperature monitoring device. The shipper must be opened immediately upon receipt.

7.7.2. Receipt of IMP

All IMP should be inspected upon receipt as indicated on the Packing List. Follow instructions on the Packing List to complete any necessary forms and report issues or product complaints as directed in the Pharmacy Manual. Sites must retain all IMP vials affected and may not perform any additional testing on the vials in question.

If use of the interactive web-based response system (IWRS) is required, follow the process found in the study-specific IWRS Manual.

The study Pharmacist, or the Principal Investigator or designee must confirm that appropriate conditions have been maintained during transit and that any discrepancies are reported per guidance found in the Pharmacy Manual.

7.7.3. Study Drug Disposal

At the end of the study, or if instructed to do so during the study, the IMP may be destroyed at the site as dictated by the appropriate standard operating procedures at the participating institutions. IMP may not be destroyed until it has been reconciled and written confirmation has been received from the sponsor Study Contact or designee.

Destruction of IMP must be documented.

If local destruction is not possible, the IMP may be returned as per the agreed upon process. Return of IMP must be documented. The sponsor Study Contact or designee assigned to your site will assist with the return of IMP once it has been deemed appropriate by the sponsor.

8. ASSESSMENT OF EFFICACY

Efficacy will not be assessed in this study.

9. OTHER EVALUATIONS

Pharmacokinetics, immunogenicity, and 'other' evaluations will not be assessed for this study.

10. ASSESSMENT OF SAFETY

10.1. Safety Parameters

10.1.1. Weight

Weight will be measured as indicated in Table 1.

10.1.2. Laboratory Assessments

All clinical laboratory samples for safety will be collected and analyzed by the site's local laboratory with appropriate clinical action taken based on the Investigator's clinical judgement. All investigations will be assessed for all subjects as indicated in Table 1. Additional and more frequent tests may be performed at the Investigator's discretion. The specific details of each assessment will be recorded on the appropriate eCRF. Clinically-significant abnormal results should be repeated within 24-48 hours or as per treating physician's discretion to confirm abnormality and followed until resolution. The panels of laboratory tests to be performed are detailed below. For subjects rolling over from IMMU-132-15 or any new parent studies in the future, Gilead's standard reference ranges will be used.

10.1.2.1. Hematology

Hemoglobin, white blood cell (WBC) count and differential (with ANC), and platelet count to be performed as indicated in Table 1. ANC levels must be confirmed prior to each dose as described in Section 6.3.2.3.

10.1.2.2. Serum Chemistry

Total protein, albumin, total bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (estimated glomerular filtration rate [GFR] using a validated model, refer to Appendix 3), blood urea nitrogen (BUN) or urea, glucose, sodium, potassium, magnesium, chloride, bicarbonate, calcium, phosphorus will be obtained for all subjects as indicated in Table 1.

10.1.2.3. Pregnancy Test

In female subjects of childbearing potential, pregnancy testing will be performed according to the Schedule of Assessments (Table 1) and as presented in Appendix 4.

10.1.2.4. Follicle-Stimulating Hormone

Follicle-stimulating hormone (FSH) testing will be conducted as needed per Appendix 4 for determination of childbearing potential.

10.2. Adverse Event Reporting

All subjects must be carefully monitored for AEs as defined below. Sufficient information must be obtained by the Investigator to determine whether the event meets criteria for immediate reporting to the sponsor (ie, SAEs and pregnancies). All AEs should be assessed in terms of their seriousness, severity, and relationship to the study drug, per the definitions in the following sections.

10.2.1. Safety Reporting Definitions

10.2.1.1. Adverse Events

An AE is defined as any untoward medical occurrence in a subject administered a medicinal product that does not necessarily have a causal relationship with this treatment. An AE can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational medicinal product.

Adverse events may include worsening or exacerbation of the disease under study; worsening or exacerbation of preexisting conditions or events; intercurrent illnesses; or drug interactions. Anticipated fluctuations of preexisting conditions that do not represent a clinically significant exacerbation or worsening are not considered AEs.

Adverse events should be recorded using medical terminology and whenever possible, a diagnosis should be provided for clearly associated signs, symptoms, and/or abnormal laboratory results. If the final diagnosis is not known at the time of initial detection, the provisional diagnosis or signs or symptoms should be recorded and updated when the final diagnosis is available.

Surgical procedures are not AEs; they are therapeutic measures for conditions that require surgery. The condition, provided it develops or is a worsening of a preexisting condition for which the surgery is required, is the AE.

10.2.1.2. Serious Adverse Events

A serious adverse event (SAE) is any untoward medical occurrence that at any dose:

- Is fatal (results in death)
- Is life-threatening: The subject was at immediate risk of death from the AE as it occurred. This does not include an event that, had it occurred in a more severe form, or was allowed to continue, might have caused death.
- Requires inpatient hospitalization or prolongation of existing hospitalization (in the absence of a precipitating, clinical AE hospitalization is not in itself an SAE)

- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect (in the child of a subject who was exposed to the study treatment)
- An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such events are intensive treatments in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

An SAE does not include:

- Progression of disease (See Section 10.2.2.9)
- Hospitalization for a routine clinical procedure
- Pre-planned treatments or surgical procedures requiring hospitalization (the conditions should be documented as appropriate in the eCRF)
- Hospitalization for non-medical reasons (ie, social admissions, hospitalizations for social, convenience or respite care)

10.2.1.3. Special Situation Reports

Special situation reports (SSRs) include all reports of medication error, abuse, misuse, overdose, occupational exposure, drug interactions, exposure via breastfeeding, unexpected benefit, transmission of infectious agents via the product, counterfeit of falsified medicine, and pregnancy regardless of an associated AE.

Medication error is any unintentional error in the prescribing, dispensing, preparation for administration or administration of a study drug while the medication is in the control of a health care professional, patient, or consumer. Medication errors may be classified as a medication error without an AE, which includes situations of missed dose, medication error with an AE, intercepted medication error, or potential medication error.

Abuse is defined as persistent or sporadic intentional excessive use of a study drug by a subject.

Misuse is defined as any intentional and inappropriate use of a study drug that is not in accordance with the protocol instructions or the local prescribing information.

An overdose is defined as an accidental or intentional administration of a quantity of a study drug given per administration or cumulatively that is above the maximum recommended dose as per protocol or in the product labeling (as it applies to the daily dose of the subject in question).

In cases of a discrepancy in drug accountability, overdose will be established only when it is clear that the subject has taken the excess dose(s). Overdose cannot be established when the subject cannot account for the discrepancy, except in cases in which the investigator has reason to suspect that the subject has taken the additional dose(s).

Occupational exposure is defined as exposure to a study drug as a result of one's professional or nonprofessional occupation.

Drug interaction is defined as any drug/drug, drug/food, or drug/device interaction.

Unexpected benefit is defined as an unintended therapeutic effect where the results are judged to be desirable and beneficial.

Transmission of infectious agents is defined as any suspected transmission of an infected agent through a sponsor study drug.

Counterfeit or falsified medicine is defined as any study drug with a false representation of (a) its identity, (b) its source, or (c) its history.

10.2.2. Adverse Event and Special Situation Reporting

10.2.2.1. Requirements for Collection of Events Before Study Drug Initiation

After informed consent, but before initiation of study drug, the following types of events must be reported on the applicable eCRFs: all SAEs and any AEs that are related to protocol-required procedures.

10.2.2.2. Reporting Period for Adverse Events

Following initiation of study drug, collect all AEs, regardless of cause or relationship, until 30 days after last administration of study drug and report the AEs on the eCRFs as instructed.

All AEs and clinically significant laboratory abnormalities should be followed until resolution or until the AE is stable, if possible. Gilead may request that certain AEs be followed beyond the protocol-defined follow-up period.

10.2.2.3. Reporting Period for Serious Adverse Events

All SAEs, regardless of cause or relationship, that occur after the subject first consents to participate in the study (ie, signing the informed consent form) and throughout the duration of the study, including the Safety Follow-up visits, must be reported on the applicable eCRFs and to Gilead Global Patient Safety. This also includes any SAEs resulting from protocol-associated procedures performed after the informed consent form is signed.

Any SAEs (including deaths; see Section 10.2.3 for exclusions) that occur during the study (including the Safety Follow-up visits detailed in the Schedule of Assessments [Table 1]) or within 30 days of the last dose of study drug or initiation of alternative therapy, whichever is later, should also be reported regardless of causality.

Investigators are not obligated to actively seek SAEs after the protocol-defined follow-up period; however, if the investigator learns of any SAEs that occur after the protocol-defined follow-up period has concluded and the event is deemed relevant to the use of study drug, the investigator should promptly document and report the event to Gilead Global Patient Safety.

10.2.2.4. Reporting Period for Special Situation Reports

All study drug SSRs that occur from study drug initiation and throughout the duration of the study, including the Safety Follow-up visits, must be reported to the sponsor.

10.2.2.5. Adverse Event Collection and Documentation

Adverse Events Reporting Process

It is the responsibility of the Investigator to document all AEs that occur during the study. All adverse events regardless of seriousness, severity, or relationship to the study drug, that occur during the safety reporting period, must be recorded in the AE page of the eCRF. AEs should be elicited by asking the subject a non-leading question (eg, “have you experienced any new or changed symptoms since we last asked/since your last visit?”). AEs can also represent abnormal findings from laboratory tests and other study procedures. The Investigator must review all laboratory and test data; abnormal findings should be assessed to determine if they meet the criteria for adverse events (Section 10.2.1.1, Section 10.2.2.8).

For all AEs, the Investigator must pursue and obtain information adequate to assess whether it meets the criteria for classification as an SAE and, therefore, requires immediate notification to the sponsor or its designee (Section 10.2.5). In addition, sufficient information must be obtained by the Investigator to perform a causality assessment, which must be done for every adverse event. Follow-up by the Investigator is required until the event or its sequelae resolve or stabilize, as assessed by the Investigator. The outcome of each AE must be provided on the eCRF.

To assist in the sponsor’s assessment of each case, further information may be requested from the Investigator to provide clarity and understanding of the event in the context of the clinical study.

Adverse events and SAEs resulting from SSRs must be reported in accordance with the AE and SAE reporting guidance summarized in Sections 10.2.2.5 and 10.2.5.

Serious Adverse Events Reporting Process

SAEs are to be recorded on the eCRF and SAE form. The SAE form must be forwarded to the sponsor or the sponsor's designee in accordance with the timelines summarized in Section 10.2.5. The Investigator should include a detailed description of the event(s), including the clinical course, criteria for seriousness, treatments administered, action taken with respect to study drug, rationale for the Investigator's assessment, including causality, and other relevant information, such as possible alternative etiologies.

Information captured on both the SAE form and entered into the eCRF should be consistent.

Special Situation Reporting Process

All SSRs will be recorded on the special situation report form and forwarded to the sponsor or sponsor's designee in accordance with the timelines summarized in Section 10.2.2.5.

10.2.2.6. Assessment of Adverse Event Severity

The severity of AEs will be graded using NCI CTCAE v5.0. For each SAE, the highest severity grade should be reported. If a CTCAE criterion does not exist, the Investigator should assess the severity according to the criteria in Table 3.

Table 3. Grading for Adverse Events Not Listed in NCI-CTCAE

CTCAE Grade	Severity	Definition
Grade 1	Mild	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate	Minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL[1]
Grade 3	Severe	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL[2,3]
Grade 4	Life-threatening	Life-threatening consequences; urgent intervention indicated[3]
Grade 5	Death	Results in death[3]

1 Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

2 Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

3 These events should be assessed to determine if they meet the definition of SAEs.

ADL = activities of daily living; NCI-CTCAE = National Cancer Institute common terminology criteria for adverse events; SAE = serious adverse event.

10.2.2.7. Assessment of Adverse Event Causality

The Investigator's causality assessment is required for all AEs including both non-serious and serious AEs. The causality assessment is the determination of whether there exists a reasonable possibility that the study treatment caused or contributed to an AE. In order to determine causality, the Investigator should consider the temporal relationship of the onset of the event to the start of study drug; the course of the event and, in particular, whether the event resolves or improves with dose reduction or study drug discontinuation; the known toxicities of the study drug; events expected to occur in subjects with the disease under study; and concomitant medications and comorbidities that may have a known association with the event. Causality is to be assessed as follows:

- Related: Plausible time relationship to study treatment administration; plausible time relationship of improvement or resolution with study drug dose reduction or discontinuation; event cannot be explained by the underlying disease, comorbidities, or concomitant medications.

- Possibly related: a reasonable time sequence to administration of study drug, but which could also be explained the underlying disease, comorbidities, or concomitant medications.

- Unlikely related: a temporal relationship to drug administration that makes a causal relationship improbable and the underlying disease, comorbidities, or concomitant medications provide a plausible explanation.

- Not related: a causal relationship to the study drug can be easily ruled out.

10.2.2.8. Adverse Events Based on Abnormal Test Findings

An abnormal test finding that meets any one of the criteria below should be considered an AE:

- Test result is associated with accompanying symptoms.

- Test result requires additional diagnostic testing or medical/surgical intervention.

- Test result leads to a change in study treatment dosing (eg, dose modification, interruption, or permanent discontinuation) or concomitant drug treatment (eg, addition, interruption, or discontinuation) or any other change in a concomitant medication or therapy

- Test result leads to any of the outcomes included in the definition of an SAE. (Note: This would be reported as an SAE, Section 10.2.5)

- Test result is considered an AE by the Investigator.

Laboratory results that fall outside the reference range and do not meet one of the criteria above should not be reported as AEs. Repeating an abnormal test, in the absence of the above conditions, does not constitute an AE. Any abnormal test result that is determined to be an error does not require reporting as an AE.

Any abnormal test finding that meets the criteria for an SAE (Section 10.2.1.2) should be reported as such.

10.2.2.9. Disease Progression

Disease progression should not be reported as an AE. It is important to differentiate expected disease progression from an AE. Events that are clearly consistent with the expected pattern of disease progression should not be considered AEs. Expected disease progression refers to an event that is unequivocally related to disease progression, and that the clinical course is consistent with what would be expected for the subject's disease. A clinical event in the setting of disease progression would be considered an AE if it could not unequivocally be attributed to or consistent with expected disease progression.

Hospitalization due to signs and symptoms of disease progression (as defined above) should not be reported as an SAE.

10.2.3. Reporting Deaths

Death is an outcome of an SAE and not, in itself, an SAE. When death is an outcome, the event(s) resulting in death should be reported (eg, "pulmonary embolism" with a fatal outcome). The appropriate diagnosis (ie, cause of death) should be recorded and assigned severity Grade 5. The time period for reporting AEs (including fatal AEs) continues up to 30 days after the last dose of study drug or initiation of alternative therapy, whichever is later. Deaths that occur more than 30 days after the last dose of study drug or initiation of alternative therapy, whichever is later, are to be reported if they are assessed by the Investigator as related to study drug. Fatal AEs meeting these criteria are SAEs and should be reported to the sponsor or the sponsor's designee in accordance with the timelines specified in Section 10.2.5.

Deaths related to progression of the underlying disease during the study will not be reported as an SAE (see Section 10.2.2.9) if, in the Investigator's judgment, the event is unequivocally due to the expected course of progression of the underlying disease, and not due to another cause.

10.2.4. Pregnancy Reporting Process

The investigator should report pregnancies in female study subjects that are identified after initiation of study drug and throughout the study (including through the protocol-required Safety Follow-up visits) or 6 months after the last study drug dose, whichever is longer, to Gilead Global Patient Safety using the pregnancy report form within 24 hours of the Investigator becoming aware of the pregnancy.

The investigator should report pregnancies in female partners of male subjects that are identified after initiation of study drug by the male subject and throughout the study (including through the protocol-required Safety Follow-up visits), or 3 months after the last study drug dose, whichever is longer, to Gilead Global Patient Safety using the pregnancy report form within 24 hours of the Investigator becoming aware of the pregnancy.

Contact details for transmitting the pregnancy report form are as follows:

Gilead Global Patient Safety
Email: Safety_FC@gilead.com
or
Fax: 1-650-522-5477

The pregnancy itself is not considered an AE, nor is an induced elective abortion to terminate a pregnancy without medical reasons.

All other premature terminations of pregnancy (eg, a spontaneous abortion, an induced therapeutic abortion due to complications or other medical reasons) must be reported within 24 hours as an SAE, as described in Section 10.2.5. The underlying medical reason for this procedure should be recorded as the AE term.

A spontaneous abortion is always considered to be an SAE and will be reported as described in Section 10.2.5. Furthermore, any SAE occurring as an adverse pregnancy outcome after the study must be reported to Gilead Global Patient Safety.

The subject should receive appropriate monitoring and care until the conclusion of the pregnancy. The outcome of the pregnancy/partner pregnancy should be reported to Gilead Global Patient Safety using the pregnancy report form. If the end of the pregnancy/partner pregnancy occurs after the study has been completed, the outcome should be reported directly to Gilead Global Patient Safety. Gilead Global Patient Safety contact information is as follows: email: Safety_FC@gilead.com and fax: +1 (650) 522-5477.

10.2.5. Investigator Immediate Reporting Requirements

All SAEs and pregnancies must be reported to the sponsor or the sponsor's designee immediately, and no later than 24 hours of becoming aware of the event.

The initial SAE report should be as complete as possible (Section 10.2.2.5); however, reporting should not be delayed in order to obtain more information. The SAE should also be entered on the applicable eCRF. All follow-up information should be reported within 24 hours of the Investigator's awareness of the information. The Investigator is required to provide follow-up information in response to queries from the sponsor or the sponsor's designee. Hospital discharge summaries should be provided for subjects who are hospitalized and autopsy findings, if available, should be provided for subjects who die.

All SAEs and pregnancies should be reported to the contact indicated on the SAE form and entered on the applicable eCRF.

10.2.6. Investigator Notification to Local Institutional Review Boards/Ethics Committees

The Investigator must notify their local Institutional Review Board (IRB)s/ECs about certain AEs including suspected unexpected serious adverse reactions (SUSARs) in accordance with their IRBs'/ECs' policies and procedures and Good Clinical Practice (GCP)/International Conference on Harmonisation (ICH) guidelines.

10.2.7. Sponsor Responsibilities

The sponsor or its designee will be responsible for reporting all AEs, SAEs and SUSARs to the appropriate regulatory authorities, Investigators, and Central IRBs/ECs in accordance with all applicable regulations and guidance documents.

11. STATISTICS

11.1. Sample Size Determination

The sample size of up to approximately 200 subjects assumes that 10-15% of subjects in an ongoing sacituzumab govitecan parent studies will rollover to this study upon closure of the parent study.

11.2. Populations for Analyses

All Treated Subjects: All subjects who received at least one dose of sacituzumab govitecan.

11.3. Statistical Analyses

These analyses will be presented by cancer types and histology when deemed appropriate and by the overall study population.CCI [redacted]

11.3.1. Endpoints

The primary endpoints are as follows:

- Percentage of participants experiencing any AE
- Percentage of participants experiencing any SAE
- Percentage of participants experiencing any laboratory abnormality

11.3.2. Efficacy Analyses

Efficacy will not be analyzed.

11.3.3. Safety Analyses

Safety analyses will be based on All Treated Subjects. All safety analyses will be presented by cancer types and histology when deemed appropriate. Safety data will be summarized using descriptive statistics. Categorical variables will be summarized by number and percentage. Continuous variables will be summarized using n (number of subjects with available data), mean, standard deviation, median, upper and lower quartiles, and range (minimum and maximum), unless otherwise specified.

A treatment-emergent AE will be defined as any AE that begins on or after the date of first dose of study drug up to the date of last dose of study drug plus 30 days. Treatment-emergent laboratory abnormalities will be defined as values that increase at least 1 toxicity grade from baseline at any time after baseline up to and including the date of last dose of study drug plus 30 days. Treatment-emergent AEs and SAEs and clinical laboratory test results will be summarized. Study drug exposure and concomitant medications will also be summarized.

12. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

12.1. Study Monitoring

Monitoring procedures developed by the sponsor or its designee will be followed, in order to comply with ICH GCP, Food and Drug Administration (FDA) and applicable guidelines. Review of the subject's eCRFs, electronic medical/health records, or paper source documentation for completeness and accuracy will be required, and a review of all applicable regulatory documents will be performed. All available source documents should be obtained by the Investigator and provided to the sponsor's designee for review at each monitoring visit. Monitoring visits to the study site will be conducted periodically during the study to ensure that GCP and all aspects of the protocol are followed.

Queries may be issued in the eCRF system to be addressed by the appropriate study site personnel within a timely manner when clarification of eCRF data is required to ensure data accuracy and completeness. The sponsor's designee will ensure that the investigation is conducted according to protocol design and regulatory requirements by frequent communications.

Regulatory authorities, the IRB/Independent Ethics Committee (IEC), and/or the sponsor's Clinical Quality Assurance group or designee may request access to all source documents, subject's eCRFs, and other study documentation for on-site audit or inspection. Access to these documents must be guaranteed by the Investigator, who must cooperate and provide support at all times for these activities as allowed by standard operating procedure or policy of their institution.

12.2. Audits and Inspections

Authorized representatives of the sponsor, a regulatory authority, an Independent EC or an IRB may visit the site to perform audits or inspections, including source data verification. The purpose of a sponsor's audit or inspection is to systematically and independently examine all study-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, Good Clinical Practice (GCP) guidelines of the ICH, and any applicable regulatory requirements. The Investigator should contact the sponsor immediately if contacted by a regulatory agency about an inspection.

12.3. Institutional Review Board /Independent Ethics Committee

The Principal Investigator must obtain IRB/IEC approval for the investigation. Initial IRB/IEC approval, and all materials approved by the IRB/IEC for this study including the subject consent form and recruitment materials must be maintained by the Investigator and made available for inspection.

13. QUALITY CONTROL AND QUALITY ASSURANCE

The sponsor has ethical, legal and scientific obligations to follow this study carefully in a detailed and orderly manner in accordance with established research principles and applicable regulations.

The study site may be subject to review by the IRB/IEC, to quality assurance audits performed by the sponsor's designee and/or to inspection by appropriate regulatory authorities. Investigator(s) and their relevant personnel must agree to be available and participate with audit visits conducted at a reasonable time in a reasonable manner, Investigator/Institution must guarantee direct access to source documents by the sponsor and its designee, and appropriate regulatory authorities.

Global regulatory authorities may also audit the Investigator during or after the study. The Investigator should contact the sponsor's designated contact immediately if this occurs and must fully cooperate with regulatory authority audits conducted at a reasonable time in a reasonable manner.

14. ETHICS

14.1. Ethics Review

The final study protocol, including the final version of the Informed Consent Form, must be approved or given a favorable opinion in writing by an IRB or IEC as appropriate. The investigator must submit written approval to the sponsor before he or she can enroll any subject into the study.

The Principal Investigator is responsible for informing the IRB or IEC of any amendment to the protocol in accordance with local requirements. In addition, the IRB or IEC must approve all advertising used to recruit subjects for the study. The protocol must be re-approved by the IRB or IEC upon receipt of amendments and annually, as local regulations require.

The Principal Investigator is also responsible for providing the IRB with reports of any reportable serious adverse drug reactions from any other study conducted with the investigational product. The sponsor will provide this information to the Principal Investigator.

Progress reports and notifications of serious adverse drug reactions will be provided to the IRB or IEC according to local regulations and guidelines.

14.2. Ethical Conduct of the Study

This study is planned to be conducted both in the US, Europe, and rest of the world countries. The study will be performed in accordance with ICH GCP guidelines, the Declaration of Helsinki, 18th World Medical Assembly, Helsinki, Finland, 1964 and later revisions (as mandated for European studies), and applicable local regulatory requirements and laws. In the United States, ethical protection is provided by compliance with GCPs as described in ICH and 21 Code of Federal Regulation (CFR) 50 (Protection of Human Subjects).

The IRB and the IEC will review all appropriate study documentation in order to safeguard the rights, safety and well-being of the subjects. The study will only be conducted at sites where IRB/IEC approval has been obtained.

The Investigator is responsible for providing their IRB/IEC with any required study documents, progress reports and safety updates and is responsible for notifying the IRB/IEC promptly of all SAEs occurring at the site.

All correspondence with the IRB/IEC should be retained in the Investigator File. Copies of IRB/IEC approvals should be forwarded to the sponsor or the designee.

The only circumstance in which an amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the Investigator must notify the IRB/IEC and the sponsor or its designee in writing within 5 working days after the implementation**.**

14.3. Written Informed Consent

It is the responsibility of the Investigator to give each subject (or the subject's legally authorized representative) full and adequate verbal and written information regarding the objective and procedures of the study including the possible risks and benefits involved. Written subject information, approved by the IRB/IEC, must be given to each subject before any study-related procedure is undertaken. During the consent process, the subject must be informed about their right to withdraw from the study at any time. The subject must also be given ample time to read the written informed consent form and have all study-related questions answered to the satisfaction of the subject (or the subject's legally acceptable representative). It is the responsibility of the Investigator to obtain a signature from each subject, the subject's legally acceptable representative (if applicable), and from the persons conducting the informed consent discussion prior to undertaking any study-related procedure. The subject (or the subject's legally acceptable representative) must be given a copy of the signed and dated informed consent form.

The Investigator is also responsible for providing the subject (or the subject's legally acceptable representative) with any clinical study updates that may affect the subject's willingness to continue participation in the study. The informed consent process must be documented in the subject's medical or source chart. The written subject information must not be changed without prior approval by the sponsor or its designee and the IRB/IEC.

Per ICH E6 4.3.3, it is recommended that the Investigator notify the subject's primary care physician of the subject's participation in the study if the subject agrees to the Investigator informing the primary care physician.

14.4. Good Clinical Practice

The study will be conducted in accordance with the ICH E6 GCP and the appropriate local and national regulatory requirement(s). The Investigator will be thoroughly familiar with the appropriate use of the study medications as described in the protocol and investigator's brochure.

Essential clinical documents will be maintained to demonstrate the validity of the study and the integrity of the data collected. Master files for this study should be established at the beginning of the study, maintained for the duration of the study, and retained according to the appropriate regulations.

14.5. Protocol Compliance

The Investigator will conduct the study in compliance with the protocol provided by the sponsor or its designee and given approval by the IRB/IEC and the appropriate regulatory authorities. Modifications to the protocol should not be made. Changes to the protocol will require written IRB/IEC approval prior to implementation, except when the modification is needed to eliminate an immediate hazard(s) to the subject. The IRB/IEC may provide, if applicable, regulatory authorities permit, expedited review and approval for minor change(s) in ongoing studies that have the approval of the IRB/IEC. The sponsor's designee will submit all protocol modifications to the regulatory authorities in accordance with the governing regulations.

When immediate deviation from the protocol is required to eliminate an immediate hazard(s) to subjects, the Investigator will contact the sponsor's designee, if circumstances permit, to discuss the planned course of action. Any departures from the protocol must be fully documented in the subject's source documentation.

14.6. Subject Data Protection

Information collected in this clinical study is subject to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) as described in 45 CFR 160 and 45 CFR 164, as well as the REGULATION (EU) 2016/679 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 April 2016 (on the protection of natural persons with regard to the processing of personal data and on the free movement of such data). The study Investigator is responsible for informing subjects of their rights under HIPAA and General Data Protection and obtaining any necessary HIPAA authorizations. In compliance with the provisions of that policy, the sponsor or designee will not collect any protected health information and will only collect de-identified health information. Any clinical study information referred to in this section is understood to be compliant with the provisions of the Privacy Act. The information obtained during the conduct of this clinical study is confidential, and disclosure to third parties other than those noted below is prohibited.

Information obtained during the conduct of this study will be used by the sponsor or designee in connection with the development of the study drug. The study Investigator is obliged to provide the sponsor or designee with complete test results and all data developed in this study. This information may be disclosed to other physicians participating in the study, to the FDA, or to national and local health authorities. To ensure compliance with all current Federal Regulations and the ICH/GCP guidelines, data generated by this study must be available for inspection upon request by representatives of the FDA, national and local health authorities, sponsor, designee, and the IRB/IEC for each study site.

14.7. Financial Disclosure

In accordance with 21 CFR Part 54, FDA requires that certain financial interests and arrangements between sponsors of clinical investigations be disclosed in marketing applications. Since the results of this study may eventually be used in a marketing application, compliance with this Federal statute is essential. In order to comply with the provisions of this regulation, the sponsor requests that every Investigator and sub-Investigator mentioned on FDA Form 1572 or its equivalent fill out a financial disclosure form. Under the provisions of 21 CFR Part 54, the term clinical Investigator includes the spouse and each dependent child of the Investigator.

The provisions of 21 CFR Part 54 specify disclosure of significant equity interests in the sponsor that exceed $50,000, or significant payments of other sorts made by the sponsor to the Investigator that have a monetary value of more than $25,000, exclusive of the costs of conducting the clinical study or other clinical studies (eg, grants to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation), during the time the clinical Investigator is carrying out the study or for 1 year following the completion of the study. If a change in financial interest occurs throughout the study, the Investigator is obligated

to notify the sponsor. To assist the sponsor or designee in providing the FDA with the required information, please complete the financial disclosure form and return a signed copy. All information provided in the financial disclosure form will be regarded as strictly confidential and will only be disclosed to the FDA.

14.8. Sponsor Discontinuation Criteria

The sponsor reserves the right to discontinue the study prior to inclusion of the intended number of subjects but intends only to exercise this right for valid scientific or administrative reasons. After such a decision, the Investigator must contact all participating subjects within a time period set by the sponsor. In the unlikely event of premature termination or discontinuation of the study, in the event the Investigator believes a subject is continuing to receive clinical benefit, the sponsor will discuss options with the Investigator in order to ensure continuing supply of sacituzumab govitecan. As directed by the sponsor's designee, all study materials will be collected and all eCRFs completed to the greatest extent possible.

15. DATA HANDLING AND RECORDKEEPING

15.1. Inspection of Records

The sponsor or its designee will be allowed to conduct site visits to the investigation facilities for the purpose of monitoring any aspect of the study. The Investigator agrees to allow the monitor to inspect the drug storage area, study drug stocks, drug accountability records, subject charts and study source documents, and other records relative to study conduct.

15.2. Retention of Records

Records and documents pertaining to the conduct of this study, including eCRFs, source documents, consent forms, laboratory test results, and medication inventory records must be retained by the Investigator for at least 15 years. No study records shall be destroyed without prior authorization from the sponsor. For studies conducted outside the US under a US Investigational New Drug (IND), the Investigator must also comply with US FDA IND regulations, ICH guidelines, and with the regulations of the relevant national and local health authorities. Current US federal law requires an Investigator to maintain such records for a period of two years following approval of a Biologic License Application, or, if the Biologic License Application is not approved, until two years following notification by the sponsor that the clinical investigations have been discontinued.

15.3. Electronic Case Report Forms

An eCRF is required and must be completed for each enrolled subject. The completed original eCRFs are the sole property of the sponsor and should not be made available in any form to third parties, except for authorized representatives of appropriate regulatory authorities, without written permission from the sponsor.

It is the Investigator's responsibility to ensure completion and to review and approve all eCRFs. eCRFs must be signed by the Investigator or by an authorized staff member. These signatures serve to attest that the information contained on the eCRFs is true. At all times, the Investigator has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the eCRFs. Subject source documents are the physician's subject records maintained at the study site. In most cases, the source documents will be the hospital's or the physician's chart. In cases where the source documents are the hospital or the physician's chart, the information collected on the eCRFs must match those charts.

Queries will be issued in the eCRF system by the sponsor or designee in cases where clarification of eCRF data entered by the study site is required. The appropriate site personnel will address all queries per site agreement with the sponsor during the course of the study and afterwards to ensure data accuracy and completeness.

16. PUBLICATION POLICY

The conditions regulating dissemination of the information derived from this clinical study are described in the Clinical Study Agreement.

17. LIST OF REFERENCES

Cardillo TM, Govindan SV, Sharkey RM, Trisal P, Arrojo R, Liu D, et al. Sacituzumab Govitecan (IMMU-132), an Anti-Trop-2/SN-38 Antibody-Drug Conjugate: Characterization and Efficacy in Pancreatic, Gastric, and Other Cancers. Bioconjug Chem 2015;26 (5):919-31.

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Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16 (1):31-41.

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18. APPENDICES

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Appendix 1. Investigator Signature Page

GILEAD SCIENCES, INC.
(IMMUNOMEDICS, INC. IS NOW PART OF THE GILEAD GROUP OF COMPANIES)
333 LAKESIDE DRIVE
FOSTER CITY, CA 94404

STUDY ACKNOWLEDGMENT

Open-label Rollover Study to Evaluate Long-Term Safety in Subjects with Metastatic Solid Tumors that are Benefiting from Continuation of Therapy with Sacituzumab Govitecan

IMMU-132-14, Protocol Amendment 1, 27 August 2021

This protocol has been approved by Gilead Sciences, Inc. (Immunomedics, Inc. is now part of the Gilead group of companies). The following signature documents this approval.

PPD

Name (Printed)
Vice President, Clinical Development

PPD

Signature

PPD

INVESTIGATOR STATEMENT

I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Gilead Sciences, Inc. I will discuss this material with them to ensure that they are fully informed about the drugs and the study.

Principal Investigator Name (Printed)

Signature

Date

Site Number

Appendix 2. Pandemic Risk Assessment and Mitigation Plan

During an ongoing pandemic, potential risks associated with subjects being unable to attend study visits have been identified for this study.

These risks can be summarized as follows:

1) Study drug supplies

   a) Subjects may be unable to return to the site for a number of visits to get the study drug, or the site may be unable to accept any subject visits. Without study drugs, the subject would not be able to continue their study treatment as planned per protocol.

      Mitigation plan: At the earliest opportunity, the site will schedule in-person subject visits and return to the regular protocol schedule of assessments.

   b) Shipments of study drug could be delayed because of transportation issues. Without study drug, enrolled subjects would not be able to continue receiving the study drug as planned per protocol.

      Mitigation plan: The site's study drug inventory should be closely monitored. Site staff should notify the sponsor or delegate if they foresee shortage in study drug inventory or if there is any interruption in local shipping service. The sponsor will continue to monitor inventory at the study drug depot and investigational sites. Manual shipments will be triggered as necessary.

2) Subject safety monitoring and follow-up:

   a) Subjects may be unable or unwilling to come to the investigational site for their scheduled study visits as required per protocol.

      Mitigation plan: For subjects who may be unable or unwilling to visit the investigational site for their scheduled study visits as required per protocol, the principal investigator or qualified delegate will conduct a remote study visit, via phone or video conferencing, to assess the subject within the target visit window date whenever possible. During the remote study visit, the following information at minimum will be reviewed:

      i) Confirm if subject has experienced any AEs/SAEs/special situations (including pregnancy) and follow up on any unresolved AEs/SAEs.

      ii) Review the current list of concomitant medications and document any new concomitant medications.

b) Subjects may be unable or unwilling to travel to the site for planned assessments (eg, safety blood draws); hence samples may not be sent for central laboratory analyses.

Mitigation plan: Local laboratories or other vendors may be used as appropriate to monitor subject safety until the subject can return to the site for their regular follow-up per protocol. Any changes in the party conducting laboratory assessments for the study due to the pandemic will be documented accordingly. Pregnancy testing may be performed using a home urine pregnancy test if local laboratory pregnancy testing is not feasible.

c) Subjects may be unable or unwilling to attend the study visit to sign an updated informed consent form version.

Mitigation plan: The site staff will follow their approved consent process and remain in compliance with the local Ethics Committee/Institutional Review Board (EC/IRB) and national laws and regulations. Remote consent will be allowed if it has been approved by the local EC/IRB. The consent process will be documented and confirmed by normal consent procedure at the earliest opportunity.

d) The safety of study subjects is important and testing of COVID-19 infection will be based on local clinical guidelines for testing based on signs/symptoms and/or suspected exposure to COVID-19.

Mitigation plan: If subject has a diagnosis of COVID-19 while on this clinical study, study drug may be held until clinical improvement or resolution in accordance with the treating physician's judgment and general sacituzumab govitecan dose delay guidance in the protocol. Additional supportive care and treatment measures for COVID-19 infection on the study will be performed in accordance with local institutional guidelines. Subjects with a COVID-19 infection while participating in the clinical study will have this event documented as an AE in the clinical database.

3) Protocol and monitoring compliance:

a) Protocol deviations may occur in case scheduled visits cannot be conducted as planned per protocol.

Mitigation plan: If it is not possible to complete a required procedure, an unscheduled visit should be conducted as soon as possible when conditions allow. The situation should be recorded and explained as a protocol deviation. Any missed subject visits or deviation to the protocol due to the pandemic must be reported in the eCRF and described in the clinical study report. Any remote study visits that are conducted in lieu of clinic visits due to the pandemic will be documented as a protocol deviation related to the pandemic.

b) Study monitors may be unable to carry out source data review or source data verification, or study drug accountability or assess protocol and Good Clinical Practice compliance. This may lead to delays in source data verification, an increase in protocol deviations, or underreporting of AEs.

Mitigation plan: The study monitor is to remain in close communication with the site to ensure data entry and query resolution. Remote source data verification may be arranged if allowed by local regulation and the Study Monitoring Plan. The study monitor is to reference the Study Monitoring Plan for guidance on how to conduct an off-site monitoring visit. The study staff is to save and document all relevant communication in the study files. The status of sites that cannot accept monitoring visits and/or subjects on-site, must be tracked centrally and updated on a regular basis.

4) Missing data and data integrity:

There may be an increased amount of missing data due to subjects missing visits/assessments. This could have an impact on the analysis and the interpretation of clinical study data.

Mitigation plan: Implications of a pandemic on methodological aspects for the study will be thoroughly assessed and documented, and relevant actions will be taken as appropriate (eg, modification of the statistical analysis plan) and in compliance with regulatory authorities' guidance. Overall, the clinical study report will describe the impact of the pandemic on the interpretability of study data.

5) Concurrent administration of the COVID-19 vaccine:

There may be potential safety issues due to concurrent administration of the COVID-19 vaccine and study drug.

Mitigation plan: There is not substantial efficacy or safety data regarding the concurrent administration of the COVID-19 vaccine and sacituzumab govitecan. Subjects are allowed to receive the COVID-19 vaccine to reduce the risk and complications of COVID-19 infection. Investigators and study personnel should provide close surveillance of subjects after COVID-19 vaccine administration and the institutional guidelines should always be followed. The administration of specific COVID-19 vaccine must be documented in the clinical database and AEs associated with COVID-19 vaccine administration should be recorded in the AE eCRF. COVID-19 vaccine administration should be recorded in the prior or concomitant medication eCRF as appropriate. The study visits should continue as planned, if possible, and clinically appropriate if vaccination occurs while the subject is on the study.

Risks will be assessed continuously, and temporary measures will be implemented to mitigate these risks as part of a mitigation plan, as described above. These measures will be communicated to the relevant stakeholders as appropriate and are intended to provide alternate methods that will ensure the evaluation and assessment of the safety of subjects who are enrolled in this study.

Since these potential risks are considered mitigated with the implementation of these measures, the expected risk/benefit assessment of sacituzumab govitecan in study subjects remains unchanged.

Appendix 3. Cockcroft-Gault Formula

$C_{Cr}=[((140–age) \times weight)/(72 \times S_{Cr})] \times 0.85$ (if female)

Abbreviations/ Units
C_{Cr} (creatinine clearance) = mL/minute
Age = years
Weight = kg
SCr (serum creatinine) = mg/dL

{Cockcroft 1976}

Appendix 4. Pregnancy Precautions, Definition for Female of Childbearing Potential, and Contraceptive Requirements

1) Definitions

a. Definition of Childbearing Potential

For the purposes of this study, a female-born subject is considered of childbearing potential following the initiation of puberty (Tanner stage 2) until becoming postmenopausal unless the subject is permanently sterile or has medically documented ovarian failure.

Women are considered to be in a postmenopausal state when they are at least 54 years of age with cessation of previously occurring menses for at least 12 months without an alternative cause. In addition, women younger than 54 years with amenorrhea of at least 12 months also may be considered postmenopausal if their FSH level is in the postmenopausal range and they are not using hormonal contraception or hormonal replacement therapy.

Permanent sterilization includes hysterectomy, bilateral oophorectomy, or bilateral salpingectomy in a female subject of any age.

b. Definition of Male Fertility

For the purposes of this study, a male-born subject is considered fertile after the initiation of puberty unless the subject is permanently sterile by bilateral orchidectomy or medical documentation.

2) Contraception Requirements for Female Subjects

a. Study Drug Effects on Pregnancy and Hormonal Contraception

Sacituzumab govitecan is contraindicated in pregnancy because a malformative effect has been demonstrated/suspected or is unknown, taking into consideration class effects and genotoxic potential. Based on the assessment of published data related to CYP450 enzyme inhibition and induction experiments for SN-38, efficacy of hormonal contraception is not expected to be impacted due to sacituzumab govitecan administration. A dedicated oral contraceptive drug-drug interaction clinical study has not been conducted. Refer to the latest version of the investigator's brochure for additional information.

b. Contraception Requirements for Female Subjects of Childbearing Potential

The inclusion of female subjects of childbearing potential requires the use of highly effective contraceptive measures that have a failure rate of less than 1% per year. A negative urine pregnancy test is required at baseline prior to study treatment administration on C1D1. The baseline urine pregnancy test does not need to be conducted if the screening pregnancy test was performed within 72 hours before study treatment administration on C1D1. Pregnancy tests will be performed thereafter on Day 1 of each treatment cycle starting from Cycle 2 through the last cycle and every 28 days after the last dose of study drug until the end of contraception requirement. If a urine pregnancy test is positive or equivocal, a confirmatory serum pregnancy test will be required.

Duration of required contraception for female subjects in this clinical study should start from the screening visit until 6 months after the last dose of study drug.

Female subjects must agree to 1 of the following contraceptive methods:

Complete abstinence from intercourse of reproductive potential. Abstinence is an acceptable method of contraception only when it is in line with the subject's preferred and usual lifestyle.

Or

Consistent and correct use of 1 of the following methods of birth control listed below:

- Nonhormonal intrauterine device (IUD)
- Hormonal IUD (must be used in conjunction with a barrier method)
- Bilateral tubal occlusion (upon medical assessment of surgical success)
- Vasectomy in the male partner (upon medical assessment of surgical success)

Or

Female subjects who wish to use a hormonally based method must use it in conjunction with a barrier method, preferably a male condom. Hormonal methods are restricted to those associated with the inhibition of ovulation. Hormonally based contraceptives and barrier methods permitted for use in this protocol are as follows:

- Hormonal methods (each method must be used with a barrier method, preferably male condom)
    a) Oral contraceptives (either combined or progesterone only) (see Appendix 5 for a list of UGT1A1 inducers and Section 6.5)
    b) Injectable progesterone
    c) Subdermal contraceptive implant
    d) Transdermal contraceptive patch
    e) Contraceptive vaginal ring
- Barrier methods (each method must be used with a hormonal method)
    a) Male condom (with or without spermicide)
    b) Female condom (with or without spermicide)

c) Diaphragm with spermicide

d) Cervical cap with spermicide

e) Sponge with spermicide

Inclusion of methods of contraception in this list of permitted methods does not imply that the method is approved in any country or region. Methods should only be used if locally approved.

Female subjects must also refrain from egg donation, cryopreservation of germ cells, and in vitro fertilization during treatment and until the end of contraception requirement. Female subjects should be advised to seek advice of the Investigator about egg donation and cryopreservation of germ cells before treatment.

3) Contraception Requirements for Male Subjects

It is theoretically possible that a relevant systemic concentration of study drug may be achieved in a female partner from exposure of the male subject's seminal fluid and poses a potential risk to an embryo/fetus. Therefore, male subjects with female partners of childbearing potential must use condoms during treatment and until 6 months after the last dose of study drug. If the female partner of childbearing potential is not pregnant, additional highly effective contraception recommendations should also be considered.

Male subjects must also refrain from sperm donation, and/or cryopreservation of germ cells during treatment and until the end of contraception requirement. Male subjects should be advised to seek advice of the Investigator about sperm donation and cryopreservation of germ cells before treatment.

4) Unacceptable Birth Control Methods

Birth control methods that are unacceptable include periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method. A female condom and a male condom should not be used together.

5) Procedures to be Followed in the Event of Pregnancy

Female subjects will be instructed to notify the Investigator if they become pregnant or suspect they are pregnant at any time from start of the study and throughout the study (including the post study drug follow-up period) or 6 months after the last dose of study drug, whichever is longer. Sacituzumab govitecan must be discontinued immediately upon consultation with the medical monitor.

Male subjects whose partner has become pregnant or suspects she is pregnant from start of study and throughout the study (including the post study drug follow-up period) or 3 months after the last dose of study drug, whichever is longer, must also report the information to the investigator. Instructions for reporting pregnancy, partner pregnancy, and pregnancy outcome are outlined in Section 10.2.4.

Appendix 5. UGT1A1 Inhibitors and Inducers

Inhibitors of UGT1A1	Inducers of UGT1A1
Amitriptyline	Carbamazepine
Atazanavir	Efavirenz
Dacomitinib	Ethinylestradiol
Dasabuvir	Lamotrigine
Deferasirox	Phenobarbital
Eltrombopag	Phenytoin
Enasidenib	Primidone
Erlotinib	Rifampicin
Flunitrazepam	Ritonavir
Flurbiprofen	Tipranavir
Fostamatinib	
Gemfibrozil	
Glecaprevir	
Indinavir	
Indomethacin	
Ketoconazole	
Nilotinib	
Ombitasvir	
Paritaprevir	
Pazopanib	
Pexidartinib	
Pibrentasvir	
Probenecid	
Propofol	
Regorafenib	
Rucaparib	
Silibinin	
Sorafenib	
Valproic acid	