CLINICAL STUDY PROTOCOL

Study Title:	A Phase 2 Open-Label Study of Sacituzumab Govitecan (IMMU-132) in Subjects with Metastatic Solid Tumors
Study Acronym:	TROPiCS-03
Short Title:	Study of Sacituzumab Govitecan in Participants With Metastatic Solid Tumors
Sponsor:	Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA
IND Number:	115621
EU CT Number:	2024-513611-28
ClinicalTrials.gov Identifier:	NCT03964727
Indication:	Metastatic Solid Tumors
Protocol ID:	IMMU-132-11
Contact Information:	The medical monitor name and contact information will be provided on the Key Study Team Contact List.
Protocol Version/Date:	Amendment 5: 17 December 2024
Amendment History:	Original: 16 January 2019 Amendment 1: 12 September 2019 Amendment 2: 24 March 2021 Amendment 3: 29 November 2021 Amendment 4: 09 October 2023 Amendment 5: 17 December 2024 A high-level summary of the changes in each amendment is provided in Appendix 17.11.
Country-specific Requirements:	Country-specific requirements, as applicable, are listed in Appendix 17.10.

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.

This study will be conducted in compliance with this protocol and in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) and applicable regulatory requirements.

The study will be conducted in accordance with European Union Clinical Trials Directive (2001/20/EC) and EU Regulation 536/2014.

PROTOCOL SYNOPSIS

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Name of Sponsor/Company: Gilead Sciences, Inc.		
Name of Investigational Product: sacituzumab govitecan (IMMU-132)		
Name of Active Ingredient: sacituzumab govitecan		
Protocol Number: IMMU-132-11	**Phase:** 2	**Region(s):** Global
Title of Study: A Phase 2 Open-Label Study of Sacituzumab Govitecan (IMMU-132) in Subjects with Metastatic Solid Tumors		
Study Acronym: TROPiCS-03		
Short Title: Study of Sacituzumab Govitecan in Participants With Metastatic Solid Tumors		
Study Center(s): Up to 95 sites		
Studied Period (years): Date first subject enrolled: 12 Sep 2019 Estimated date last subject enrolled: 30 May 2023	**Phase of development:** 2	

Objectives and Endpoints:

Primary Objective	Primary Endpoint
Assess the ORR of sacituzumab govitecan in subjects with metastatic solid tumors by Investigator's assessment according to the Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) criteria.	Objective response rate (ORR) according to RECIST 1.1 by Investigator's assessment.
Secondary Objectives	**Secondary Endpoints**
• Assess the ORR, duration of response (DOR), clinical benefit rate (CBR), and progression-free survival (PFS) of sacituzumab govitecan in subjects with metastatic solid tumors by blinded independent central review (BICR) according to RECIST 1.1 criteria. • Assess the DOR, CBR, and PFS of sacituzumab govitecan in subjects with metastatic solid tumors by Investigator's assessment according to RECIST 1.1 criteria. • Assess the OS of sacituzumab govitecan in subjects with metastatic solid tumors. • Assess the safety of sacituzumab govitecan in subjects with metastatic solid tumors. • Assess the PK and immunogenicity of sacituzumab govitecan in subjects with metastatic solid tumors.	• ORR, DOR, CBR, and PFS according to RECIST 1.1 by BICR. • DOR, CBR, and PFS, according to RECIST 1.1 by Investigator's assessment. • Overall survival (OS). • Incidence of treatment-emergent adverse events (AEs) and clinical laboratory abnormalities. • Serum concentrations of sacituzumab govitecan over time and incidence of anti-drug antibody (ADA) to sacituzumab govitecan.
Exploratory Objectives	**Exploratory Endpoints**
• CCI [redacted]	[redacted]

Study Design:

This is a multi-cohort, open-label, Phase 2 study designed to assess the efficacy and safety of sacituzumab govitecan in adult subjects with metastatic solid tumors. Upon meeting the eligibility criteria, the subjects are treated with sacituzumab govitecan at 10 mg/kg via intravenous infusion on Days 1 and 8 of a 21-day cycle. The original protocol included the following cohorts: non-small cell lung cancer (NSCLC; adenocarcinoma and squamous cell carcinoma [SCC]), head and neck squamous cell carcinoma (HNSCC), and endometrial carcinoma.

With Amendment 3, this is a single stage cohort evaluation for proof of concept (POC) with recalculation of sample sizes for all the cohorts. An additional cohort for small cell lung cancer (SCLC) has been added. The Sponsor will evaluate the totality of efficacy and safety data at the end of the POC stage independently for each of the cohorts, and may potentially expand the HNSCC, endometrial carcinoma and SCLC cohorts to enroll additional subjects up to a total sample size of 100 to 120 subjects in each selected cohort. In addition, OS is included as a secondary endpoint and will be assessed for all cohorts CCI [redacted]

Study modifications after implementation of Protocol Amendment 5 (PA5):

Following implementation of PA5, subjects who are still receiving treatment may continue treatment as part of the study for as long as they are deriving clinical benefit. Radiographic tumor assessments per protocol will be discontinued; however, treatment response should continue to be evaluated per standard of care. Information on study drug administration and safety assessments will continue to be collected. Subjects who have discontinued treatment and were being followed for survival and subsequent therapy at the time of PA5 implementation, will be discontinued from the study and survival follow-up with subsequent therapy information will no longer be collected.

At the completion of the study, subjects who were deriving benefit from sacituzumab govitecan may continue to receive treatment in a rollover study (Study IMMU-132-14) in locations where the study is available.

Methodology:

Baseline/Screening evaluations that must be performed after providing written informed consent and within 28 days prior to Cycle 1, Day 1 (C1D1) include subject's medical and surgical history, histology or cytology documentation, computed tomography (CT) or magnetic resonance imaging (MRI) imaging with intravenous (IV) contrast (chest, abdomen, pelvis, and other areas of known/suspected involvement), unless known anaphylaxis to contrast and/or medically contraindicated (imaging options described below), complete physical examination with vital signs and Eastern Cooperative Oncology Group (ECOG) Performance Score, electrocardiogram (ECG), complete blood count (CBC) with differential, routine serum chemistries including liver function tests, lactate dehydrogenase (LDH), uric acid, hepatitis B and C testing, HIV testing, and pregnancy test in women of childbearing potential. Routine chemistries and liver function tests need to be repeated for C1D1 if they were obtained for Screening > 72 hours prior to C1D1 dosing. In females of childbearing

potential, a negative serum pregnancy test during screening and a negative urine pregnancy test is required at baseline prior to study treatment administration on C1D1. The urine pregnancy test at baseline (prior to study treatment administration on C1D1) does not need to be conducted if the serum pregnancy at screening was performed within 72 hours before study treatment administration on C1D1.

All subjects who previously failed screening may be rescreened only once.

Twelve-lead ECG will be obtained at baseline and prior to the C1D1 infusion. Abnormal findings should be evaluated as clinically indicated, including repeated ECGs. ECGs may be done at other timepoints during the study if clinically indicated.

Tumor blocks (preferably obtained within 12 months of study entry if clinically feasible) or 20 newly sectioned unstained slides (6 slides minimum) of archived biopsy/surgical specimens are requested. A baseline biopsy is required if archival tissue is not available. Fine needle aspirates and bone biopsies are not suitable samples. These specimens should be submitted within the 28-day screening period, after the subject provides written informed consent.

Serum samples will be collected from all subjects for PK and immunogenicity assessments. A blood sample will be collected for UGT1A1 genotype.

Blood samples will be collected from all subjects for biomarker analyses.

CCI [redacted]

Adverse events (AEs), concomitant medications (continued, changed), and hematology and chemistry blood work will be obtained during every study visit with appropriate follow-up of clinically significant abnormal laboratory assessments or AEs.

Response assessments by CT or MRI scan with IV contrast (chest, abdomen, and pelvis with scanning of other regions including brain MRI as clinically indicated) unless known anaphylaxis to contrast and/or medically contraindicated. If the use of IV contrast is medically contraindicated for a subject, 1 of the following options may be used (listed in order of preference): CT without contrast, MRI without contrast, or attempt to desensitize the subject with steroids. For each subject, the same imaging technique should be used throughout the study for tumor assessment. If a subject had brain lesions at study entry, brain MRI will be needed at all assessments. The timing of imaging is based on calendar time from the date of C1D1. Scans will be performed for all subjects at baseline and every 6 weeks for the first 6 months after C1D1 and then every 9 weeks thereafter until the occurrence of radiologic progression of disease (progressive disease; PD), as per RECIST 1.1, requiring discontinuation of treatment. Dose delays and cycle delays should not result in delays in the timing of imaging. For subjects with evidence of complete response (CR) or partial response (PR), a confirmatory scan must be obtained at least 4 to 6 weeks after initial documentation of CR or PR.

Subjects will be treated until PD (according to RECIST 1.1 by Investigator's assessment), unacceptable toxicity, study withdrawal, or death, whichever comes first. However, treatment may be continued beyond PD if there is evidence of clinical benefit per the Investigator and the subject is tolerating study treatment. The following clinical criteria should be met for subjects to continue to receive treatment beyond the Investigator-assessed progression:

- Absence of symptoms and signs indicating clinically significant progression of disease.
- No decline in performance status.
- Absence of symptomatic rapid disease progression requiring urgent medical intervention (eg, symptomatic pleural effusion, spinal cord compression).

Sponsor consultation is required before subjects initiate the treatment beyond progression. If this occurs, the subject will remain in the study and continue to be monitored according to the protocol schedule of assessments).

Subjects who discontinue treatment because of toxicity will continue with radiologic response assessments per protocol-required schedule, until PD or initiation of new therapy. The reason for treatment discontinuation will be documented and any treatment-related AEs or clinically significant abnormal laboratory values at that time will be followed until resolution or stabilization.

The EOT Visit will be conducted within 30 days of the date when the decision is made to discontinue treatment. A Safety Follow-up Visit will be conducted 30 days after the last treatment dose. If the EOT Visit and Safety Follow-up Visit coincide within 2 weeks of each other, the same assessments may be utilized for both events. Subjects will then be followed every 12 weeks for survival, unless the subject explicitly indicates a desire to forego survival follow-up to their study Investigator. Subjects will be followed until death, withdrawal of consent, loss to follow-up, Sponsor-terminated study or completion of survival follow-up (24 months after the last subject is dosed), whichever occurs first.

For subjects who are lost to follow-up, study staff may use public records (eg, public health records) to obtain information about survival status where allowable by local regulation.

Following implementation of PA5, subjects who previously discontinued treatment will no longer be followed for survival follow-up and subsequent therapy and will discontinue the study.

The end of study for a subject occurs when they have completed all periods of the study including long-term survival follow-up due to the following reasons: death, the subject withdraws consent, there is documented loss to follow-up of the subject, or the Sponsor terminated the study, whichever comes first. The end of the entire study for all subjects is defined as the date on which the last subject remaining on study completes the last study visit/call/survival follow-up or when the Sponsor decides to end the study. The Sponsor reserves the right to terminate the study at any time for any reason (including safety).

National Cancer Institute-Common Terminology Criteria for Adverse Events version 5.0 (NCI-CTCAE v5.0) toxicity grades will be used to classify safety evaluations and AEs, including serious adverse events (SAEs). SAEs must be reported to the Sponsor's designee within 24 hours of the event, and treatment-related AEs and SAEs will be followed until recovery or stabilization in the event of residual effects. Abnormal clinically significant laboratory values must be repeated within 48 hours and followed until resolution.

Following implementation of PA5:

- Subjects may continue treatment as part of the study, for as long as they are deriving

clinical benefit. After they meet one of the criteria for treatment discontinuation, they will have an EOT visit and a 30-Day Safety Follow-up Visit. There will be no additional assessments including survival follow-up and subsequent therapy collection.

- Subjects will have the end of study at the same time as the EOT visit. However, if at the time of an EOT visit, subjects have unresolved AEs, the end of study may be delayed until all AEs have been resolved or stabilized.

Number of Subjects (Planned):

CCI [redacted]

Diagnosis and Main Criteria for Inclusion:

Target Population:

Adult subjects with histologically documented advanced or metastatic NSCLC (adenocarcinoma and SCC), HNSCC, endometrial carcinoma, or SCLC. All subjects must meet the eligibility criteria described in the following inclusion criteria and exclusion criteria.

Inclusion Criteria:

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

1) Female or male subjects, $\geq$ 18 years of age, who are able to understand and give written informed consent.
2) Subjects with the following histologically documented metastatic (M1, Stage IV) or locally advanced solid tumors.
   a) NSCLC (adenocarcinoma or SCC) that has progressed after prior platinum-based chemotherapy and programmed death-(ligand) 1 (PD-(L)1) directed therapy given sequentially (in either order) or in combination. These agents could have been taken as monotherapy or in combination with other agents. If subjects have had recurrence/relapse or lack of response within 6 months of completing chemotherapy with or without PD-(L)1 directed therapy for locally advanced disease, that line of therapy may be counted for eligibility.
   b) HNSCC that has progressed after prior platinum-based chemotherapy and anti-PD-(L)1 directed therapy given sequentially (in either order) or in combination. These agents

could have been taken as monotherapy or in combination with other agents. No more than 3 prior lines of systemic treatment is allowed.

c) Endometrial carcinoma that has progressed after prior platinum-based chemotherapy and anti- PD-(L)1 directed therapy given sequentially (in either order) or in combination. These agents could have been taken as monotherapy or in combination with other agents. No more than 3 prior lines of systemic treatment is allowed. Endometrial carcinoma with any histology including microsatellite instability-high /mismatch repair deficient and microsatellite stable (MSI-h/dMMR and MSS) are allowed.

d) Extensive stage SCLC that has progressed after prior platinum-based chemotherapy and PD-(L)1 directed therapy. No more than one prior line of systemic treatment is allowed (re-challenge with the same initial regimen is not allowed).

3) ECOG Performance Status score of 0 or 1 (see Appendix 17.2).

4) Adequate hematologic counts without transfusional or growth factor support within 2 weeks of study drug initiation (hemoglobin ≥ 9 g/dL, absolute neutrophil count (ANC) ≥ 1,500/mm^3, and platelets ≥ 100,000/μL).

5) Adequate hepatic function (bilirubin ≤ 1.5 institutional upper limit of normal [IULN], aspartate aminotransferase [AST], and alanine aminotransferase [ALT] ≤ 2.5 × IULN or ≤ 5 × IULN if known liver metastases and serum albumin ≥ 3 g/dL).

6) Creatinine clearance ≥ 30 mL/min as assessed by Cockcroft-Gault (see Appendix 17.3).

7) Subjects must have at least a 3-month life expectancy.

8) Have measurable disease by CT or MRI scan as per RECIST 1.1 criteria (see Appendix 17.4). Tumor lesions situated in a previously irradiated area may be utilized if they are considered measurable and PD has been demonstrated in such lesions.

9) 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 17.5.

10) Tumor blocks (preferably obtained within 12 months of study entry if clinically feasible) or 20 newly sectioned unstained slides (6 slides minimum) of archived biopsy/surgical specimens are requested. A baseline biopsy is required if archival tissue is not available. Fine needle aspirates and bone biopsies are not suitable samples. These specimens should be submitted within the 28-day screening period, after the subject provides written informed consent.

Exclusion Criteria:

Subjects meeting any of the following exclusion criteria at Screening will not be enrolled in the study.

1) Positive serum pregnancy test (Appendix 17.5) or women who are lactating.

2) Are currently participating in or has participated in a study of an investigational agent or using an investigational device within 4 weeks prior to the first dose of study drug. Subjects participating in observational studies are eligible.
3) Have had a prior anti-cancer biologic agent within 4 weeks prior to study Day 1 or have had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1.
4) Have not recovered (ie, ≤ Grade 1) from AEs due to a previously administered agent.
   - **Note**: Subjects with ≤ Grade 2 neuropathy or ≤ Grade 2 alopecia are exceptions to this criterion and may qualify for the study.
   - **Note**: If subjects underwent major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study drug.
   - **Note**: Subjects with Grade ≤ 2 immune-mediated toxicities (except colitis) related to immunotherapy and/or radiation treatment that are long lasting, but stable on treatment and not requiring agents that are excluded by this protocol may qualify for the study.
5) Have previously received topoisomerase I inhibitors (for SCLC cohort: Etoposide with platinum combination in first-line setting is allowed).
6) Have an active second malignancy.
   - **Note**: Subjects with a history of malignancy that has been completely treated, with no evidence of active cancer for 3 years prior to enrollment, or subjects with surgically cured tumors with a low risk of recurrence, may be enrolled.
7) Have known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they have stable CNS disease for at least 4 weeks prior to the first dose of study drug and all neurologic symptoms have returned to baseline, no evidence of new or enlarging brain metastases and are taking ≤ 20 mg/day of prednisone or its equivalent. All subjects with carcinomatous meningitis are excluded regardless of clinical stability.
8) Have active cardiac disease, defined as:
   - Myocardial infarction or unstable angina pectoris within 6 months of Day 1.
   - History of serious ventricular arrhythmia (ie, ventricular tachycardia or ventricular fibrillation), high-grade atrioventricular block, or other cardiac arrhythmias requiring anti-arrhythmic medications (except for atrial fibrillation that is well controlled with anti-arrhythmic medication); history of QT interval prolongation.
   - New York Heart Association (NYHA) Class III or greater congestive heart failure or left ventricular ejection fraction of < 40%.
9) Have active chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease), immune-mediated colitis, or gastrointestinal (GI) perforation within 6 months of C1D1.
10) Have an active infection requiring IV antibiotics.

11) Have positive human immunodeficiency virus (HIV)-1 or HIV-2 antibody with detectable viral load or taking medications that may interfere with SN-38 (the active metabolite of sacituzumab govitecan).

12) Have active hepatitis B virus (HBV) or hepatitis C virus (HCV), subjects with a detectable viral load will be excluded.

- Subjects who test positive for hepatitis B surface antigen (HBsAg). Subjects who test positive for hepatitis B core antibody (anti-HBc) will require HBV DNA by quantitative polymerase chain reaction (PCR) for confirmation of active disease.
- Subjects who test positive for HCV antibody. Subjects who test positive for HCV antibody will require HCV RNA by quantitative PCR for confirmation of active disease. Subjects with a known history of HCV or a positive HCV antibody test will not require an HCV antibody at screening and will only require HCV RNA by quantitative PCR for confirmation of active disease.

13) 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.

14) Impending need for palliative radiation therapy or surgery for pathological fractures and/or for medullary compression within 4 weeks prior to initiating study treatment.

15) Additional cohort-specific exclusion criteria:

NSCLC cohort (adenocarcinoma and SCC):

a) Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder (ie, pulmonary emboli within 3 months of enrollment, severe asthma, severe chronic obstructive pulmonary disease, restrictive lung disease, pleural effusion, etc); any autoimmune, connective tissue, or inflammatory disorders with pulmonary involvement (ie, rheumatoid arthritis, Sjogren syndrome, sarcoidosis, etc); or prior pneumonectomy.

HNSCC cohort:

b) Subjects with nasopharynx carcinoma.

c) Subjects who had progressive disease within 6 months of completion of curative therapy.

Endometrial carcinoma cohort:

d) Subjects who have carcinosarcoma (malignant mixed Mullerian tumor), endometrial leiomyosarcoma, and/or endometrial stromal sarcomas.

Small cell lung cancer cohort:

e) Subjects who never received platinum-containing regimen for SCLC.

f) Limited-stage subjects who are candidates for local or regional therapy.

Investigational product, dosage, and mode of administration:

Sacituzumab govitecan will be administered at 10 mg/kg as an IV infusion on Days 1 and 8 of a 21-day cycle until PD, unacceptable toxicity, or withdrawal of consent. Treatment beyond PD is permitted if there is evidence of clinical benefit per the Investigator and the subject is tolerating study treatment. The clinical criteria for treatment beyond PD are described in the Methodology section of the Synopsis.

Statistical Methods:

This study was originally designed to limit enrollment to subjects with elevated TROP-2 expression. In Amendment 2, the enrollment criterion for elevated TROP-2 expression was removed, and the study was expanded to include subjects with any level of TROP-2 expression. Clinical activity will be correlated with TROP-2 expression assessed retrospectively.

In Amendment 3, the primary endpoint is ORR according to RECIST 1.1 by Investigator assessment. Secondary endpoints include ORR, DOR, CBR (defined as complete response + partial response + stable disease [CR + PR + SD] for at least 6 months), and PFS according to RECIST 1.1 by BICR; DOR, CBR, and PFS according to RECIST 1.1 by the Investigator assessment; OS; incidence of treatment-emergent AEs and clinical laboratory abnormalities; and serum concentrations of sacituzumab govitecan and incidence of ADAs to sacituzumab govitecan. Summary tables and listings will be prepared using SAS®. Continuous data will be summarized using descriptive statistics: n, mean, median, standard deviation, minimum, and maximum. Categorical data will be summarized using frequency counts and percentages. Data listings will be created to support tables and figures. Any statistical analyses impacted by the coronavirus disease 2019 (COVID-19) pandemic will be detailed in the statistical analysis plan (SAP).

Statistical analyses will be performed using SAS® (SAS Institute, Version 9.2 or later, Cary, NC) and other software.

In Amendment 3, the sample size for the POC stage was not based on formal power calculation but to ensure the accuracy for the estimation of ORR. For each cohort of NSCLC, assuming the true ORR is 25%, a sample size of 30 subjects will ensure the half-width of the 95% CI is ≤ 0.155; for the HNSCC cohort, assuming the true ORR is 22%, a sample size of 30 subjects in the POC stage will ensure the half-width of the 95% CI is ≤ 0.148; for the endometrial carcinoma cohort, assuming the true ORR is 23%, a sample size of 35 subjects will ensure the half-width of the 95% CI is ≤ 0.139; for the SCLC cohort, assuming the true ORR is 25%, a sample size of 40 subjects will ensure the half-width of the 95% CI is ≤ 0.134.

Once the minimal number of responses (CR or PR) are observed at the end of POC stage in any of the cohorts of HNSCC, endometrial carcinoma or SCLC, the Sponsor may evaluate the totality of data and choose to expand the specific cohort and enroll approximately a total of 100 to120 subjects. This total sample size of 100 to 120 subjects in the cohort provides adequate power to reject the null hypothesis for ORR H_0:$r \leq r_0$ versus the alternative

hypothesis $H_1{:}r = r_1$, where r_0 is the futile response rate based on historical control data and r_1 is the target response rate.

The minimal number of responses that are required to trigger the potential expansion, the specific power for each sample size, along with the assumed target ORR r_1 and null r_0, are provided by cohort in the table below. The power is calculated using an exact binomial test with a one-sided α of 0.025.

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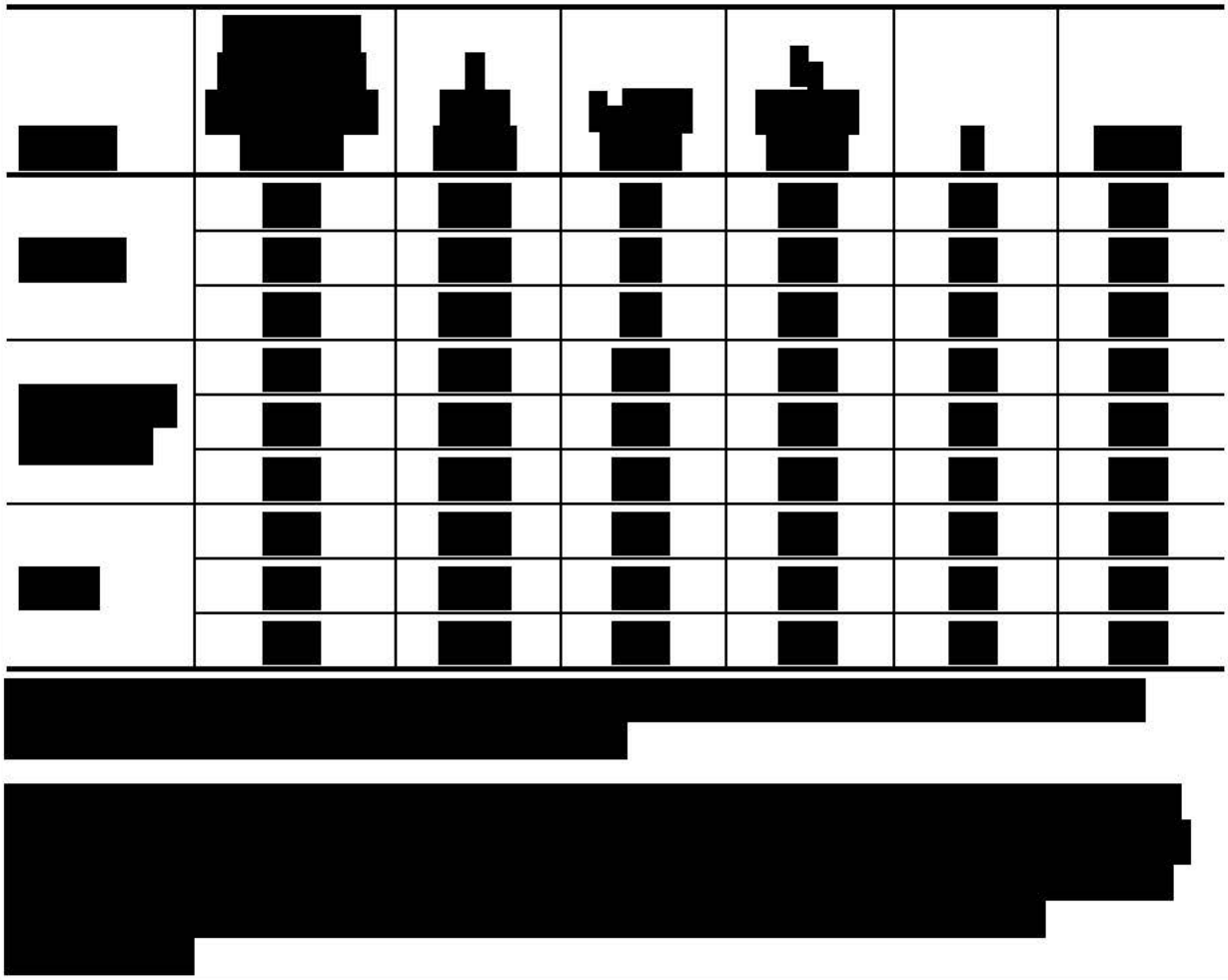

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

5-HT_3	5-hydroxytryptamine
ADA	Anti-drug antibody
ADC	Antibody-drug conjugate
AE	Adverse event
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
ASCO	American Society of Clinical Oncology
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration-time curve
β-hCG	Beta-human chorionic gonadotropin
BICR	Blinded independent central review
BUN	Blood urea nitrogen
C1D1	Cycle 1, Day 1
C_{max}	Maximum plasma concentration
CBC	Complete blood count
CBR	Clinical benefit rate
CFR	Code of Federal Regulation
CI	Confidence interval
CNS	Central nervous system
CO_2	Carbon dioxide
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus disease 2019
CPS	Combined positive score
CR	Complete response
CT	Computed tomography
dMMR	Mismatch repair deficient
DNA	Deoxyribonucleic acid
DOR	Duration of response
ECG	Electrocardiogram
EDC	Electronic data collection
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EMA	European Medicines Agency
EOI	End of infusion
EOT	End of treatment
EU	European Union
EU CT	European Clinical Trials Database

FDA	Food and Drug Administration
FSH	Follicle-stimulating hormone
GCP	Good Clinical Practice
G-CSF	Granulocyte-colony stimulating factor
GI	Gastrointestinal
GLP	Good Laboratory Practice
HBc	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCO_3	Bicarbonate
HCV	Hepatitis C virus
HED	Human equivalent dose
HER2−	Human epidermal growth factor receptor 2-negative
HIPAA	Health Insurance Portability and Accountability Act of 1996
HIV	Human immunodeficiency virus
HNSCC	Head and neck squamous cell carcinoma
HR+	Hormone receptor positive
IC_{50}	Concentration of drug required for 50% inhibition
ICH	International Council for Harmonization
IEC	Independent ethics committee
IO	Immuno-oncology
IgG	Immunoglobulin G
IND	Investigational new drug
IRB	Institutional review board
IULN	Institutional upper limit of normal
IV	Intravenous
LD	Longest diameter
LDH	Lactate dehydrogenase
M1	Metastatic, Stage IV
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic resonance imaging
MSI-H	Microsatellite instability-high
MSS	Microsatellite stable
MTD	Maximum tolerated dose
mTNBC	Metastatic triple-negative breast cancer
mUC	Metastatic urothelial cancer
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Events
NK1	Neurokinin 1
NOAEL	No-observable adverse effect level
NSCLC	Non-small cell lung cancer

NYHA	New York Heart Association
ORR	Objective response rate
OS	Overall survival
PA5	Protocol Amendment 5
PC-3	Epithelial tumor-prostate
PCP	Primary care physician
PCR	Polymerase chain reaction
PD	Progressive disease
PD-1	Programmed cell death protein 1
PD-L1	Programmed death-ligand 1
PET	Positron emission tomography
PFS	Progression-free survival
PK	Pharmacokinetic
POC	Proof of concept
PR	Partial response
PT	Preferred Term
QTc	Corrected QT interval
QTcF	Corrected QT interval using Fridericia's formula
RBC	Red blood cell
RECIST 1.1	Response Evaluation Criteria in Solid Tumors Version 1.1
RNA	Ribonucleic acid
SAE	Serious adverse event
SAP	Statistical analysis plan
SC	Subcutaneous
SCC	Squamous cell carcinoma
SCLC	Small cell lung cancer
SD	Stable disease
SOC	System Organ Class
SUSAR	Suspected unexpected serious adverse reaction
T_{max}	Maximum plasma concentration
TACSTD	Tumor-associated calcium signal transducer
TID	Three (3) times per day
TMB-H	Tumor mutational burden-high
TNBC	Triple-negative breast cancer
TROP-2	Trophoblastic cell-surface antigen-2
UC	Urothelial cancer
UGT1A1	Uridine diphosphate -glucuronosyltransferase 1A1
US	United States
USP	United States Pharmacopoeia
WBC	White blood cell

1. INTRODUCTION

1.1. Sacituzumab Govitecan Background

1.1.1. Mechanism of Action of Sacituzumab Govitecan

Sacituzumab govitecan is an antibody-drug conjugate (ADC) composed of the following 3 components:

1) The humanized monoclonal antibody, hRS7 IgG1κ, which binds to trophoblastic cell-surface antigen-2 (TROP-2), a transmembrane calcium signal transducer that is overexpressed in many epithelial cancers, including triple-negative breast cancer (TNBC).
2) The camptothecin-derived agent SN-38, a topoisomerase I inhibitor.
3) A hydrolyzable linker, with the company designation as CL2A, that links the humanized monoclonal antibody to SN-38.

Binding of TROP-2 by the parental RS7 antibody has been shown to result in internalization and processing of the antibody by the targeted cells {Shih 1994, Stein 1995}. Because of its hydrolyzable linker, sacituzumab govitecan will release its SN-38 payload both intra- and extracellularly in the tumor microenvironment {Goldenberg 2015, Govindan 2013}. Sacituzumab govitecan delivers significantly greater amounts of SN-38 to a TROP-2-expressing tumor than conventional irinotecan chemotherapy {Sharkey 2015}. The extracellular release of SN-38 from sacituzumab govitecan also allows for bystander killing of TROP-2 negative tumor cells {Lopez 2020, Perrone 2020, Zeybek 2020}. Thus, sacituzumab govitecan can deliver cytotoxic chemotherapy to tumors, including adjacent cancer cells, in concentrations that are higher than those with standard chemotherapy and may reduce toxic effects in normal tissues that do not express the target.

For further information on sacituzumab govitecan, refer to the current Investigator's Brochure.

1.1.2. Nonclinical Experience

1.1.2.1. Pharmacology

In vitro cytotoxicity of sacituzumab govitecan was assessed in multiple cell lines representative of several different epithelial tumors; PC-3 (prostate), Calu-3, COLO 205, Capan-1, SK-MES-1, and BxPC-3. In general, the concentration of drug required for 50% inhibition (IC_{50}) values ranged from 1.95 nM to 23.14 nM {Cardillo 2011}.

The antitumor activity and significant inhibition of tumor growth was shown in various epithelial cancer xenograft models including non-small cell lung cancer (NSCLC), colorectal cancer, pancreatic cancer, and triple-negative breast cancer (TNBC) when sacituzumab govitecan was compared to saline or unconjugated antibody controls {Cardillo 2015, Cardillo 2011, Goldenberg 2015}.

1.1.2.2. Pharmacokinetics

Toxicokinetic analysis of the 3-month repeat-dose study in cynomolgus monkeys using validated assays showed a dose-proportional exposure (maximum plasma concentration [C_{max}] and area under the curve [AUC]) to sacituzumab govitecan, total antibody, total SN-38, and free SN-38 with no relevant gender differences after the first dose. Serum half-life was estimated in recovery animals and ranged from 67.3 to 152 hours. On average, the amount of free SN-38 in circulation was low, < 3% free SN-38 compared with the total SN-38 bound to sacituzumab govitecan. This confirms that the majority of SN-38 administered as sacituzumab govitecan remains bound to the ADC in serum and is not circulating as the free cytotoxic payload. The inactive metabolite, SN-38G, readily appeared in serum with a mean time to the maximum plasma concentration (T_{max}) ranging from 4 to 12 hours.

1.1.2.3. 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 1,500 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, which had returned to normal by the end of the study.

In cynomolgus monkeys, sacituzumab govitecan administered at 50 mg/kg/dose (human equivalent dose [HED] = 16 mg/kg/dose) for 4 treatment cycles (Days 1 and 8 of a 21-day cycle) was considered a no-observable 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 blood cells (RBCs), white blood cells (WBCs), and platelets; and the gastrointestinal (GI) tract (necrosis, erosions, inflammation, fibrosis, hemorrhage, edema).

Local tolerance was evaluated in the Good Laboratory Practice (GLP)-compliant monkey studies. Although changes were observed at the injection site, the study pathologist interpreted these findings as related to procedural trauma and not the test article. These changes consisted of mild to moderate perivascular hemorrhage, moderate hemorrhage in the dermis and subcutis, and minimal to mild perivascular mixed cell infiltration.

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 prenatal and postnatal development have been assessed. However, SN-38 is a camptothecin and hence might be carcinogenic. Furthermore, SN-38 is a known developmental toxicant {CAMPTOSAR 2020}.

1.1.3. Clinical Experience

Sacituzumab govitecan is approved in several countries and regions including the US, Canada, Australia, Great Britain, Europe, Asia, and Switzerland, for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received 2 or more prior therapies, at least 1 of them for metastatic disease and for the treatment of adult patients with unresectable locally advanced or metastatic hormone receptor positive (HR+)/human epidermal growth factor receptor 2-negative (HER2−; immunohistochemistry [IHC] 0, IHC 1+, or IHC 2+/in-situ hybridization [ISH]−) breast cancer who have received endocrine-based therapy and at least 2 additional systemic therapies in the metastatic setting.

Clinical data are available for 3 clinical studies (2 completed and 1 ongoing) in which 795 patients were treated with sacituzumab govitecan:

- Study IMMU-132-01, a Phase 1/2, open-label, basket study in patients with metastatic epithelial cancers that were either relapsed or refractory after at least 1 standard therapeutic regimen for their tumor type (N = 495 patients in the safety population, 402 patients received 10 mg/kg sacituzumab govitecan). Patients were enrolled regardless of TROP-2 expression and treated with sacituzumab govitecan monotherapy. Doses of 8 to 18 mg/kg were tested, with the 10 mg/kg dose selected for further investigation. Of over 15 histologies tested, 4 histologies were selected for further expansion because of the clinical activity noted. These histologies include TNBC, NSCLC, SCLC, and urothelial cancer (UC).

- Study IMMU-132-05, a Phase 3 study of sacituzumab govitecan compared with single-agent chemotherapy in patients with unresectable locally advanced or mTNBC who had received at least 2 prior therapies (N = 582 patients in the safety population including 258 patients with sacituzumab govitecan and 224 patients with single-agent chemotherapy); included a pharmacokinetic (PK)-electrocardiogram (ECG) substudy of 29 patients from the sacituzumab govitecan treated group to assess the effects of sacituzumab govitecan on cardiac repolarization (QTc interval) and other ECG parameters.

- Study IMMU-132-06, an ongoing Phase 2 study in patients with locally advanced or mUC (N = 135) that included: 1) a cohort of patients who progressed after prior platinum-based and PD-1/PD-L1 inhibitor therapy (N = 113) and 2) a cohort of patients who were platinum ineligible and received PD-1/PD-L1 inhibitor therapy in the first-line metastatic setting (N = 22).

1.1.3.1. Pharmacokinetics and Immunogenicity

The serum PK of sacituzumab govitecan and free SN-38 were evaluated in a Phase 1/2 study in a population of subjects with mTNBC who received sacituzumab govitecan as a single agent at a dose of 10 mg/kg. The mean PK parameters of sacituzumab govitecan and free SN-38 as determined by non-compartmental analysis are presented in Table 1.

Table 1. Summary of Mean Pharmacokinetic Parameters (± Standard Deviation) of Sacituzumab Govitecan and Free SN-38

	Sacituzumab Govitecan	Free SN-38
CCI [redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Abbreviations: AUC_{0-168} = area under the plasma concentration-time curve from time zero (0) through 168 hours; C_{max} = maximum plasma concentration.

CCI [redacted]

Metabolism

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

Excretion

As reported, SN-38 and SN-38G appear to be mainly eliminated via biliary excretion.

Immunogenicity

As with all therapeutic proteins, there is a potential for an immune response to sacituzumab govitecan. Based on available data in the Overall Safety Population (n = CCI [redacted]), the rate of treatment-emergent and persistent anti-drug antibodies (ADAs) is very low and has been limited to 3 subjects (0.7%), with an additional 17 subjects (4%) having a transient ADA-positive sample. None of the treatment-emergent and confirmed positive subjects experienced infusion reactions or adverse events (AEs) suggestive of immunogenicity.

1.1.3.2. Summary of Clinical Efficacy

NSCLC

Sacituzumab govitecan has been evaluated in patients with metastatic NSCLC in a clinical study: Study IMMU-132-01 (based on a database cutoff date of 01 March 2019 – completed; 54 patients enrolled). The NSCLC population in this study was heavily pretreated with a median of 3 prior therapies (range: 2 to 7 prior therapies) {Heist 2017}.

In Study IMMU-132-01, objective response rate (ORR) based on local response assessment was 16.7% for the NSCLC population; all responses were partial responses (PRs). The majority of patients had at least a 30% reduction in the size of the target lesion.

Median duration of response (DOR) by local assessment was 6.0 months (range: 2.5 to 21.0 months). The Kaplan-Meier estimate of the percentage of patients with a response of 6 months was 44.4% (95% CI: 13.6, 71.9).

Endometrial Cancer

Sacituzumab govitecan has been evaluated in patients with metastatic endometrial cancer in a clinical study: Study IMMU-132-01 (based on a database cutoff date of 01 March 2019 – completed; 18 patients enrolled).

In Study IMMU-132-01, ORR based on local response assessment was 22.2% for the endometrial population; all responses were PRs. The majority of patients had at least a 30% reduction in the size of the target lesion.

Median DOR had not been reached as of the data cutoff.

SCLC

Sacituzumab govitecan has been evaluated in patients with metastatic SCLC in a clinical study: Study IMMU-132-01 (based on a database cutoff date of 01 March 2019 – completed; 62 patients enrolled). The SCLC population in this study was heavily pretreated with a median of 2 prior therapies including patients who were chemosensitive or chemoresistant to first-line chemotherapy and also in patients who failed second-line topotecan therapy {Gray 2017}.

In Study IMMU-132-01, ORR based on local response assessment was 17.7% for the SCLC population; all responses were PRs. The majority of patients had at least a 30% reduction in the size of the target lesion.

Median DOR by local assessment was 5.7 months (range: 3.6 to 19.9 months). The Kaplan-Meier estimate of the percentage of patients with a response of 6 months was 45.5% (95% CI: 16.7, 70.7).

Additional information regarding the efficacy data can be found in the current edition of the Investigator's Brochure.

1.1.3.3. Summary of Sacituzumab Govitecan Safety Data

The safety profile of sacituzumab govitecan has been characterized based on 795 patients who received a starting dose of 10 mg/kg of sacituzumab govitecan in Studies IMMU-132-01 (N = 402, regardless of tumor type; data cutoff date 01 March 2019), IMMU-132-05 (N = 258; data cutoff date 11 March 2020), and IMMU-132-06 (N = 135; data cutoff date 18 September 2020). As of the data cutoff dates for these studies, the median treatment duration was 4.1 months (6 cycles). The following is a summary of the safety profile; additional details can be found in the current edition of the Investigator's Brochure.

Nearly all subjects experienced at least 1 AE; approximately 77% of subjects experienced at least 1 National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) ≥ Grade 3 AE; 37% experienced at least 1 serious adverse event (SAE). The protocol provided instructions for dose reduction and dose interruption, and treatment discontinuation based on toxicities. AEs led to treatment interruption in 55% of subjects; however, only 8% of subjects discontinued because of AEs. Fatal AEs (within 30 days of the last dose) occurred in 2% of subjects; 2 were assessed as treatment-related (sepsis in the setting of febrile neutropenia in a subject with UC; aspiration pneumonia in the setting of disease progression in a subject with NSCLC who had persistent nausea and vomiting after each infusion of sacituzumab govitecan).

The most common AEs (all grade, NCI-CTCAE Grade 3-4 frequencies) were nausea (66.3%, 4.2%), diarrhea (64.8%, 10.6%), neutropenia (58.4%, 43.8%), fatigue (54.5%, 7.4%), alopecia (44.7%, 0), anemia (41.5%, 13.0%), vomiting (38.7%, 2.5%), and constipation (37.2%, 0.6%). The most clinically relevant Grade 3 or Grade 4 AEs with sacituzumab govitecan were neutropenia and diarrhea. Febrile neutropenia occurred in 6.5% of subjects. The most frequent AEs that led to treatment interruption (occurring in ≥ 2% of subjects) were neutropenia (34%), anemia (5%), leukopenia (5%), diarrhea (4%), fatigue (3%), nausea (2%), vomiting (2%), febrile neutropenia (2%), and upper respiratory tract infection (2%). The most frequent AEs leading to dose reduction (occurring in ≥ 2% of subjects) were neutropenia (5%), diarrhea (3%), and fatigue (2%). The most frequent AEs leading to permanent discontinuation of sacituzumab govitecan (occurring in ≥ 0.5% of subjects) were fatigue (0.8%), diarrhea (0.6%), pneumonia (0.6%), and neutropenia (0.5%).

Neutropenia typically 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. Fatal infections in the setting of neutropenia have been observed in clinical trials with sacituzumab govitecan (SG), primarily in the first 2 cycles of treatment.

Diarrhea with sacituzumab govitecan typically 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.

Hypersensitivity and infusion-related reactions have been observed. One subject in Study IMMU-132-01 experienced a grade 3 serious adverse event of anaphylactic reaction during Cycle 4 Day 1 that resolved with antihistamine, corticosteroids, and epinephrine treatment; sacituzumab govitecan was permanently discontinued.

As noted in Section 1.1.3.1, SN-38 (the active metabolite of irinotecan) is metabolized by *UGT1A1*. Irinotecan-treated subjects who are homozygous for the *UGT1A1 *28* allele are at increased risk for neutropenia and diarrhea {CAMPTOSAR 2020}. Pooled data from Studies IMMU-132-01, IMMU-132-05, and IMMU-132-06 who received 10 mg/kg of sacituzumab govitecan indicate higher incidences of neutropenia, febrile neutropenia, and anemia in patients who were homozygous for the *UGT1A1*28* allele compared with patients who were heterozygous for the *UGT1A1*28* allele and patients who were homozygous for the wild-type allele.

1.1.4. Rationale for Dose Regimen

The proposed sacituzumab govitecan dosing regimen for this study (10 mg/kg on Day 1 and 8 of a continuous 21-day cycle) is the same as the labeled dosage currently approved in TNBC. Selection of this regimen was based on the dose-optimization performed in the Phase 1 part of Study IMMU-132-01, where dose escalation was performed according to a standard 3 + 3 design, and based on planned initial dose levels of 8, 12, and 18 mg/kg. A sacituzumab govitecan dose of 12 mg/kg was formally identified as the maximum tolerated dose (MTD), but it was associated with dose delays and reductions in several subjects. To determine a maximum acceptable dose, additional subjects were treated at the 8 mg/kg dose level, and an intermediate dose cohort of 10 mg/kg was added to the study. Both dose levels were shown to be better tolerated in the first cycle than the previously determined MTD of 12 mg/kg, allowing for repeated cycles with a better safety profile. Interim analyses demonstrated that subjects receiving the 10 mg/kg dose achieved a treatment duration that was comparable with subjects receiving the 8 mg/kg dose. However, compared with the 8 mg/kg dose level, there was no worsening of AE incidence or severity with the 10 mg/kg dose. The 10 mg/kg dose achieved a better ORR, clinical benefit rate (CBR), and progression-free survival (PFS) than the 8 mg/kg dose in subjects with TNBC, specifically {Ocean 2017}. Based on these results, 10 mg/kg was chosen as the dose for further study. Additional information regarding the safety and efficacy of sacituzumab govitecan can be found in the current edition of the Investigator's Brochure and TRODELVY™ labeling information.

1.2. Study Rationale

TROP-2, the trophoblastic cell-surface antigen-2, is a transmembrane calcium signal transducer glycoprotein of the TACSTD (tumor-associated calcium signal transducer) gene family, expressed in many normal tissues, including the epithelial barrier/lining of the stratum basale epidermis, breast, cervix, cornea, the epithelial secretory tissue of the endocrine and exocrine glands, esophagus, lung, pancreas, salivary gland, tonsils, trachea, urothelium, and uterus, in addition to several other tissues {Shvartsur 2015, Trerotola 2010}. In contrast to normal tissues, TROP-2 is overexpressed in many epithelial cancers {Alberti 2007} and has been implicated as an oncogene. It is thought to be a poor prognostic factor and is found in more aggressive tumors {Cubas 2009, Cubas 2010, Fang 2009, Fong 2008a, Fong 2008b, Guerra 2008, Kobayashi 2010, Köbel 2008, Ohmachi 2006, Stepan 2011, Wu 2013}. TROP-2 may confer the capability for proliferation and invasion to cancer cells, regulating cell growth, transformation, regeneration, and proliferation. Evidence of TROP-2 expression has been noted on several tumors including NSCLC, head and neck squamous cell carcinoma (HNSCC), SCLC, endometrial carcinoma, UC, and TNBC.

As described in Section 1.1.3, sacituzumab govitecan has been investigated in several clinical studies and has demonstrated clinical activity in a TROP-2 unselected population. While data indicate significant activity in a TROP-2 unselected population of TNBC {Bardia 2017, Bardia 2021} and UC {Bardia 2021} subjects, encouraging clinical activity was demonstrated in multiple types of cancers {Bardia 2021} including NSCLC {Heist 2017}, SCLC {Gray 2017}, HNSCC, and endometrial cancer in TROP-2 unselected subjects enrolled in Study IMMU-132-01. Limited data are available in HNSCC.

Despite recent approvals of novel agents like programmed death-ligand 1 (PD-L1) or programmed cell death protein 1 (PD-1) inhibitors in NSCLC, HNSCC, endometrial carcinoma, and SCLC, for subjects with advanced disease who have exhausted multiagent chemotherapy and PD-L1 or PD-1 therapy, the therapeutic options are often single agent chemotherapy which provided limited benefit.

A) NSCLC

The current treatment paradigm for patients with advanced NSCLC is the combination of platinum-based therapy with immune checkpoint inhibitors. Patients who do not receive this treatment in combination are treated with this agent sequentially. Upon progression with immune checkpoint inhibitors and platinum-based chemotherapy, a very few treatment options exist with the most common treatment being docetaxel. Other options include docetaxel + ramucirumab, pemetrexed (if not already given) and other single agent chemotherapy. These treatments provide poor outcomes with minimal benefit and overall survival (OS) less than 1 year {Hanna 2004, Horn 2017, Mazieres 2021, Shepherd 2000} and hence they represent a patient population of high unmet medical need.

TROP-2 is highly expressed in NSCLC and sacituzumab govitecan has shown encouraging single agent clinical activity in a heavily pretreated NSCLC patient population in Study IMMU-132-01. In this study, the aim is to obtain clinical data on additional NSCLC patients in the current clinical landscape.

B) HNSCC

Platinum agents have been the mainstay for initial treatment in patients with metastatic and recurrent HNSCC. Recently the addition of immune checkpoint inhibitors has revolutionized the treatment for patients whose tumors express PD-L1. These immune checkpoint inhibitors are used either alone (combined positive score [CPS] $\geq$ 20%) or in combination with platinum-based chemotherapy (CPS < 20%). However, most patients progress after these treatments. Limited treatment options exist after patients have exhausted platinum-based chemotherapy and immune checkpoint inhibitors. Current options include single agent chemotherapy such as methotrexate or docetaxel, or cetuximab. Efficacy results from studies using these treatments show ORR in range of 5.8 to 10.6%, median PFS around 2.3 months, and OS ranging from 5.1 to 6.9 months {Cohen 2019, Ferris 2018}. Therefore, a high unmet need exists for improved treatments in this setting. TROP-2 is highly expressed in HNSCC and therefore, sacituzumab govitecan provides an opportunity for improved clinical outcomes in this setting.

C) Endometrial carcinoma

The initial treatment for patients with advanced endometrial carcinoma is largely standardized by platinum chemotherapy. Upon progression on platinum agents, the subsequent treatment has been pembrolizumab monotherapy in a small subgroup of patients with microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR)/high tumor mutational burden-high (TMB-H). Very recently pembrolizumab in combination with lenvatinib received full approval in this patient population regardless of the MSI-H/dMMR status {Merck 2021}. For patients whose

cancer(s) has failed the aforementioned treatments, single agent chemotherapy (ie, docetaxel, doxorubicin, or paclitaxel) remains the main stay of treatment and that has very poor outcomes. Hence, these patients represent a population of high unmet medical need.

Sacituzumab govitecan has demonstrated activity in endometrial carcinoma in TROP-2 unselected subjects enrolled in Study IMMU-132-01. In this study, the aim is to obtain clinical data on additional endometrial carcinoma patients in the current clinical landscape.

D) SCLC

Single agent chemotherapy with topotecan is a common current standard of care treatment in patients with extensive stage SCLC whose tumors have progressed on platinum and PD-(L)1 combination and has been evaluated in several randomized clinical studies. Efficacy results from studies using these treatments show ORR in the range of 16.5 to 25%, median PFS from 2.7 to 3.8 months, and OS ranging from 7.4 to 8.4 months {Baize 2020, Spigel 2021}

More recently lurbinectedin has been evaluated in the post-platinum and immuno-oncology (IO) setting as well. Results from initial trial were encouraging showing ORR of 35%. However, subsequent confirmatory study failed to show benefit over current standard of care. In the Phase 3 ATLANTIS trial, comparing the combination of lurbinectedin and doxorubicin versus chemotherapy (topotecan or cyclophosphamide, doxorubicin, and vincristine), the lurbinectedin arm had an ORR of 31.6% with PFS of 4 months and median OS of 8.6 months and the chemotherapy arm had an ORR of 29.7% with median PFS of 4 months and median OS of 7.6 months {Paz-Ares 2021}.

Given the lack of durable response and with the median survival is ≤ 1 year, there is a significant unmet medical need for additional therapeutic options in SCLC cohort. Sacituzumab govitecan is an ADC that uses an SN-38 payload which has been proven to be an effective agent in SCLC. It has achieved encouraging activity in Study IMMU-132-01 and therefore, it warrants further evaluation in SCLC.

This study will enroll subjects with NSCLC (adenocarcinoma and squamous cell carcinoma [SCC]), HNSCC, endometrial carcinoma, and SCLC. This study will provide further clinical data to support the clinical activity of sacituzumab govitecan in the current landscape and to further explore the relationship between clinical data and TROP-2 expression levels CCI [redacted]

1.2.1. Potential Benefits

Sacituzumab govitecan has demonstrated encouraging activity in multiple cancer types as described in the earlier Section 1.1.3.2. Sacituzumab govitecan seems well-tolerated and induced durable responses in heavily pretreated patients; therefore, the potential therapeutic benefit for the patient populations targeted in this study seems substantial and worth evaluating further in additional patients.

1.2.2. Benefit-Risk Assessment

Sacituzumab govitecan has a significant risk of causing fatigue, diarrhea, nausea, and cytopenia with an overall treatment discontinuation rate of 8%. Further, there is a potential increase in risk of toxicities in subjects bearing *UGT1A1**1/*28 and *28/*28 genotypes as reported with the SN-38 metabolite of irinotecan. However, the rates of toxicity are manageable with dose modifications and the judicious use of dose delays. Neutropenia may be further managed with the addition of growth factor support. Fatal infections in the setting of neutropenia have been observed in clinical trials with SG, primarily in the first 2 cycles of treatment, hence primary prophylaxis with G-CSF is recommended starting in the first cycle in patients at increased risk of febrile neutropenia eg, older patients (in particular aged 65 years and older), patients with previous neutropenia, poor performance status, organ dysfunction (including renal, liver or cardiovascular dysfunction), or multiple comorbid conditions. Absolute neutrophil count must be monitored during treatment. Despite the risk of these toxicities, the potential therapeutic benefit for the patient populations targeted in this study is substantial. In patients with limited treatment options with little benefit, in terms of approved therapies, and a limited expectation of survival, sacituzumab govitecan may offer a survival benefit by targeting a protein highly expressed on these specific tumor types. The favorable benefit-risk profile of this product warrants further investigation given the high unmet medical need in the targeted patient populations.

An unanticipated event such as a disaster or public health emergency may pose additional risks to study drug availability, the study visit schedule, and adherence to protocol-specified safety monitoring or laboratory assessments. For details on the risk and mitigation strategy refer to Appendix 17.7.

2. STUDY OBJECTIVES AND ENDPOINTS

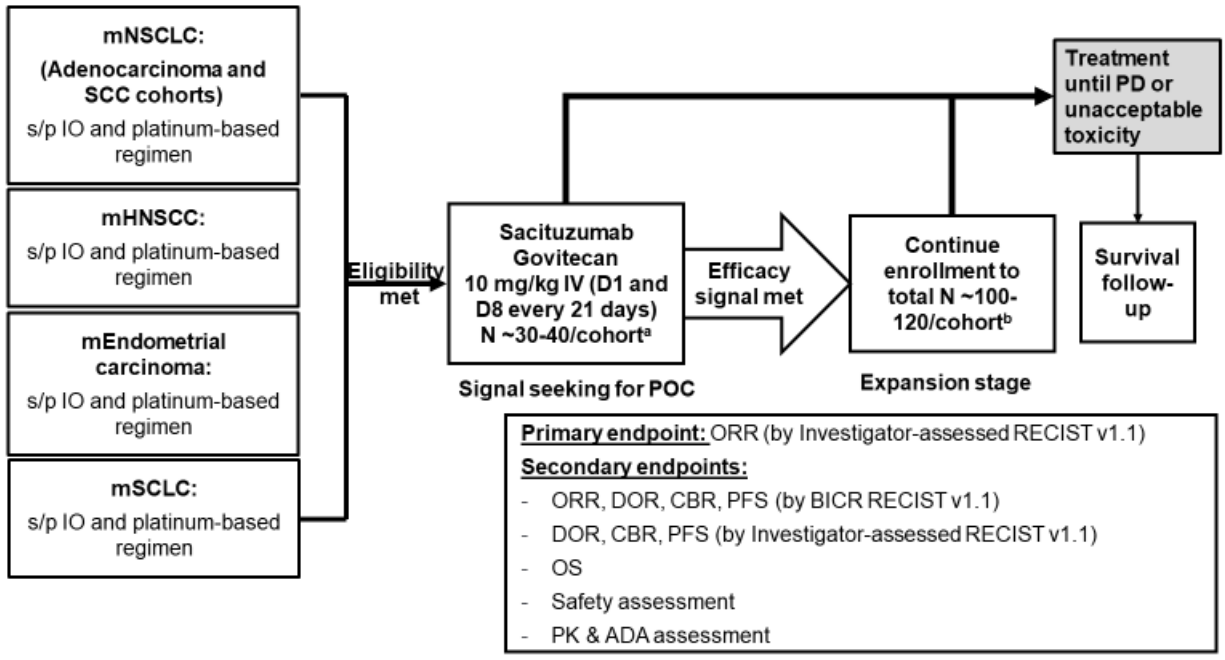
Primary Objective	Primary Endpoint
Assess the ORR of sacituzumab govitecan in subjects with metastatic solid tumors by Investigator's assessment according to the Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) criteria.	Objective response rate (ORR) according to RECIST 1.1 by Investigator's assessment.
Secondary Objectives	**Secondary Endpoints**
• Assess the ORR, DOR, CBR, and PFS of sacituzumab govitecan in subjects with metastatic solid tumors by blinded independent central review (BICR) according to RECIST 1.1 criteria. • Assess the DOR, CBR, and PFS of sacituzumab govitecan in subjects with metastatic solid tumors by Investigator's assessment according to RECIST 1.1 criteria. • Assess the OS of sacituzumab govitecan in subjects with metastatic solid tumors. • Assess the safety of sacituzumab govitecan in subjects with metastatic solid tumors. • Assess the PK and immunogenicity of sacituzumab govitecan in subjects with metastatic solid tumors.	• ORR, DOR, CBR, and PFS according to RECIST 1.1 by BICR. • DOR, CBR, and PFS according to RECIST 1.1 by Investigator's assessment. • Overall survival (OS). • Incidence of treatment-emergent AEs and clinical laboratory abnormalities. • Serum concentrations of sacituzumab govitecan over time and incidence of anti-drug antibody (ADA) to sacituzumab govitecan.
CCI [redacted]	[redacted]
• CCI [redacted]	[redacted]

3. INVESTIGATIONAL PLAN

This is a multi-cohort, open-label, Phase 2 study designed to assess the efficacy and safety of sacituzumab govitecan in adult subjects with metastatic solid tumors. Upon meeting the eligibility criteria, the subjects are treated with sacituzumab govitecan at 10 mg/kg via intravenous infusion on Days 1 and 8 of a 21-day cycle. The original protocol included the following cohorts: NSCLC (adenocarcinoma and SCC), HNSCC, and endometrial carcinoma.

With Amendment 3, this study is a single stage cohort evaluation for proof of concept (POC) with recalculation of sample sizes for all the cohorts. An additional cohort for SCLC has been added. OS is included as a secondary objective and endpoint and will be assessed for all cohorts. The correlation of clinical activity to TROP-2 expression is included as an exploratory endpoint (see study schema in Figure 1).

Figure 1. Study IMMU-132-11 Schema



ADA = anti-drug antibody; BICR = blinded independent central review; CBR = clinical benefit rate; D = day; DOR = duration of response; IO = immuno-oncology; IV = intravenous; m = metastatic; mHNSCC = metastatic head and neck squamous cell carcinoma; mNSCLC = metastatic non-small cell lung cancer; mSCLC = metastatic small cell lung cancer; ORR = objective response rate; OS = overall survival; PA5 = Protocol Amendment 5; POC = proof of concept; PD = progressive disease; PFS = progression-free survival; PK = pharmacokinetic; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors Version 1.1; SCC = squamous cell carcinoma; s/p = status post

a. Exact sample size calculations for each of the cohorts for POC stage are outlined in Section 11.1.

b. Expansion stage planned only for HNSCC, endometrial, and SCLC cohorts (if efficacy signal met in the POC stage). Following implementation of PA5, subjects who previously discontinued treatment will no longer be followed for survival follow-up and subsequent therapy and will discontinue the study as per sponsor's decision.

Approximately, a total of 165 subjects will be enrolled for the initial POC stage, that is, 30 subjects for each of the NSCLC (adenocarcinoma and SCC) and HNSCC cohorts, 35 subjects for the endometrial carcinoma cohort, and 40 subjects for the SCLC cohort. Once the efficacy bars are reached in any of the endometrial carcinoma, HNSCC, or SCLC cohorts, the Sponsor may choose to expand the specific cohort(s) and continue to enroll additional subjects, so that approximately a total of 100 to 120 subjects (including subjects enrolled in the initial stage) in each selected cohort will be accrued. If one or more cohorts are expanded, the total study sample size combining subjects in both the POC and the expansion stage can be up to approximately 225 to CCI subjects.

Subjects will be treated until PD (according to RECIST 1.1 by Investigator's assessment), unacceptable toxicity, study withdrawal, or death, whichever comes first. However, treatment may be continued beyond PD if there is evidence of clinical benefit per the Investigator and the subject is tolerating study treatment. The clinical criteria for subjects to continue to receive treatment beyond the Investigator-assessed progression are defined in Section 4.3.1.

Subjects will then be followed every 12 weeks for survival, unless the subject explicitly indicates a desire to forego survival follow-up to their study Investigator. Subjects will be followed until death, withdrawal of consent, lost to follow-up, Sponsor-terminated study or completion of survival follow-up (24 months after the last subject is dosed), whichever occurs first.

The end of study for a subject occurs when there is a death event, withdrawal of consent, or loss to follow-up is documented. The end of the entire study for all subjects is defined as the date on which the last subject remaining on study completes the last study visit/call/survival follow-up or when the Sponsor decides to end the study. The Sponsor reserves the right to terminate the study at any time for any reason (including safety). At the completion of the study, subjects who are deriving benefit from sacituzumab govitecan may continue to receive treatment in a rollover study (Study IMMU-132-14) in locations where the study is available.

Study modifications after implementation of Protocol Amendment 5 (PA5):

Following implementation of PA5, subjects who are still receiving treatment may continue treatment as part of the study for as long as they are deriving clinical benefit. Radiographic tumor assessments per protocol will be discontinued; however, treatment response should continue to be evaluated per standard of care. Information on study drug administration and safety assessments will continue to be collected. Subjects who have discontinued treatment and were being followed for survival and subsequent therapy at the time of PA5 implementation, will be discontinued from the study and survival follow-up with subsequent therapy information will no longer be collected.

4. STUDY PROCEDURES

All subjects must be dosed within 28 days of providing written informed consent. Unless otherwise specified, visit windows are within −1 and +2 days for the treatment schedule and ± 7 days for response assessments. Absolutely no waivers for subject eligibility will be permitted.

Samples for PK, ADA, and biomarker analyses will be collected according to the protocol schedule of assessments and are to be shipped to the Sponsor's designee. Otherwise, all other laboratory procedures are to be performed locally at each study site (Table 2).

The schedule of assessments for all subjects before implementation of PA5 is presented in Table 2. The schedule of assessments for all subjects who continue treatment following implementation of PA5 is presented in Table 3.

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 their legally authorized representative. However, procedures such as laboratory work or imaging that were performed per standard of care may be utilized for Screening if they were performed within the proposed screening window with the subject's consent. The Investigator will explain the nature and scope of the study, potential risks and benefits of participation, and answer all questions for the subject or their 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.

CCI [redacted]

4.2. Screening Evaluations

Screening evaluations conducted to establish eligibility will be performed within 28 days prior to Cycle 1, Day 1 (C1D1) (Table 2):

- Signed informed consent (prior to any screening evaluations).
- Tumor blocks (preferably obtained within 12 months of study entry if clinically feasible) or 20 newly sectioned unstained slides (6 slides minimum) of archived biopsy/surgical specimens are requested. A baseline biopsy is required if archival tissue is not available.

Fine needle aspirates and bone biopsies are not suitable samples. These specimens should be submitted within the 28-day screening period, after the subject provides written informed consent.

- CCI [redacted]
- Eligibility (inclusion/exclusion criteria).
- Medical/surgical history review with treatment history to include treatment response and time to progressive disease (PD) from the last therapy regimen.
- Complete physical examination including, height, weight, and Eastern Cooperative Oncology Group (ECOG).
- 12-lead electrocardiogram (ECG).
- Vital signs defined as heart rate, blood pressure, respiratory rate, and body temperature, taken after the subject has been resting for at least 5 minutes.
- Serum beta-human chorionic gonadotropin (β-hCG), in women of childbearing potential during screening, and urine pregnancy test at baseline (prior to study treatment administration on C1D1). The urine pregnancy test at baseline does not need to be conducted if the serum pregnancy test at screening was performed within 72 hours before study treatment administration on C1D1.
- Serum follicle-stimulating hormone (FSH) testing will be conducted as needed per Appendix 17.5 for determination of childbearing potential.
- Complete blood count (CBC) with differential. If the baseline sample was collected > 72 hours prior to C1D1, then it must be repeated to confirm eligibility prior to dosing.
- HIV antibody test.
- Hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc) test. Subjects who test positive for the anti-HBc test will require hepatitis B virus (HBV) DNA by quantitative polymerase chain reaction (PCR).
- Hepatitis C (HCV) antibody test. Subjects with a known history of HCV or a positive HCV antibody test will not require an HCV antibody at Screening and will only require HCV ribonucleic acid (RNA) by quantitative PCR for confirmation of active disease.
- Routine serum chemistries including liver function tests, glucose, creatinine, blood urea nitrogen (BUN), total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, serum albumin, total protein, sodium, potassium, calcium, chloride, bicarbonate, magnesium, and phosphorus, lactate dehydrogenase (LDH), and uric acid. If routine chemistries and liver function tests were collected > 72 hours prior to C1D1, then it must be repeated to confirm eligibility prior to dosing.

- Urinalysis only for Screening.
- Brain MRI in subjects with known central nervous system (CNS) disease or with suspicion of CNS disease. Target and non-target lesions must be determined by the study site at baseline.
- Computed tomography (CT) or magnetic resonance imaging (MRI) scan with intravenous (IV) contrast as appropriate (chest, abdomen, pelvis, and other regions of known/suspected involvement) unless there is a known anaphylaxis to contrast and/or medically contraindicated as described in Section 9.
- Record AEs.
- Prior/concomitant medications review.
- All subjects who previously failed screening may be rescreened only once (Section 6.1).

4.3. Procedures During Treatment

Note: CBC with differential, serum chemistries, and liver function tests, as well as pregnancy tests in women of childbearing potential need not be repeated for C1D1 if they were obtained for Screening within 72 hours prior to dosing.

- Sacituzumab govitecan dosing is based on the subject's body weight at enrollment (C1D1). The dose is to remain constant throughout the study unless there is a > 10% change in body weight from enrollment (C1D1) (Table 2).
- Vital signs including blood pressure, heart rate, pulse, respiratory rate, and body temperature on C1D1 prior to infusion. Additional collection of vital signs will be needed in the event of suspected infusion-related reaction.
- Blood samples prior to infusion for:
  - CBC with differential on Days 1 and 8 of each cycle. CBC does not need to be repeated at C1D1 if the screening sample was collected within the previous 72 hours. If the baseline sample was collected > 72 hours prior to C1D1, then it must be repeated to confirm eligibility prior to dosing. Hematology tests may be performed and reviewed up to 24 hours prior to scheduled study treatment administration.
  - Serum chemistry panel including liver function tests, glucose, creatinine, BUN, total bilirubin, AST, ALT, alkaline phosphatase, serum albumin, total protein, sodium, potassium, calcium, chloride, bicarbonate, magnesium, and phosphorus. Serum chemistries are required for all subjects on Days 1 and 8 of every subsequent cycle (repeated assessment at C1D1 is not required if the screening sample was collected within the previous 72 hours). These laboratory assessments may be performed more frequently at the discretion of the treating physician if abnormal results warrant follow-up. Serum chemistries may be performed and reviewed up to 24 hours prior to scheduled study treatment administration.

- Blood for PK serum samples will be collected from all subjects at pre-sacituzumab govitecan infusion and at End of Infusion (EOI) on Day 1 of Cycles 1, 2, 3, 7, 11, and every 6 cycles thereafter (17, 23, etc), EOT with sacituzumab govitecan, and at the 30-Day Safety Follow-up Visit. There will be an additional collection pre-dose on C1D8. The collection window for PK samples is -30 minutes for predose (prior to the start of infusion), +10 minutes for postdose samples (at EOI), and ±10 minutes for all other timepoints. PK serum samples for subjects continuing sacituzumab govitecan treatment following implementation of PA5 will not be collected.

- Blood for immunogenicity samples (ADA) will be collected from all subjects at pre-sacituzumab govitecan infusion on Day 1 of Cycles 1, 2, 3, 7, 11, and every 6 cycles thereafter (17, 23, etc), EOT with sacituzumab govitecan, and at the 30-Day Safety Follow-up Visit. All ADA samples will be collected predose with a collection window of -30 minutes prior to the start of infusion. ADA samples for subjects continuing sacituzumab govitecan treatment following implementation of PA5 will not be collected.

- Blood for biomarker samples will be collected from all subjects receiving sacituzumab govitecan before infusion on Day 1 of Cycles 1, 3, 5, 7, 9, 11, and every 3 cycles thereafter (Cycles 14, 17, etc) and at EOT. Biomarker samples for subjects continuing sacituzumab govitecan treatment following implementation of PA5 will not be collected.

- CCI [redacted]

- Blood sample collection for UGT1A1 genotyping. This sample should be collected at the C1D1 visit. If the sample is not collected at C1D1, then it can be collected at any other visit. UGT1A1 genotyping blood samples for subjects continuing treatment following implementation of PA5 will not be collected.

- A 12-lead ECG will be obtained prior to the C1D1 infusion. Abnormal findings should be evaluated as clinically indicated, including repeated ECGs. ECGs may be done at other timepoints during the study if clinically indicated.

- Urinalysis will be performed only if clinically indicated with abnormal results captured on the electronic case report form (eCRF).

- Clinically targeted physical examination including weight.

- Record AEs (at every visit).

- Record concomitant medications; continued, changed (at every visit).

- CT or MRI scan with IV contrast (chest, abdomen, and pelvis with scanning of other regions including brain MRI as clinically indicated) examinations, unless known anaphylaxis to contrast and/or medically contraindicated as described in Section 9. Subjects who continue treatment following implementation of PA5 will be expected to have scans performed per standard of care, as indicated by local practice. Tumor response data will no longer be collected for this study; however, disease status should still be monitored by the treating physician to determine if progression has occurred, and whether the subject is continuing to derive clinical benefit.
- CCI [redacted]
- Pregnancy testing at monthly intervals.

4.3.1. Treatment After Progression

Subjects will be treated until PD (according to RECIST 1.1 by Investigator's assessment), unacceptable toxicity, study withdrawal, or death, whichever comes first. However, treatment may be continued beyond PD if there is evidence of clinical benefit per the Investigator and the subject is tolerating study treatment. The following clinical criteria should be met for subjects to continue to receive treatment beyond the Investigator-assessed progression:

- Absence of symptoms and signs indicating clinically significant progression of disease.
- No decline in performance status.
- Absence of symptomatic rapid disease progression requiring urgent medical intervention (eg, symptomatic pleural effusion, spinal cord compression).

Sponsor consultation is required before subjects initiate the treatment beyond progression. If this occurs, the subject will remain in the study and continue to be monitored according to the protocol schedule of assessments (Table 2).

4.4. End of Treatment Visit

The End of Treatment (EOT) Visit should be conducted within 30 days after the decision has been made to discontinue treatment. If this is scheduled for 30 days (± 14 days) after the last dose, the results from these assessments may also be used for the 30-Day Safety Follow-up Visit. Subjects who discontinue treatment because of toxicity will continue with radiologic response assessments at the protocol-required schedule, until PD or initiation of new therapy with capture of radiologic evidence of PD if clinically feasible. The reason for treatment discontinuation will be documented and any treatment-related AEs or clinically significant abnormal laboratory values at that time will be followed until resolution or stabilization.

- Complete physical examination including weight.
- Blood samples for:

  - CBC with differential.
  - Serum chemistry panel and liver function tests, glucose, creatinine, BUN, total bilirubin, AST, ALT, alkaline phosphatase, serum albumin, sodium, potassium, calcium, chloride, bicarbonate, magnesium, and phosphorus.

- Urine pregnancy test.
- Tumor assessment: CT or MRI scan with IV contrast as appropriate (chest, abdomen, pelvis, and other regions of known/suspected involvement), unless known anaphylaxis to contrast or medically contraindicated as described in Section 9. If imaging was obtained within 2 weeks of the EOT Visit, imaging does not need to be repeated.
- Blood collection for PK and ADA serum samples.
- Blood collection for biomarker samples.
- Record AEs.
- Concomitant medications.
- CCI [redacted]

For subjects continuing treatment following implementation of PA5, EOT assessments will be performed according to Table 3.

4.5. 30-Day Safety Follow-Up Visit

A single Safety Follow-up Visit will occur 30 days (± 3 days) after the last dose of study drug and will include:

- Complete physical examination including weight.
- Urine pregnancy test.
- Blood samples for:
  - CBC with differential.
  - Serum chemistry panel and liver function tests, glucose, creatinine, BUN, total bilirubin, AST, ALT, alkaline phosphatase, serum albumin, sodium, potassium, calcium, chloride, bicarbonate, magnesium, and phosphorus.
- Blood collection for PK and ADA serum samples.
- Concomitant medications.
- Record AEs.
- Collection of subsequent anti-cancer treatment.

If the EOT Visit occurs at the same time or within 14 days of the scheduled 30-Day Safety Follow-up Visit, the same assessments may be utilized for both visits.

For subjects continuing treatment following implementation of PA5, the 30-Day Safety Follow-up Visit assessments will be performed according to Table 3.

4.6. Treatment Discontinuation

Subjects may discontinue the study drug under any of the following conditions:

1) Withdrawal of consent from further treatment with study drug.

2) Lost to follow-up (see Section 4.6.1).

3) An AE that, in the opinion of the Investigator or the Sponsor, contraindicates further dosing.

4) Initiation of alternative anti-tumor therapy, including any other investigational product.

5) Pregnancy.

6) More than a 3-week dose delay from the planned treatment date due to treatment-related toxicity or 5-week dose delay for all other reasons.

7) PD without evidence of clinical benefit with continued therapy.

8) Subject non-compliance.

9) Suspension of the study by the Sponsor.

10) Death.

11) Investigator's or treating physician decision in the absence of any of the above.

Study drug discontinuation should not result in subject discontinuation from the study, and the subject should continue to be followed up in the study for disease progression and survival per Section 4.7. Reasons for discontinuation from the study are described in Section 4.8.

If a subject discontinues study treatment (eg, as a result of an AE), every attempt should be made to keep the subject in the study and continue to perform the required study-related follow-up procedures (see Section 4.7). If this is not possible or acceptable to the subject or Investigator, the subject may be withdrawn from the study.

4.6.1. Lost to Follow-up

A subject will be considered lost to follow-up if the subject repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a subject fails to return to the clinic for a required study visit:

- The site must attempt to contact the subject and reschedule the missed visit as soon as possible, counsel the subject on the importance of maintaining the assigned visit schedule and ascertain whether the subject wishes to and/or should continue in the study.

- Before the subject is deemed lost to follow-up, the Investigator or designee must make every effort to regain contact with the subject (where possible, 2 telephone calls, and if necessary, a certified letter to the subject's last known mailing address or local equivalent methods). These contact attempts should be documented in the subject's source documents.

- Should the subject continue to be unreachable, the subject will be considered lost to follow-up.

For subjects who are lost to follow-up, study staff may use public records (eg, public health records) to obtain information about survival status where allowable by local regulation.

4.7. Safety/End of Treatment and Survival Follow-up

After discontinuation of treatment (see Section 4.6), all subjects must complete an EOT Visit 30 days after the last dose of study drug and a 30-Day Safety Follow-up Visit (Table 2). Subjects will then be followed every 12 weeks for survival, unless the subject explicitly indicates a desire to forego survival follow-up to their study Investigator. Subjects will be followed until death, withdrawal of consent, lost to follow-up, Sponsor-terminated study or completion of survival follow-up (24 months after the last subject is dosed), whichever occurs first. This follow-up assessment may be conducted by telephone or in-clinic visit and will include documentation of any subsequent therapy for their cancer.

For subjects who are lost to follow-up, study staff may use public records (eg, public health records) to obtain information about survival status where allowable by local regulation.

Following implementation of PA5, subjects who previously discontinued treatment will no longer be followed for survival follow-up and subsequent therapy and will discontinue the study as per sponsor's decision.

4.8. End of Study

The end of the study for a subject's participation occurs when they have completed all periods of the study including long-term or survival follow-up due to the following reasons: death, the subject withdraws consent, there is documented loss to follow-up of the subject, or the Sponsor terminated the study, whichever comes first.

Please note, the End-of-Study page is also expected to be entered into the Electronic Data Collection (EDC) system once a subject completes the study even if there was no death event, withdrawal of consent, or loss to follow-up. The End-of-Study page is required to be completed in addition to the End-of-Treatment page.

Following implementation of PA5:

- Subjects may continue treatment as part of the study, for as long as they are deriving clinical benefit. After they meet one of the criteria for treatment discontinuation (Section 4.6), they will have an EOT visit and a 30-Day Safety Follow-up Visit. There will be no additional assessments including survival follow-up and subsequent therapy collection.

- Subjects will have the end of study at the same time as the EOT visit (Section 4.4). However, if at the time of an EOT visit, subjects have unresolved AEs, the end of study for that subject may be delayed until all AEs have been resolved or stabilized per Section 10.2.2.1.

The end of the entire study for all subjects is defined as the date on which the last subject remaining on study completes the last study visit/call/survival follow-up or when the Sponsor decides to end the study. The Sponsor reserves the right to terminate the study at any time for any reason (including safety).

At the completion of the study, subjects who are deriving benefit from sacituzumab govitecan monotherapy may continue to receive treatment in a rollover study (Study IMMU-132-14) in locations where the study is available. This rollover study is designed to provide continued access to sacituzumab govitecan for eligible subjects who have previously participated in a Gilead-sponsored parent study, who are tolerating sacituzumab govitecan, have no evidence of PD, or are still deriving clinical benefit despite progression (as assessed by the Investigator). Subjects may receive the dose of sacituzumab govitecan currently receiving in the parent study at the time of consenting to participate in the rollover study, if applicable.

CCI [redacted]

5. STUDY EVALUATIONS

All subjects must be dosed within 28 days of providing written informed consent. No subject may be dosed until the Sponsor or their representative has approved the eligibility packet. Clear documentation as to the reason the subject was not dosed should be provided on the relevant eCRF. Unless otherwise specified, visit windows are permitted either 1 day before or + 2 days after scheduled visits and ± 7 days for response assessments. Treatment delays for reasons other than required for resolution of treatment-related toxicity are not permitted.


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Table 3. Modified Schedule of Assessments/Study Calendar (After Implementation of PA5)

Visit	**Treatment**			
Cycle	**ALL Cycles**			
Day[a]	**1**	**8**	**EOT Visit**[b]	**30-Day Safety Follow-up Visit**[c]
Weight[d]	X		X	X
Physical examination[e]	Per standard of care		X	X
Vital signs[f]	As needed			
Study drug administration	X	X		
Urine Pregnancy test (if applicable)[g]	X		X	X
Serum Follicle-Stimulating Hormone (FSH)[h]	As needed			
Hematology[i]	X	X	X	X
Serum chemistry including liver function tests[j]	X	X	X	X
Tumor assessment (CT or MRI scan)[k]	Per standard of care			
AE reporting[l]	X	X	X	X
Prior/concomitant medications	X	X	X	X
Subsequent anti-cancer treatment				X

Abbreviations: AE = adverse event; ALT = alanine aminotransferase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; BUN = blood urea nitrogen ; CBC = complete blood count; CT = computed tomography; eCRF = electronic case report form; EOT = end of treatment; MRI = magnetic resonance imaging; PA5 = Protocol Amendment 5; SAE = serious adverse event.

a Unless otherwise specified, visit windows are within −1 to +2 days of the schedule visits and ±7 days for response assessments.

b The EOT Visit should occur within 30 days of the decision to discontinue treatment. If the EOT Visit and 30-Day Safety Follow-up Visit occur within 14 days of each other, the same assessment results may be utilized for both study visits.

c The Safety Follow-up Visit should be conducted 30 days (± 3 days) after the last dose of study drug.

d During treatment, subject's body weight will be measured on Day 1 of each treatment cycle (or more frequently if the subject's body weight changed by >10% since the previous administration), at the EOT Visit, and at the 30-Day Safety Follow-up Visit.

e Complete physical examinations will be performed at the EOT Visit and the 30-Day Safety Follow-up Visit. At study visits during the Treatment Phase, physical examinations should be performed per institutional practice.

f Collection of vital signs will be needed in the event of suspected infusion-related reaction. Vital signs will include blood pressure, heart rate, pulse, respiratory rate, and body temperature and will be taken after the subject has been resting for at least 5 minutes.

g In females of childbearing potential, pregnancy testing will be performed on Day 1 of each treatment cycle, and every 28 days after the last dose of study drug up to 6 months after the last dose of study drug per the duration of required contraception, as described in Appendix 17.5. Testing during the posttreatment period may be performed at home and the result is to be self-reported by the subject. If the urine test is positive or equivocal, a confirmatory serum pregnancy test will be required.

h Conduct as needed per Appendix 17.5.

i CBC with differential for all subjects is required at Days 1 and 8 of each cycle, and the EOT Visit and 30-Day Safety Follow-up Visit. Hematology tests may be performed and reviewed up to 24 hours prior to scheduled study treatment administration. See Section 7.5.2.5 for when sacituzumab govitecan should be administered based on ANC.

j Serum chemistries include liver function test, glucose, creatinine, BUN, total bilirubin, AST, ALT, alkaline phosphatase, serum albumin, total protein, sodium, potassium, calcium, chloride, bicarbonate, magnesium, and phosphorus. Serum chemistries are required in all subjects at Days 1 and 8 of every cycle, the EOT Visit, and 30-Day Safety Follow-up Visit. These laboratory assessments may be obtained more frequently at the discretion of the treating physician if abnormal results warrant follow-up. Serum chemistries may be performed and reviewed up to 24 hours prior to scheduled study treatment administration.

k Subjects who continue treatment following implementation of PA5 will be expected to have scans performed per standard of care, as indicated by local practice. Tumor response data will no longer be collected for this study; however, disease status should still be monitored by the treating physician to determine if progression has occurred, and whether the subject is continuing to derive clinical benefit.

l All AEs and SAEs must be reported in eCRF and to Gilead Global Patient Safety from first dose of study drug until 30 days after last dose of study drug or initiation of alternative therapy for underlying disease in accordance with instructions in Section 10.2.5. SAEs that occur after initiation of a new anticancer therapy will not be reported.

5.1. Medical History and Demographic/Baseline Characteristics

Basic demographic and baseline characteristics will be collected during Screening. In addition to the evaluation of a subject's medical history to determine study eligibility, all relevant medical conditions will be documented on the appropriate eCRF. Events that occur after signing of informed consent but prior to initiation of study drug(s), unless it was due to a protocol-mandated procedure, should be recorded on the Medical History eCRF.

The subject's entire oncology history for the tumor of interest will be collected on the appropriate eCRF including cancer histology, stage, and date of diagnosis, prior surgeries/treatments received for cancer, dates of treatment administration, intent of administered regimen (neoadjuvant, adjuvant, or metastatic), best response achieved, and date of PD.

5.2. Prior and Concomitant Medication Assessments

Medications administered prior to the first dose of study drug will be recorded as prior medications, whereas medications initiated after administration 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 AEs as outlined in the protocol should be documented along with the rationale for prophylactic intent.

5.3. Other Study Evaluations

For other study evaluation parameters, please refer to the following sections:

- Efficacy evaluation (Section 9).
- Safety evaluations (Section 10.1 and Section 10.2).
- PK evaluations (Section 10.3).
- Immunogenicity (ADA) evaluations (Section 10.4).
- Biomarker evaluations (Section 10.6).

6. TARGET POPULATION

Adult subjects with histologically documented advanced or metastatic NSCLC (adenocarcinoma or SCC), HNSCC, endometrial carcinoma, or SCLC histology. All subjects must meet the eligibility criteria as described in Section 6.2 and Section 6.3.

6.1. Screen Failures

Subjects who consent to participate in the clinical study, and who do not meet at least 1 criterion required for participation in the study during the screening procedures are considered screen failures. All subjects who have signed informed consent and were deemed ineligible will be recorded in a log with the reason for ineligibility. 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, screen failure date, and any AEs and SAEs.

All subjects who previously failed screening may be rescreened only once.

All screening tests must be obtained during the 28-day screening period after the subject provides written informed consent and prior to C1D1. Subjects who are rescreened are considered previous screen failures and they will be enrolled in the study and assigned a new subject number at the time of rescreening.

6.2. Subject Inclusion Criteria

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

1) Female or male adults, > 18 years of age, who are able to understand and give written informed consent.

2) Subjects with the following histologically documented metastatic (M1, Stage IV) or locally advanced solid tumors.

    a) NSCLC (adenocarcinoma or SCC) that has progressed after prior platinum-based chemotherapy and programmed death-(ligand) 1 (PD-(L)1) directed therapy given sequentially (in either order) or in combination. These agents could have been taken as monotherapy or in combination with other agents. If subjects have had recurrence/relapse or lack of response within 6 months of completing chemotherapy with or without PD-(L)1 directed therapy for locally advanced disease, that line of therapy may be counted for eligibility.

    b) HNSCC that has progressed after prior platinum-based chemotherapy and anti-PD-(L)1 directed therapy given sequentially (in either order) or in combination. These agents could have been taken as monotherapy or in combination with other agents. No more than 3 prior lines of systemic treatment is allowed.

c) Endometrial carcinoma that has progressed after prior platinum-based chemotherapy and anti-PD-(L)1 directed therapy given sequentially (in either order) or in combination. These agents could have been taken as monotherapy or in combination with other agents. No more than 3 prior lines of systemic treatment is allowed. Endometrial carcinoma with any histology including MSI-h/dMMR and MSS are allowed.

d) Extensive stage SCLC that has progressed after prior platinum-based chemotherapy and PD-(L)1 directed therapy. No more than one prior line of systemic treatment is allowed (re-challenge with the same initial regimen is not allowed).

3) ECOG Performance Status score of 0 or 1 (see Appendix 17.2).

4) Adequate hematologic counts without transfusional or growth factor support within 2 weeks of study drug initiation (hemoglobin ≥ 9 g/dL, absolute neutrophil count (ANC) ≥ 1,500/mm3, and platelets ≥ 100,000/μL).

5) Adequate hepatic function [bilirubin ≤ 1.5 institutional upper limit of normal (IULN), AST and ALT ≤ 2.5 × IULN or ≤ 5 × IULN if known liver metastases and serum albumin ≥ 3 g/dL].

6) Creatinine clearance ≥ 30 mL/min as assessed by Cockcroft-Gault (see Appendix 17.3).

7) Subjects must have at least a 3-month life expectancy.

8) Have measurable disease by CT or MRI scan as per RECIST 1.1 criteria (see Appendix 17.4). Tumor lesions situated in a previously irradiated area may be utilized if they are considered measurable and PD has been demonstrated in such lesions.

9) 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 17.5.

10) Tumor blocks (preferably obtained within 12 months of study entry if clinically feasible) or 20 newly sectioned unstained slides (6 slides minimum) of archived biopsy/surgical specimens are requested. A baseline biopsy is required if archival tissue is not available. Fine needle aspirates and bone biopsies are not suitable samples. These specimens should be submitted within the 28-day screening period, after the subject provides written informed consent.

6.3. Subject Exclusion Criteria

Subjects meeting any of the following exclusion criteria at Screening will not be enrolled in the study.

1) Positive serum pregnancy test (Appendix 17.5) or women who are lactating.

Article I. Are currently participating in or have participated in a study of an investigational agent or using an investigational device within 4 weeks prior to the first dose of study drug. Subjects participating in observational studies are eligible.

Article II. Have had a prior anti-cancer biologic agent within the 4 weeks prior to Day 1 or have had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1.

Article III. Have not recovered (ie, ≤ Grade 1) from AEs caused by a previously administered agent.

- **Note**: Subjects with ≤ Grade 2 neuropathy or ≤ Grade 2 alopecia are exceptions to this criterion and may qualify for the study.
- **Note**: If subjects underwent major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study drug.
- **Note**: Subjects with Grade ≤ 2 immune-mediated toxicities (except colitis) related to immunotherapy and/or radiation treatment that are long lasting, but stable on treatment and not requiring agents that are excluded by this protocol may qualify for the study.

2) Have previously received topoisomerase I inhibitors (for SCLC cohort: Etoposide with platinum combination in first-line setting is allowed).

3) Have an active second malignancy.

- **Note**: Subjects with a history of malignancy that has been completely treated, with no evidence of active cancer for 3 years prior to enrollment, or subjects with surgically cured tumors with a low risk of recurrence may be enrolled.

4) Have known active CNS metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they have stable CNS disease for at least 4 weeks prior to the first dose of study drug and all neurologic symptoms have returned to baseline, have no evidence of new or enlarging brain metastases, and are taking ≤ 20 mg/day of prednisone or its equivalent. All subjects with carcinomatous meningitis are excluded regardless of clinical stability.

5) Have active cardiac disease, defined as:

   - Myocardial infarction or unstable angina pectoris within 6 months of Day 1.
   - History of serious ventricular arrhythmia (ie, ventricular tachycardia or ventricular fibrillation), high-grade atrioventricular block, or other cardiac arrhythmias requiring anti-arrhythmic medications (except for atrial fibrillation that is well controlled with anti-arrhythmic medication); history of QT interval prolongation.
   - New York Heart Association (NYHA) Class III or greater congestive heart failure or left ventricular ejection fraction of < 40%.

6) Have active chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease), immune-mediated colitis, or GI perforation within 6 months of C1D1.

7) Have an active infection requiring IV antibiotics.

8) Have positive HIV-1 or HIV-2 antibody with detectable viral load or taking medications that may interfere with SN-38 metabolism (the active metabolite of sacituzumab govitecan).

9) Have active HBV or HCV, subjects with a detectable viral load will be excluded.

   - Subjects who test positive for HbsAg. Subjects who test positive for anti-HBc will require HBV DNA by quantitative PCR for confirmation of active disease.
   - Subjects who test positive for HCV antibody. Subjects who test positive for HCV antibody will require HCV RNA by quantitative PCR for confirmation of active disease. Subjects with a known history of HCV or a positive HCV antibody test will not require an HCV antibody at screening and will only require HCV RNA by quantitative PCR for confirmation of active disease.

10) 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.

11) Impending need for palliative radiation therapy or surgery for pathological fractures and/or for medullary compression within 4 weeks prior to initiating study treatment.

12) Additional cohort-specific exclusion criteria:

NSCLC cohort (adenocarcinoma and SCC):

a) Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder (ie, pulmonary emboli within 3 months of enrollment, severe asthma, severe chronic obstructive pulmonary disease, restrictive lung disease, pleural effusion, etc); any autoimmune, connective tissue, or inflammatory disorders with pulmonary involvement (ie, rheumatoid arthritis, Sjogren syndrome, sarcoidosis, etc); or prior pneumonectomy.

HNSCC cohort:

a) Subjects with nasopharynx carcinoma.

b) Subjects who had progressive disease within 6 months of completion of curative therapy.

Endometrial carcinoma cohort:

a) Subjects who have carcinosarcoma (malignant mixed Mullerian tumor), endometrial leiomyosarcoma, and/or endometrial stromal sarcomas.

Small cell lung cancer cohort:

a) Subjects who never received platinum-containing regimen for SCLC.

b) Limited-stage subjects who are candidates for local or regional therapy.

7. TREATMENT OF SUBJECTS

7.1. Description of Study Drug

Sacituzumab govitecan is an ADC composed of hRS7, a humanized immunoglobulin G (IgG)1κ monoclonal antibody, which binds to TROP-2 (trophoblast cell-surface antigen-2), SN-38, a camptothecin analog which is an inhibitor of topoisomerase I, and CL2A, a linker that couples SN-38 to hRS7.

7.2. Concomitant Medications

No anti-cancer therapies, aside from the study drug (sacituzumab govitecan) 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 of non-target lesions is permitted, but presence of new or worsening metastases will be considered PD. Palliative radiation of target lesions should be avoided and will make the subject unevaluable per protocol. However, if there is clear evidence of clinical benefit, treatment may be continued after completion of palliative radiotherapy to lesions that are not target lesions. In this case, sacituzumab govitecan administration should be interrupted 1 week before the procedure and reinstated no earlier than 2 weeks after the procedure. If a subject requires surgery, administration of sacituzumab govitecan should be interrupted 1 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, or cranial surgeries, may require suspension of dosing for 4 weeks to allow for an adequate period for healing before the subject may resume treatment. The medical monitor for the study must approve continuation of therapy with sacituzumab govitecan prior to resumption of dosing.

There is not substantial 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. The study visits should continue as planned if vaccination occurs while the subject is on the study. For details on the risk and mitigation strategy for concurrent administration of the COVID-19 vaccine, refer to Appendix 17.7.

7.3. Treatment Compliance

Sacituzumab govitecan will be administered at scheduled study sites 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 height and weight, and total study 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.

7.4. Randomization and Blinding

Not applicable.

7.5. Treatment of Sacituzumab Govitecan-Associated Toxicities

Instructions for the preparation and administration of the infusion of sacituzumab govitecan are provided in Section 8.4 and Section 8.5, respectively. 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 assessed and managed in accordance with standard clinical and institutional practices and accepted treatment guidelines.

7.5.1. Preventative Medications

Guidance for premedication for prevention of toxicities associated with sacituzumab govitecan is presented in Table 4.

CCI

ANC = absolute neutrophil count; ASCO = American Society of Clinical Oncology; ESMO = European Society for Medical Oncology; G-CSF = granulocyte-colony stimulating factor; IV = intravenous; NCCN = National Comprehensive Cancer Institute; PO = orally; SG = sacituzumab govitecan

All patients should be given medications to take home with clear instructions for the prevention and treatment of nausea, vomiting, and diarrhea. At the onset of diarrhea, promptly initiate treatment with anti-diarrheals (eg, loperamide at 4 mg initially followed by an additional 2 mg with every episode of diarrhea for a maximum of 16 mg daily or follow local label guidelines for loperamide). Discontinue anti-diarrheals 12 hours after diarrhea resolves. Additional supportive measures (eg, fluid and electrolyte substitution) may also be employed as clinically indicated. Subjects who exhibit an excessive cholinergic response to treatment with sacituzumab govitecan (eg, abdominal cramping, diarrhea, salivation) can receive appropriate premedication (eg, anti-cholinergics such as atropine) for subsequent infusions.

Additional details of recommended treatment of infusion-related reactions are described in Section 7.5.2.1 The recommended treatment of delayed nausea and vomiting is described in Section 7.5.2.2.

7.5.2. 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 because of increased episodes of diarrhea or neutropenia, should have their polymorphism assessed. If found to have the *1/*28 or *28/*28 polymorphism, this data should be recorded in the eCRF with dosing adjusted per institutional standards. Instructions for sacituzumab govitecan dose reduction for treatment-related toxicities are provided in Section 7.5.2.5.

7.5.2.1. 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. 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 infusion-related reactions, sacituzumab govitecan should only be administered in a setting in which appropriately trained medical staff, emergency equipment, and medications are available if resuscitation is required. NCI-CTCAE v5.0 is used to grade the severity of all infusion-related AEs. Premedication for the prevention of infusion-related reactions is described in Section 7.5.1.

Grade 4 Events

Grade 4 reactions include potentially life-threatening reactions, requiring urgent intervention. If Grade 4 infusion-related reactions occur, sacituzumab govitecan should be permanently discontinued (Table 6).

Grade 2 and Grade 3 Events

Grade 2 infusion-related reactions are defined as those that require infusion interruption and respond to symptomatic treatment; prophylactic medications are indicated for ≤ 24 hours. For Grade 2 infusion-related reactions, the infusion should be interrupted until symptoms resolve. After symptoms resolve, the infusion should be resumed at a slower infusion rate determined by the managing physician. Grade 3 infusion-related reactions are defined as those which 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 and Grade 3 infusion-related reactions despite optimal management, sacituzumab govitecan should be permanently discontinued (Table 6).

7.5.2.2. Gastrointestinal Toxicities

Nausea, vomiting, and diarrhea are toxicities that are frequently associated with sacituzumab govitecan. Appropriate treatment, including 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 GI toxicities are provided in Section 7.5.2.5.

Nausea and Vomiting

Instructions for the use of pre-medications for prophylactic treatment of nausea and vomiting and anticipatory nausea are provided in Section 7.5.1. 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. Subjects may be treated for delayed nausea and vomiting on Days 2 and 3 with 5-HT_3 receptor antagonist (ondansetron or palonosetron) monotherapy and other agents if needed. Steroids may be added if symptoms do not resolve with these agents. Consider olanzapine for persistent or anticipatory nausea; an olanzapine dose of 2.5 mg or 5 mg at bedtime is recommended. Neurokinin 1 (NK1) receptor antagonists (fosaprepitant and aprepitant) may be administered.

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, the Investigator (or treating physician) should consider adding diphenoxylate/atropine and/or opium tincture, as clinically indicated.

Consider adding octreotide 100 to 150 µg subcutaneous (SC) 3 times per day (TID) if diarrhea persists. Withhold sacituzumab govitecan for Grade 3 or Grade 4 diarrhea at the time of scheduled treatment administration and resume when resolved to Grade ≤ 1. For Grade 3 or Grade 4 diarrhea, the subject may be hospitalized, and treated 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) can receive appropriate premedication (eg, atropine) for subsequent treatment with sacituzumab govitecan.

7.5.2.3. Neutropenia

Information regarding the prophylaxis and management of neutropenia and febrile neutropenia with G-CSF are included in Table 4. Fever, fatigue, lethargy, malaise, loss of appetite, and decreased production of urine are potential early symptoms of febrile neutropenia. In subjects who develop neutropenia or febrile neutropenia, treat with G-CSF and consider prophylaxis in subsequent cycles as clinically indicated. Initiation of anti-infective treatment in subjects with febrile neutropenia without delay is strongly recommended. SG dosing should be interrupted and modified in accordance with Table 6.

7.5.2.4. Overdose

Overdose is defined as administration of more than 10% higher dose 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.

7.5.2.5. Sacituzumab Govitecan Dose Delays, Dose Reductions, and Discontinuation Guidelines

CCI

[redacted]

CCI [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Event NCI-CTCAE v5.0	Occurrence	Recommended dose reduction or action
Any Grade 3 or Grade 4 nausea, vomiting or diarrhea due to treatment that is not controlled with anti-emetics and anti-diarrheal agents OR Other Grade 3 or Grade 4 non-hematologic toxicity persisting > 48 hours despite optimal medical management OR At time of scheduled treatment, Grade 3 or Grade 4 non-neutropenic hematologic or non-hematologic toxicity, that delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1	Third	Discontinue treatment
In the event of Grade 3 or Grade 4 non-neutropenic hematologic or non-hematologic toxicity that does not recover to ≤ Grade 1 within 3 weeks	First	Discontinue treatment
Infusion-Related Toxicities		
Grade 2 or Grade 3 infusion-related reactions despite optimal management	Recurrent	Discontinue treatment
Grade 4 infusion-related reaction	First	Discontinue treatment

Abbreviations: G-CSF = granulocyte-colony stimulating factor; NCI-CTCAE = National Cancer Institute-Common Terminology Criteria for Adverse Events.

7.6. 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* (Appendix 17.6), with sacituzumab govitecan, should be avoided because of the potential to either increase (inhibitors) or decrease (inducers) the exposure to SN-38, unless there are no therapeutic alternatives.

7.6.1. UGT1A1 Inhibitors

Co-administration of sacituzumab govitecan with inhibitors of *UGT1A1* 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 17.6.

7.6.2. 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 17.6.

8. STUDY DRUG MATERIALS AND MANAGEMENT

8.1. Study Drug

Sacituzumab govitecan 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 buffer containing trehalose and polysorbate 80 and contains no preservatives. Following reconstitution, the concentration of sacituzumab govitecan is 10 mg/mL. The pH of the reconstituted solution is approximately 6.5.

8.2. Study Drug Packaging and Labeling

Sacituzumab govitecan is packaged in single-use, 50R, glass vials, closed with coated elastomeric stoppers and capped with flip-off caps with aluminum over seals. Study drug to be distributed to centers in the US and other participating countries shall be labeled to meet applicable requirements of the US Food and Drug Administration (FDA), European Union (EU) Guideline to Good Manufacturing Practice–Annex 13 (Investigational Medicinal Products), and/or other local regulations.

8.3. Study Drug Storage

The glass vials of sacituzumab govitecan must be stored under refrigeration (2-8 °C) and protected from light until use. Since the formulated drug product contains no preservative, vials should be used only once. Refer to the current version of the Pharmacy Manual for additional details.

8.4. Study Drug Preparation

Calculate the prescribed dose in mg based on the subject's body weight at enrollment (C1D1) (unless there is a > 10% change in body weight from enrollment or if required by institutional policy). Calculate the number of vials required for a dose, based on maximum concentration of 10 mg/mL after reconstitution.

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

8.5. Administration

Do not administer as an IV push or bolus. Sacituzumab govitecan is administered via IV infusion as described below with additional information available in the current version of the Pharmacy Manual.

- Administer the **first** infusion over 3 hours (±15 minutes). Subsequent infusions may be administered over 1 to 2 hours if previous infusions were well tolerated. Monitor the subject during the infusion, and for at least 30 minutes after infusion.

9. ASSESSMENT OF EFFICACY

CT or MRI scans with IV contrast of the chest, abdomen, pelvis, and any other involved disease sites (including brain MRI if appropriate) are to be obtained in all subjects (unless known anaphylaxis to contrast and/or medically contraindicated). If the use of IV contrast is medically contraindicated for a subject, 1 of the following options may be used (listed in order of preference): CT without contrast, MRI without contrast, or attempt to desensitize the subject with steroids. For each subject, the same imaging technique should be used throughout the study for tumor assessment. If a subject had brain lesions at study entry, brain MRI will be needed at all assessments. The timing of imaging is based on calendar time from the date of C1D1. Scans will be performed for all subjects at baseline and every 6 weeks for the first 6 months after C1D1 and then every 9 weeks thereafter until the occurrence of radiologic PD, as per RECIST 1.1, requiring discontinuation of treatment. Dose delays and cycle delays should not result in delays in the timing of imaging. For subjects with evidence of CR or PR, a confirmatory scan must be obtained at least 4 to 6 weeks after initial documentation of response CR or PR. Scans will be transferred to a central reader for collection and analysis by blinded independent central review (BICR).

Target and non-target lesions must be determined by the clinical site at baseline. Subjects who discontinue from treatment because of toxicity or clinical progression will continue to obtain radiologic response assessments at the protocol-required schedule until radiologic evidence of PD or initiation of new therapy, if clinically feasible. Additional CT or MRI studies may be performed at the discretion of the subject's treating physician to assess disease status, as medically indicated. Tumor response and progression will be determined using RECIST 1.1. For subjects who continue treatment despite radiologic evidence of PD as defined in Section 4.3.1, the subject will remain in the study and continue to be monitored according to the protocol required schedule of assessments (Table 2). The results of all imaging including those not specified as protocol assessments will be recorded on the eCRF.

Subjects who continue treatment following implementation of PA5 will be expected to have scans performed per standard of care, as indicated by local practice. Tumor response data will no longer be collected for this study; however, disease status should still be monitored by the treating physician to determine if progression has occurred, and whether the subject is continuing to derive clinical benefit.

10. ASSESSMENT OF SAFETY

10.1. Safety Parameters

10.1.1. Clinical Laboratory Investigations

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 judgment. All investigations will be assessed for all subjects at Screening, during treatment, and upon treatment discontinuation per the schedule of assessments (Table 2). Clinical laboratory samples will also be collected at the 30-Day Safety Follow-up Visit. 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. In the event of clinically significant abnormal results, tests should be repeated within 24 to 48 hours to confirm abnormality. Results for these laboratory tests should be followed until resolution. The panels of laboratory tests to be performed are shown below:

Hematology: hemoglobin, white blood cell (WBC) count and differential (with ANC), and platelet count.

Clinical Chemistry: total protein, albumin, total bilirubin, alkaline phosphatase (ALP), ALT, AST, creatinine (see Appendix 17.3) and clinical chemistries including glucose, sodium, potassium, magnesium, chloride, bicarbonate (CO_2/HCO_3^-), calcium, phosphorus.

Urinalysis: performed locally on a freshly voided clean sample by dipstick for protein, glucose, blood, pH, and ketones. If dipstick findings are abnormal based on the Investigator's judgment, then a microscopic evaluation will be performed to assess the abnormal findings. Urinalysis will be performed at Screening only and as clinically indicated with details regarding casts, WBC count and RBC count, and bacteria recorded. Only abnormal results will be captured on the eCRF.

Pregnancy and FSH Testing: Female subjects of childbearing potential must have a negative serum or urine pregnancy test result within 72 hours prior to administration of the first dose of study drug and a negative urine pregnancy test result of Day 1 of every cycle while on study drug. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. Serum FSH testing will be conducted as needed per Appendix 17.5 for determination of childbearing potential.

LDH and Uric Acid: will only be required at Screening. May be obtained more frequently at the discretion of the treating physician if abnormal results warrant follow-up. Results of unscheduled tests should be documented.

10.1.2. Vital Signs

Vital signs will be taken at Screening, and C1D1 prior to infusion. Additional collection of vital signs will be needed in the event of suspected infusion-related reaction. Vital signs will include blood pressure, heart rate, pulse, respiratory rate, and body temperature and will be taken after the subject has been resting for at least 5 minutes. All vital signs will be recorded on the eCRF.

10.1.3. Electrocardiogram

Local 12-lead ECGs will be obtained for all subjects at baseline and prior to the C1D1 infusion. Abnormal findings should be evaluated as clinically indicated, including repeated ECGs. ECGs may be done at other timepoints during the study if clinically indicated.

ECGs are to be performed at rest in the supine position. Clinically significant abnormal findings should be noted and the appropriate clinical work-up initiated until the condition has stabilized.

The following will be measured or calculated: heart rate, PR, QRS, QT interval, corrected QT interval using Fridericia's formula (QTcF), and rhythm.

10.1.4. Physical Examinations, Body Weight, and Height

Complete physical examinations (a minimum assessment of the following systems: head/eyes, ears/neck/throat, cardiac, lungs, abdomen, and extremities) will be performed during Screening, at the EOT Visit, and at the 30-Day Safety Follow-up Visit. Clinically targeted physical examinations will be performed at study visits during the Treatment Phase.

Height will be measured during the Screening Visit only. Weight will be measured per institutional guidelines during Screening, on Day 1 of each cycle, and at the EOT Visit and 30-Day Safety Follow-up Visit. Only clinically significant abnormalities will be recorded on the appropriate eCRF.

Physical exam data for subjects following implementation of PA5 will not be collected at treatment visits; however, physical exams should be performed per institutional practice. Any abnormal findings identified should be recorded as an AE, unless already documented as part of medical history or if the abnormal finding is a manifestation of the disease under study.

10.1.5. ECOG Performance Status

ECOG Performance Status will be assessed during Screening (see Appendix 17.2).

10.2. Adverse and Serious Adverse Events

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. Definition of Adverse Events

10.2.1.1. Adverse Events (AEs)

An adverse event (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 it is related to the investigational medicinal product.

Adverse events may include worsening or exacerbation of the disease under study; worsening or exacerbation of pre-existing conditions or events; intercurrent illnesses; or drug interactions. Anticipated fluctuations of pre-existing 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 pre-existing condition for which the surgery is required, is the AE.

10.2.1.2. Serious Adverse Events (SAE)

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 allowed to continue, might have caused death.
- Requires inpatient hospitalization or prolongation of existing hospitalization (in the absence of a precipitating clinical AE is not in itself an SAE).
- Results in persistent or significant disability or incapacity.
- Is a congenital anomaly/birth defect (in the child of a subject who was exposed to the study drug).

- 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:

- PD (See Section 10.2.2.6).
- Hospitalization for a routine clinical procedure as stipulated by the protocol.
- 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).

10.2.2. Adverse Event Reporting and Assessment

10.2.2.1. Adverse Event Reporting Period

During the period after the informed consent has been obtained and before the first dose of study drug, all SAEs and AEs caused by a protocol-mandated intervention (eg, biopsy) should be reported. All AEs and SAEs must be reported in eCRF and to Gilead Global Patient Safety from first dose of study drug until 30 days after last dose of study drug or initiation of alternative therapy for underlying disease. Subsequently, only SAEs assessed as related to study drug by the investigator that occur during long-term follow-up must be reported to Gilead Global Patient Safety in accordance with instructions in Section 10.2.5. In addition, SAEs that occur after initiation of a new anticancer therapy will not be reported.

- Investigators are not obligated to actively seek SAEs after the long-term 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.

10.2.2.2. Adverse Event Collection and Documentation

Identification and Recording of Adverse Events

It is the responsibility of the Investigator to document all AEs that occur during the study. 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 physical examinations, laboratory tests, and other study procedures such as ECGs. The Investigator must review all laboratory and test data; abnormal findings should be assessed to determine if they meet the criteria for AEs (Section 10.2.1.1 and Section 10.2.2.5).

For all AEs, the Investigator must pursue and obtain information adequate to assess whether it meets the criteria for classification as an SAE (Section 10.2.1.2) 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 AE. 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.

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.

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.

Serious Adverse Events

Serious adverse events (SAEs) are to be recorded on the Initial or Follow-up SAE Report Form and transmitted by emailing or faxing the report to the Sponsor or the Sponsor's designee within 24 hours of investigator's awareness 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 any other relevant information, such as possible alternative etiologies.

Information captured on both the SAE Form and entered in the eCRF should be consistent.

10.2.2.3. Assessment of Adverse Event Severity

The severity of AEs will be graded using the latest version of NCI-CTCAE v5.0. For each SAE, the highest severity grade should be reported. If an NCI-CTCAE criterion does not exist, the Investigator should assess the severity according to the criteria in Table 7.

Table 7. 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

Abbreviations: ADL = activities of daily living; NCI-CTCAE = National Cancer Institute-Common Terminology Criteria for Adverse Events; SAE = serious adverse event.

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.

10.2.2.4. 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 drug caused or contributed to an AE. 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, more specifically 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 which may have a known association with the event. Causality is to be assessed as follows:

- **Related:** Plausible time relationship to study drug 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 study drug administration which 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.

10.2.2.5. Adverse Events Based on Abnormal Test Findings

An abnormal test finding that meets any 1 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 drug 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 1 of the criteria above should not be reported as AEs. Repeating an abnormal test, in the absence of the above conditions, does not constitute as 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.

10.2.2.6. Disease Progression

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

Hospitalization because of signs and symptoms of PD (as defined above) should not be reported as SAEs.

In most cases, PD will be based on RECIST 1.1 criteria. If PD is based on the subject's symptoms, every effort should be made to document progression using objective criteria.

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. Deaths which occur more than 30 days after the last dose of study drug 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 SAEs (see Section 10.2.2.6) if, in the Investigator's judgment, the event is unequivocally because of the expected course of progression of the underlying disease, and not because of another cause.

10.2.4. Reporting Exposure During Pregnancy

Pregnancy occurring in a female subject from start of the study and throughout the study (including the post study drug follow-up period) or within 6 months after the end of treatment, whichever is longer, should be reported to the Sponsor or the Sponsor's designee on the Pregnancy Form within 24 hours of the Investigator's becoming aware of the event. Pregnancy occurring in female partners of male subjects from start of the study and throughout the study (including the post study drug follow-up period) or within 3 months after the final dose, whichever is longer, should be reported to the Sponsor or the Sponsor's designee within 24 hours of becoming aware of the event.

The Investigator should counsel the subject, and in the case of a male subject, the subject's partner, regarding the risks of continuing with the pregnancy and the possible effects on the fetus.

If the female partner of a male subject becomes pregnant, the Investigator should obtain informed consent from the pregnant partner prior to monitoring the pregnancy, so that information regarding the pregnancy outcome can be reported to the Sponsor.

Information regarding the pregnancy should include estimated date of conception, duration of study drug exposure (or number of days/months after treatment discontinuation) as of the estimated conception date, expected delivery date, date of last menstrual period, all concomitant medications (including recreational drug use such as alcohol, tobacco, and illicit drugs) and other maternal medical conditions.

The Investigator should make every effort to follow the subject (or female partner of a male subject) through the resolution of the pregnancy, ie, delivery or pregnancy termination. If the pregnancy results in abortion (spontaneous or induced), or premature birth, or if the infant is born with a congenital anomaly, these events are considered SAEs and should be reported as described in Section 10.2.5. The outcome of all pregnancies must be reported to the Sponsor,

even for normal births. The condition of the infant at birth should be reported, including any anomalies, and the infant should be followed until 3 months of age and any illnesses should be reported.

All information regarding the pregnancy in a female subject or female partner of a male subject and the infant should be reported on the Pregnancy Form.

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** after becoming aware of the event.

In accordance with 10.2.2.1, all applicable SAEs will be recorded on the paper Initial SAE Report Form (Section 10.2.2.2) and transmitted by emailing or faxing the report form using the contact information below within 24 hours of the investigator's knowledge of the event to the attention of the Sponsor. Any follow-up information for a previously reported SAE (including updates to the reported event term[s]) will be submitted to the Sponsor using the paper Follow-up SAE Report Form within 24 hours of the investigator's knowledge of the follow-up/updated information using the contact information below. Additionally, the SAE must be captured on the applicable CRFs.

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

The Investigator is required to provide follow-up information in response to queries from the Sponsor or 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 must be reported to the Sponsor or the Sponsor's designee by email provided in the SAE Completion Guidelines and the SAE Report Forms (initial and follow-up).

10.2.6. Investigator Notification to Local Institutional Review Boards

The investigator will receive a safety letter or a quarterly SAE line listing notifying them of relevant suspected unexpected serious adverse reactions (SUSAR) reports associated with any study drug. The Investigator must notify their local institutional review boards (IRBs)/independent ethics committees (IECs) about certain AEs including SUSARs in accordance with the policies and procedures of their IRBs/IECs and International Council for Harmonization (ICH) Good Clinical Practice (GCP) 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/IECs in accordance with all applicable regulations and guidance documents.

10.3. Pharmacokinetics Evaluations

Blood for PK serum samples will be collected from all subjects at pre-sacituzumab govitecan infusion and at EOI on Day 1 of Cycles 1, 2, 3, 7, 11, and every 6 cycles thereafter (17, 23, etc), EOT with sacituzumab govitecan, and at the 30-Day Safety Follow-up Visit. There will be an additional collection pre-dose on C1D8. The collection window for PK samples is -30 minutes for predose (prior to start of infusion), +10 minutes for postdose samples (at EOI), and ±10 minutes for all other timepoints. Serum concentration data for total antibody, total SN-38, free SN-38 and free SN-38G (metabolites of SN38) will be generated from serum samples using assays performed by the Sponsor's designee.

PK samples for subjects continuing sacituzumab govitecan treatment following implementation of PA5 will not be collected.

10.4. Immunogenicity (Anti-drug Antibodies) Evaluations

Immunogenicity will be assessed using a tiered approach (screen, confirmatory, and titer) on study samples. Confirmed positive study samples will additionally be tested for hRS7 domain specificity and neutralizing ability. Blood for immunogenicity analysis (anti-drug antibody [ADA]) will be collected from all subjects at pre-sacituzumab govitecan infusion on Day 1 of Cycles 1, 2, 3, 7, 11, and every 6 cycles thereafter (17, 23, etc), EOT with sacituzumab govitecan, and at the 30-Day Safety Follow-up Visit. Immunogenicity (ADA) will be evaluated in serum by the Sponsor's designee. All ADA samples will be collected predose with a collection window of -30 minutes prior to the start of infusion.

ADA samples for subjects continuing sacituzumab govitecan treatment following implementation of PA5 will not be collected.

10.5. UGT1A1 Genotype

UGT1A1 genotype will be evaluated from the UGT1A1 genotyping blood sample collected as specified in Table 2. This sample should be collected at the C1D1 visit. If the sample is not collected at C1D1, then it can be collected at any other visit.

UGT1A1 genotyping blood samples for subjects continuing sacituzumab govitecan treatment following implementation of PA5 will not be collected.

CCI [redacted]

CCI

[redacted]

- CCI [redacted]

[redacted]

[redacted]

[redacted]

Biomarker Samples for Optional Future Research

CCI [redacted]

[redacted]

[redacted]

CCI [redacted]

[redacted]


CCI

11. STATISTICS

Primary and secondary endpoints, populations for analysis, and statistical methods are described in this section. Additional details will be included in the statistical analysis plan (SAP).

The primary endpoint is ORR according to RECIST 1.1 by the Investigator assessment.

Secondary endpoints include ORR, DOR, CBR (defined as CR + PR + stable disease [SD] for at least 6 months), PFS according to RECIST 1.1 by BICR; DOR, CBR, and PFS according to RECIST 1.1 by the Investigator's assessment; OS; the incidence of treatment-emergent AEs and clinical laboratory abnormalities; and serum concentrations of sacituzumab govitecan over time and incidence of ADA to sacituzumab govitecan.

Summary tables and listings will be prepared using SAS®. Continuous data will be summarized using descriptive statistics: n, mean, median, standard deviation, minimum, and maximum. Categorical data will be summarized using frequency counts and percentages. Data listings will be created to support tables and figures. Any statistical analyses affected by the COVID-19 pandemic will be detailed in the SAP.

Statistical analyses will be performed using SAS® (SAS Institute, Version 9.2 or later, Cary, NC) and other software.

11.1. Determination of Sample Size

CCI

This study was originally designed to limit enrollment to subjects with elevated TROP-2 expression. In Amendment 2, the enrollment criterion for elevated TROP-2 expression was removed, and the study was expanded to include subjects with any level of TROP-2 expression. Clinical activity will be correlated with TROP-2 expression assessed retrospectively.

There were approximately 40 subjects enrolled in the NSCLC (adenocarcinoma and SCC) cohorts before the criteria of TROP-2 expression was removed in Amendment 2 of the protocol. These subjects will not be counted toward the sample size above. Data from these subjects may be analyzed together with data from subjects enrolled under or after Amendment 2.

11.2. Efficacy Endpoint Definitions and Analyses

Efficacy analyses will be performed on all subjects who received at least 1 dose of sacituzumab govitecan. For sensitivity purpose, selected efficacy endpoints including ORR, CBR, and PFS will also be analyzed based on the Response Evaluable population, which is defined as all enrolled subjects who have received at least 1 dose of sacituzumab govitecan with a baseline radiologic assessment and at least 1 on-treatment radiological assessment.

Analysis will be conducted separately for each histologic cohort. The primary endpoint, ORR, is defined as the rate of the overall best response, CR or PR, based on the Investigator-assessed tumor response using RECIST 1.1 criteria for each histologic cohort. ORR according to RECIST 1.1 by BICR will be used as a secondary endpoint. The ORR rate will be calculated with a two-sided exact 95% CI using the Clopper-Pearson method.

The secondary endpoint, CBR, is defined as CR + PR + SD for at least 6 months, according to RECIST 1.1 by the Investigator's assessment or BICR. The CBR rate will be calculated with a two-sided exact 95% CI interval using the Clopper-Pearson method.

The secondary endpoint, PFS, is defined as the time from first dose until objective tumor progression or death, whichever comes first. Subjects not experiencing PD or not having died at the time of data cutoff or the database lock will have their event times censored at the last adequate tumor assessment. Tumor progression will be based on Investigator's assessment of tumor response according to RECIST 1.1. A Kaplan-Meier analysis will be performed for the PFS data, and a 95% CI for the median PFS using the Brookmeyer-Crowley CI will be provided. If deemed necessary, PFS analyses according to RECIST 1.1 by BICR-assessed tumor response will also be produced.

The secondary endpoint, DOR, is calculated as the date of the first evaluation showing documented response, either PR or CR, to the date of the first PD or death (or date of last adequate response assessment in case objective PD is censored) according to RECIST 1.1 by the Investigator's assessment. A Kaplan-Meier analysis will be performed for the DOR data, and a 95% Brookmeyer-Crowley CI for the median DOR will be provided. If deemed necessary, DOR analyses according to RECIST 1.1 by BICR-assessed tumor response will also be produced.

The secondary endpoint OS is defined as the time from first dose to death due to all causes. Subjects not having died at the time of the data cutoff or the database lock will have their event times censored on the last date of their known alive date. A Kaplan-Meier analysis will be performed for OS, and a 95% CI for the median OS using Brookmeyer-Crowley CI will be provided.

Analyses may be performed to understand efficacy in relation to tumor biomarkers. CCI [redacted] CCI [redacted]

11.3. Safety Analyses

All subjects administered at least 1 dose of sacituzumab govitecan will be included in the evaluation of safety.

Safety will be evaluated based on AEs, standard safety laboratories (CBC with differential), serum chemistries, and urinalysis (if clinically indicated).

The total amount of study drug and number of cycles and doses received will be summarized by the histological cohort.

The frequency and severity of AEs, classified by Medical Dictionary for Regulatory Activities (MedDRA), will be summarized overall and by histological cohort using MedDRA Preferred Term (PT) and System Organ Class (SOC). An AE that occurs more than once within each subject will be counted only once in the summaries, using the worst NCI-CTCAE grade and relationship category. AEs will be consolidated using the worst NCI-CTCAE grade and relationship category observed for classification into each MedDRA SOC summary.

AEs leading to death or to discontinuation from treatment as well as all SAEs will be summarized or listed separately. A listing of all death information will be generated. The reasons for study treatment discontinuation will also be summarized for each histological cohort.

Routine safety laboratories, based on hematology and routine serum chemistry data (glucose, creatinine, BUN, total bilirubin, AST, ALT, LDH, uric acid, alkaline phosphatase, serum albumin, total protein, sodium, potassium, calcium, chloride, bicarbonate, magnesium, and phosphorus), will be summarized using values at each visit and change from baseline using descriptive statistics for each histological cohort.

Laboratory test results for platelets, neutrophils, white blood count, lymphocytes and hemoglobin will be graded according to NCI-CTCAE severity grade. The worst NCI-CTCAE grade observed on-treatment will be tabulated for each laboratory parameter and presented in a frequency table by baseline grade. For parameters for which an NCI-CTCAE scale does not exist, the proportion of subjects with abnormal values will be summarized by histological cohort.

11.4. Pharmacokinetics Analyses

Serum concentrations of sacituzumab govitecan, free SN-38, total antibody and SN-38G will be summarized over each scheduled sampling time and PK analysis will be performed using available data from all subjects. The PK parameters to be estimated and reported may include, but may not be limited to, maximum observed drug concentration (C_{max}), area under the concentration time curve ($AUC_{0\text{-}168h}$), and time (observed time point) to C_{max} (T_{max}) for subjects with adequate serum concentration data, if feasible.

Data from this study may be combined with data from other studies with sacituzumab govitecan for population PK and exposure-response analyses. If applicable, results from such analyses may be summarized in a separate report, rather than in a clinical study report. Population PK and exposure-response analyses of data from this study only may not be conducted.

11.5. Immunogenicity (Anti-Drug Antibodies) Analyses

The rate and magnitude of ADA incidence, prevalence, persistence, and transience will be characterized by descriptive statistics and summarized. Titer summaries may also be generated, if relevant. CCI [redacted]

12. ADMINISTRATIVE AND ETHICAL REQUIREMENTS

12.1. Good Clinical Practice

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

Essential clinical documents will be maintained to permit evaluation of the conduct 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.

12.2. Ethical Considerations

This study is a global study and will be conducted in North America, Europe, Asia-Pacific, and potentially other regions. Regulatory agencies require that the study be conducted in accordance with ethical principles founded in the Declaration of Helsinki. 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, and applicable local regulatory requirements and laws. In the US, ethical protection is provided by compliance with ICH GCP guidelines and 21 Code of Federal Regulations (CFR) 50 (Protection of Human Subjects).

The IRB/IEC will review all appropriate study documentation 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 as required by the IRB/IEC.

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**.**

12.3. Subject Information and 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 general practitioner/primary care physician (PCP) of the subject's participation in the study if the subject agrees to the Investigator informing their PCP.

12.4. Protocol Compliance

The Investigator will conduct the study in compliance with the protocol provided by the Sponsor or its designee and approved by the IRB/IEC and the appropriate regulatory authority. Modifications to the protocol should not be made. Changes to the protocol will require written IRB/IEC approval prior to implementation, and acceptance by the appropriate regulatory health authority, except when the modification is needed to eliminate an immediate hazard(s) to the subject. The IRB/IEC may provide, and if applicable regulatory authorities' approval, expedited review and approval for any minor change(s) in this ongoing study that has 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 any immediate hazard(s) to subjects, the Investigator will contact the Sponsor's designee, if circumstances permit, and their local IRB/IEC if required, to discuss the planned course of action. Any departures from the protocol must be fully documented as a protocol deviation within source documentation.

12.5. Site Monitoring and On-Site Audits

Monitoring and auditing procedures developed by the Sponsor or its designee will be followed, to comply with ICH GCP guidelines; the US Food and Drug Administration (FDA) guidance, the European Medicines Agency (EMA), and all applicable guidelines. Review of subject's eCRFs, Electronic Medical Records or paper source documentation for completeness, and accuracy will be required. In addition, a review of all applicable regulatory documents will be performed according to the monitoring plan. All available source documents should be obtained by the Investigator and provided to the Sponsor's designee at each monitoring visit.

The Site Monitor may also issue queries in the eCRF system to be addressed by the appropriate study site personnel in a timely manner when clarification of eCRF data is required to ensure data accuracy and completeness. The Site Monitor will ensure that the investigation is conducted according to protocol design and regulatory requirements through frequent communication.

Regulatory authorities, the IRB/IEC, and/or the Sponsor' clinical quality assurance group or designee may request access to all source documents, subject's eCRFs, and other study documentation for onsite audit or inspection. Direct access, or remote access when permissible and deemed necessary, to these documents must be guaranteed by the Investigator, who must always provide cooperation and support for these activities.

12.6. Subject Data Protection

Enterprise level technical and organizational controls have been developed at Gilead for the purpose of data protection. This includes user authentication and identification, fine grained access controls, end-to-end data encryption, security monitoring, network segregation, and physical security controls. Users of Gilead systems are provided training for security awareness and privacy.

To prepare for the possibility of a data security breach, Gilead maintains a business continuity and disaster recovery plan and conducts regular disaster recovery testing to ensure that Gilead systems are recoverable if a cyber or data security incident is experienced. Gilead's detailed incident response plan for any cyber or data security incident is based on the following 5 steps: detection, analysis, containment, eradication, and recovery.

Information collected in this clinical study is subject to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) as described in 45 CFR Part 160 and 45 CFR Part 164 (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, the Sponsor, their designee, and the IRB/IEC for each study site.

Gilead and institutions will both act in accordance with the applicable data protection law. Furthermore, the study site and Gilead will cooperate with each other to take the necessary measures in order to comply with the applicable data protection law. Both Gilead and the study site shall implement appropriate technical and organizational measures to meet the requirements of the EU General Data Protection Regulation. If either party becomes aware of a personal data breach related to data processed under this agreement, that party shall promptly notify the other party. In such a case, parties will fully cooperate with each other to remedy the personal data breach and promptly fulfill the (statutory) notification obligations. A personal data breach refers to a personal data breach as described in Article 4, Article 33, and Article 34 of the EU General Data Protection Regulation and applicable national data protection laws.

12.7. 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. Because the results of this study may eventually be used in a marketing application, compliance with this Federal statute is essential. To comply with the provisions of this regulation, the Sponsor requests that every Investigator and sub-Investigator mentioned on FDA Form 1572 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 Investigators 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 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, Investigators are asked to 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.

12.8. 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 period of time specified by the Sponsor. In the unlikely event of premature termination or discontinuation of the study, or in the event the Investigator believes a subject is continuing to receive clinical benefit, the Sponsor will discuss options with the Investigator 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.

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.

Monitoring visits to the study site will be conducted periodically during the study to ensure that GCP guidelines and all aspects of the protocol are followed. The study site may also 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. Investigators and their relevant personnel must agree to be available and participate with visits conducted at a reasonable time in a reasonable manner, and the Investigator/Institution must guarantee direct access to source documents by the Sponsor and its designee, and appropriate regulatory authorities.

Regulatory authorities worldwide may also inspect 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 inspections conducted at a reasonable time in a reasonable manner.

14. DATA HANDLING AND RECORD KEEPING

14.1. Electronic Case Report Forms (eCRFs)

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, which must be signed by the Investigator. 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. The subject's source documents are the treating 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. The identification of any data to be recorded directly on the eCRFs (ie, no prior written or electronic record of data), and to be considered to be source data will be specified in this protocol.

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 study site personnel must address all queries in a timely manner during the study and afterwards to ensure data accuracy and completeness.

14.2. Retention of Records

Records and documents pertaining to the conduct of this study, including eCRFs, source documents, consent forms, laboratory test results, and study drug inventory records must be retained by the Investigator as per local regulations. No study records shall be destroyed without prior authorization from the Sponsor. For studies conducted outside the US under an investigational new drug (IND) application, 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 2 years after approval of a Biologic License Application, or, if the Biologic License Application is not approved, until 2 years after notification by the Sponsor that the clinical investigations have been discontinued.

15. PUBLICATION POLICY

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

A clinical study report (CSR) will be prepared and provided to the regulatory agency(ies) when applicable and in accordance with local regulatory requirements. Gilead will ensure that the report meets the standards set out in the ICH Guideline for Structure and Content of Clinical Study Reports (ICH E3). Note that an abbreviated report may be prepared in certain cases. For studies with sites in countries following the EU Regulation No. 536/2014, a CSR will be submitted within 1 year (6 months for pediatric studies, in accordance with Regulation [EC] No. 1901/2006) after the global end of study (as defined in Section 4.8).

Investigators in this study may communicate, orally present, or publish study data in scientific journals or other scholarly media in accordance with the Gilead clinical trial agreement. Study results will be made publicly available (including posted to the Clinical Trials Information System and ClinicalTrials.gov) in accordance with local regulatory requirements.

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17. APPENDICES

17.1. Investigator Signature Page

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 study drugs and the study.

Principal Investigator Name (Printed)	Signature
Date	Site Number

17.2. Performance Status Criteria

ECOG Performance Status Scale	
Grade	**Descriptions**
0	Normal activity Fully active, able to carry on all pre-disease performance without restriction
1	Symptoms, but ambulatory Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (eg, light housework, office work)
2	In bed <50% of the time Ambulatory and capable of all self-care, but unable to carry out any work activities, up and about more than 50% of waking hours
3	In bed >50% of the time Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	100% bedridden Completely disabled Cannot carry on any self-care Totally confined to bed or chair
5	Dead

17.3. Cockcroft-Gault Formula

C_{Cr}={((140–age) x weight)/(72xS_{Cr})} x 0.85 (if female)

Abbreviations/Units

C_{Cr} (creatinine clearance) = mL/minute

Age = years

Weight = kg

SCr (serum creatinine) = mg/dL

References

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

17.4. Response Evaluation Criteria in Solid Tumors (RECIST) 1.1

New Response evaluation criteria in Solid tumors: Revised RECIST criteria {Eisenhauer 2009} are summarized below. Timing of assessments has been modified to fit this protocol.

Measurable/Non-Measurable Lesions: Each tumor lesion or site of disease identified at baseline is categorized as either a measurable lesion or a non-measurable lesion according to the following definitions.

Lesion Type	Qualifying Definition
Measurable	Tumor lesions: Must be accurately measured in ≥ 1 dimension (longest diameter in the plane of measurement is to be recorded) with a minimum size of: • 10 mm by CT scan (CT scan slice thickness no greater than 5 mm). • 10 mm caliper measurement by clinical exam (lesions which cannot be accurately measured with calipers should be recorded as non-measurable) • 20 mm by chest X-ray. Malignant lymph nodes: To be considered pathologically enlarged and measurable, a lymph node must be 15 mm in short axis when assessed by CT scan (CT scan slice thickness recommended to be no greater than 5 mm). At baseline and in follow-up, only the short axis will be measured and followed.
Non-Measurable	All other lesions, including small lesions (longest diameter < 10 mm or pathological lymph nodes with 10 to < 15 mm short axis) as well as truly non-measurable lesions. Lesions considered truly non-measurable include leptomeningeal disease, ascites, pleural, or pericardial effusion, inflammatory breast disease, lymphangitic involvement of skin or lung, and abdominal masses/abdominal organomegaly identified by physical exam that is not measurable by reproducible imaging techniques.

Special considerations regarding lesion measurability:

Bone lesions, cystic lesions, and lesions previously treated with local therapy require particular comment.

Bone lesions:

- Bone scan, positron emission tomography (PET) scan, or plain films are not considered adequate imaging techniques to measure bone lesions. However, these techniques can be used to confirm the presence or disappearance of bone lesions.

- Lytic bone lesions or mixed lytic-blastic lesions, with identifiable soft tissue components, that can be evaluated by cross-sectional imaging techniques such as CT or MRI scan can be considered as measurable lesions if the soft tissue component meets the definition of measurability described above.

Blastic bone lesions are non-measurable. Cystic lesions:

- Lesions that meet the criteria for radiographically defined simple cysts should not be considered as malignant lesions (neither measurable nor non-measurable) because they are, by definition, simple cysts.

- 'Cystic lesions' thought to represent cystic metastases can be considered as measurable lesions, if they meet the definition of measurability described above. However, if non-cystic lesions are present in the same subject, these are preferred for selection as target lesions.

Lesions with prior local treatment: Tumor lesions situated in a previously irradiated area, or in an area subjected to other loco-regional therapy, are usually not considered measurable unless there has been demonstrated progression in the lesion. All measurements should be recorded in metric notation, using calipers if clinically assessed. All baseline evaluations should be performed after the subject has provided written informed consent and as close as possible to the treatment start.

Target Lesions: Target lesions are selected from measurable lesions at baseline based on their size and suitability for accurate repeated measurements by imaging techniques or clinical judgment. The sum of the longest diameter (LD) for all target lesions provides a quantitative means of characterizing objective tumor response to treatment as follows:

Evaluation Criteria Used for Categorizing Treatment Response of Target Lesions

Response Category	Definition
Complete Response (CR)	Disappearance of all target lesions
Partial Response (PR)	> 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD
Progressive Disease (PD)	> 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of ≥ 5 mm. (**Note:** The appearance of ≥ 1 new lesions is also considered progression)
Stable Disease (SD)	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started

Non-Target Lesions: Non-target lesions are other lesions (or sites of disease) not identified as target lesions at baseline. These include both non-measurable lesions as well as measurable lesions exceeding the maximum number allowed per organ or in total. The response of non-target lesions to treatment is evaluated based on their presence or absence as follows:

Evaluation Criteria Used for Categorizing Treatment Response of Non-Target Lesions	
Response Category	**Definition**
Complete Response (CR)	Disappearance of all non-target lesions and normalization of tumor marker levels initially above upper limits of normal
Progressive Disease (PD)	Appearance of ≥ 1 new lesions and/or unequivocal progression of existing non-target lesions
Stable Disease (SD)	Persistence of ≥ 1 non-target lesion(s) or/and maintenance of tumor marker level above the normal limits

New Lesions: New lesions not present at baseline should be recorded at time of occurrence.

Overall Response: The overall response is the best response recorded from the start of the treatment until disease progression or recurrence (taking as reference for progressive disease the smallest measurements recorded since the treatment started). To be assigned a status of PR or CR, changes in tumor measurements must be confirmed by repeat assessments 4 to 6 weeks after initial documentation. In the case of SD, follow-up measurements must have met the SD criteria at least once with a minimum interval of at least 6 to 8 weeks from enrollment.

Target Lesions	Non-target Lesions	New Lesions	Overall Response
CR	CR	No	CR*
CR	Incomplete response/SD	No	PR
PR	Non-PD	No	PR
SD	Non-PD	No	SD
PD	Any	Yes or No	PD**
Any	PD	Yes or No	PD**
Any	Any	Yes	PD**

CR = complete response; PD = progressive disease; PR = partial response; SD = stable disease.
*When evaluation of possible CR depends on distinguishing residual disease from normal tissue, fine needle aspirate/biopsy is recommended before confirming the complete response status.
**Subjects without objective evidence of disease progression, but with globally deteriorated health status requiring discontinuation of treatment should be classified as having "symptomatic deterioration" at that time, with every effort made to document the objective progression, even after discontinuation of treatment.

Duration of Response: The duration of overall response is measured from the time measurement criteria are met for CR or PR (whichever is first recorded) until the first date that recurrent or progressive disease is objectively documented (taking as reference for progressive disease the smallest measurements recorded since the treatment started). Stable disease is measured from the start of the treatment until the criteria for progression are met, taking as reference the smallest measurements recorded since the treatment started.

17.5. Pregnancy Precautions, Definitions of Childbearing Potential, and Contraceptive Requirements

1) Definitions

a. Definition of Childbearing Potential

For the purposes of this study, a patient assigned female at birth 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.

Patients 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, patients younger than 54 years with amenorrhea of at least 12 months also may be considered postmenopausal if their follicle-stimulating hormone 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 patient of any age.

b. Definition of Fertility in a Participant Assigned Male at Birth

For the purposes of this study, a patient assigned male at birth is considered fertile after the initiation of puberty unless the patient is permanently sterile by bilateral orchidectomy or medical documentation.

2) Contraception Requirements for Patients Assigned Female at Birth and of Childbearing Potential

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. Subjects must have a negative serum pregnancy test during screening and a negative urine pregnancy test is required at baseline prior to study treatment administration on Cycle 1 Day 1 (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 last cycle

and every 28 days after the last dose of study drug until the end of contraception requirement. If a urine 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. True 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 17.6 for a list of UGT1A1 inducers and Section 7.6.)
    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 Patients Assigned Male at Birth

It is theoretically possible that a relevant systemic concentration of study drug may be achieved in a female partner from exposure of the male patient's seminal fluid and poses a potential risk to an embryo/fetus. Therefore, male patients with female partners of childbearing potential must use condoms during treatment and until 3 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 patients must also refrain from sperm donation, and/or cryopreservation of germ cells during treatment and until the end of contraception requirement. Male patients 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), declaration of abstinence for the duration of exposure to investigational medicinal product, 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

Patients assigned female at birth 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. Study drug must be discontinued immediately upon consultation with the medical monitor.

Patients assigned female at birth 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 study drug dose, 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.

17.6. UGT1A1 Inhibitors and Inducers

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

UGT1A1 = uridine diphosphate glucuronosyltransferase 1A1

17.7. Disaster and Public Health Emergency Risk Assessment and Mitigation Plan

During an ongoing disaster or public health emergency (hereafter referred to as an event), 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 procedures.

   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 adverse events (AEs)/serious adverse events (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.

      iii) If applicable, confirm electronic diary questionnaires and patient-reported outcomes have been completed and transmitted.

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 event 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 coronavirus disease 2019 (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 event 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 event will be documented as a protocol deviation.

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:

   a) 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 an event 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 event 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 drugs.

   Mitigation plan: There is not substantial 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.

17.8. Marketing Authorization Status of Study Interventions

Study Intervention Name	Category	Authorized in ≥ 1 Country Following EU Regulation No. 536/2014	Authorized in ≥ 1 ICH Country
Sacituzumab govitecan	Study drug	No[a]	No[a]
Hydrocortisone	AxMP	Yes	Yes
Palonosetron	AxMP	Yes	Yes
Fosaprepitant	AxMP	Yes	Yes
Aprepitant	AxMP	Yes	Yes
Dexamethasone	AxMP	Yes	Yes
Olanzapine	AxMP	Yes	Yes
Loperamide	AxMP	Yes	Yes
Diphenoxylate	AxMP	Yes	Yes
Atropine	AxMP	Yes	Yes
Opium tincture	AxMP	Yes	Yes
Octreotide	AxMP	Yes	Yes
G-CSF	AxMP	Yes	Yes

AxMP = auxiliary medicinal product; EU = European Union, ICH = International Council for Harmonisation; G-CSF = granulocyte colony-stimulating factor; Requirements for Pharmaceuticals for Human Use
a. Rationale described in Section 1.1.4

17.9. Risk Factors for Febrile Neutropenia

Subjects should be evaluated for risk factors of febrile neutropenia according to local guidelines or American Society of Clinical Oncology (ASCO)/European Society for Medical Oncology (ESMO)/National Comprehensive Cancer Network (NCCN) guidelines. Risk factors per ASCO guidelines are provided as an example below.

Patient Risk Factors for Febrile Neutropenia
Age > 65 years
Advanced disease
Previous chemotherapy or radiation therapy
Preexisting neutropenia or bone marrow involvement with tumor
Infection
Open wounds or recent surgery
Poor performance status or nutritional status
Poor renal function
Liver dysfunction, most notably elevated bilirubin
Cardiovascular disease
Multiple comorbid conditions
HIV infection

HIV = human immunodeficiency virus; ASCO = American Society of Clinical Oncology
Source: Patient characteristics associated with high risk for febrile neutropenia per ASCO guidelines {Smith 2015}

17.10. Country-Specific Requirements

Not applicable.

17.11. Amendment History

High-level summaries of the history of this study's amendments are provided in tabular form in the subsections below (from most recent amendment to oldest). Minor changes such as the correction of typographic errors, grammar, or formatting are not detailed.

Separate summary of change documents for earlier amendments are available upon request.

A separate tracked change (red-lined) document comparing the previous version of the protocol to this amendment will be made available upon the publication of this protocol.

17.11.1. Amendment 5 (17 December 2024)

Rationale for Key Changes Included in Amendment 5	Affected Sections
Updated European Union Clinical Trial (EU CT) number to comply with EU-Clinical Trials Regulation (CTR) requirements.	Title page
Updated to add information on study modifications after implementation of Protocol Amendment 5 (PA5). The modifications reduce the schedule of assessments for subjects remaining on treatment and terminate survival follow-up for subjects who have previously discontinued treatment.	Synopsis, Sections 3, 4, 5, and 10.1.4
Information on survival follow-up for subjects was updated with procedures following implementation of PA5.	Synopsis and Section 4.7
Information on end of study for subjects was updated with procedures following implementation of PA5.	Synopsis and Section 4.8
Updated text to align with the approval status of sacituzumab govitecan (SG) in the United States.	Sections 1.1.3 and 1.1.4
Updated safety recommendations for subjects who are at risk for complications from neutropenia.	Sections 1.1.3.3, 1.2.2, 7.5.1, 7.5.2.3, and Appendix 17.9
Updated to expand pandemic risk and mitigation plan to disasters and public health emergencies to align with recent regulatory guidance.	Section 1.2.2 and Appendix 17.7
Added text to clarify that pharmacokinetic (PK), anti-drug antibody (ADA), biomarker samples, and uridine diphosphate-glucuronosyltransferase 1A1 (UGT1A1) genotyping will not be collected following implementation of PA5. Added information for scans, tumour response data, and disease following implementation of PA5.	Sections 4.3, 10.3, 10.4, 10.5, and 10.6
Table summarizing recommendations for SG dose reductions and discontinuations for treatment-related toxicities was added.	Section 7.5.2.5
Updated text to clarify that while tumor response data will no longer be collected after implementation of PA5, subjects who continue treatment will be expected to have scans performed per standard of care.	Sections 5 and 9
Text updated to align with adverse event and suspected unexpected serious adverse reaction (SUSAR) reporting requirements and procedures.	Sections 10.2.2.2, 10.2.5, and 10.2.6
Added text to clarify that enterprise level technical and organizational controls have been developed at Gilead Sciences for the purpose of data protection.	Section 12.6

Rationale for Key Changes Included in Amendment 5	Affected Sections
Updated text to clarify that a clinical study report (CSR) will be prepared and provided to the regulatory agency(ies) and study results will be made publicly available when applicable and in accordance with local regulatory requirements.	Section 15
Minor clarifications and changes to correct typographic errors.	Throughout, as needed

17.11.2. Amendment 4 (09 October 2023)

Rationale for Key Changes Included in Amendment 4	Affected Sections
A statement to clarify that the hematology and serum chemistry **tests** may be performed and reviewed up to 24 hours prior to scheduled study treatment administration was added	Section 4.3, Section 5 (Table 2: footnotes 'j' and 'l')
Text was updated to align with SG content library	Section 8.5
Changes from administrative amendment 3.0.1 were added to the protocol	Sections 4.6 and 7.5.2.5
Changes from administrative amendment 3.0.2 were added to the protocol	Sections 4.3, 5, (Table 2: footnote 't'), 8.3, 8.4, and 10.2.2.1
A separate page for the Sponsor Signature Page was added to the appendices to align with Clinical Trials Information System (CTIS) requirements for a consolidated and harmonized protocol	Appendix 17.11
A separate page for Amendment History and Country-Specific Requirement was added to align with EU CTR requirement	Appendix 17.9 and 17.10
A separate page for Marketing Authorization Status of Study Interventions was added to align with EU CTR requirement	Appendix 17.8
Minor changes to correct typographic errors	Throughout, as needed

17.12. Sponsor Signature Page

GILEAD SCIENCES, INC.
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STUDY ACKNOWLEDGMENT

A Phase 2 Open-Label Study of Sacituzumab Govitecan (IMMU-132) in Subjects with Metastatic Solid Tumors IMMU-132-11, Protocol Amendment 5, 17 December 2024

This protocol has been approved by Gilead Sciences, Inc. The following signature documents this approval.

PPD	*[See appended electronic signature]*
Name (Printed) Associate Director, Clinical Development	Signature
[See appended electronic signature]	
Date	

Prot_IMMU-132-11_amd-5

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Clinical Development eSigned	18-Dec-2024 16:21:00