PRIVILEGED COMMUNICATION
FOR INVESTIGATIONAL USE ONLY

SWOG CANCER RESEARCH NETWORK

TITLE *insert title*
(for CTEP IND studies include NSC# of investigational agent)

(include if relevant) **This trial is part of the National Clinical Trials Network (NCTN) program, which is sponsored by the National Cancer Institute (NCI). The trial will be led by SWOG with the participation of the network of NCTN organizations: Alliance for Clinical Trials in Oncology; ECOG-ACRIN Medical Group; and NRG.**

(include if relevant) **This is a potential FDA Registration Trial. Additional site requirements include:**

- **maintenance of a Trial Master File (https://www.swog.org/sites/default/files/docs.2017-10/Guidance on FDA.Inspection.pdf)**
- **completion of a protocol specific Delegation of Task Log (DTL) (see Section 13)**
- **additional monitoring (see Appendix 18.x)**

NCT#TBD *(insert once available on ct.gov)*

(include if relevant) **This study is being conducted under CTEP/SWOG IND XXXXX**

STUDY CHAIRS:
Name *(Discipline)*
Institution
Address
Address
Phone:
FAX:
E-mail:

AGENTS:
Commercially Available Agents:
NCI Supplied Investigational Agents:
SWOG-Held IND Agents:
Company-Held IND Agents:

Insert as necessary
NCI Supplied IDE Devices:
OR SWOG-Held IDE Devices:
OR Company-Held IDE Devices:

BIOSTATISTICIANS:

NCTN-Group **CHAMPION:**

List study chairs and indicate which is the primary one. There may be one Study Chair per discipline, with one being appointed Study Chair (i.e., one medical oncologist, one pathologist [if study includes path review], one radiation oncologist [if study includes treatment with radiation], etc.). Persons performing correlative studies may also be listed. When deemed necessary, a Study Co-Chair may be appointed whose discipline may overlap any already listed.

List biostatisticians and indicate which is the primary one.

List any Study Champions from participating NCTN groups that have assigned them.

List drugs in appropriate category

Note that section numbers/letters throughout this document will automatically renumber/letter once the correct version of each standard has been chosen.

PARTICIPANTS

U.S.-Only Participants:

[list NCTN groups as appropriate]

ALLIANCE/Alliance for Clinical Trials in Oncology
ECOG-ACRIN/ECOG-ACRIN Cancer Research Group
NRG/NRG Oncology
SWOG/SWOG Cancer Research Network
COG / Children's Oncology Group *(required for studies with participants < 18)*

[if there are other non-NCTN groups/sites list as follows]

GROUP ACRONYM/CTEP Organization ID
e.g. **BMTCTN** / Bone and Marrow Transplant Clinical Trials Network

[if there are limited institutions where sites are affiliated with more than one Group, list as follows]

CTEP ID/Site Name/Affiliated Group
e.g. **CA016**/Cedars-Sinai Medical Center/Alliance, ECOG-ACRIN

[if there are limited institutions where sites are all affiliated with only one institution, list as follows]

SWOG:
CTEP ID/Site Name

ALLIANCE:
CTEP ID/Site Name

Etc.

International Participants: ***[include from above/below as appropriate]***

CCTG / Canadian Cancer Trials Group

SWOG:
48007 / Instituto Nacional de Cancerologia, Mexico City, Mexico
15002 / Instituto Nacional de Cancerologia, Bogota, Columbia
55004 / Instituto Nacional de Enfermedades Neoplasicas, Lima Peru
43006 / National Cancer Center, Seoul, Korea
95002 / King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia
11081 / British Columbia Cancer Agency, Vancouver, British Columbia
ALLIANCE:
[insert any international ALLIANCE sites]

Etc.

TABLE SHOULD BE INCLUDED ON PG 1, IF IT FITS

*****For international participation in CTEP studies, remember the CTEP Request for International Participation in CTEP Studies Form.***

TABLE OF CONTENTS

PROTOCOL CONTACT INFORMATION

Note to PC: PCs may consider limiting the title page to the Study Chair names and adding the detailed contact information on this page.

Participant Advocate	
Eligibility, RAVE, Data Submission:	SWOG Statistics and Data Management Center E-mail: XXXXquestion@crab.org *(insert correct email address)* or Phone: 206/652-2267
Regulatory, Protocol, Informed Consent:	SWOG Operations Office E-mail: protocols@swog.org or Phone: 210/614-8808
Medical Queries (treatment or toxicity related questions):	Email: *(insert Study Chair contact information)* or call: Dr. XXX at Phone: *XXX/XXX-XXXX*
QOL/PRO questions: *(if applicable)*	Email: *(insert Study Chair contact information)* or call: Dr. XXX at Phone: *XXX/XXX-XXXX*
Investigational Drug questions: Requests for Investigator's Brochures: Access issues for the PMB Online Agent Ordering Processing (OAOP) application:	See Protocol Section 3.0 or PMBAfterHours@mail.nih.gov See Protocol Section 3.0 or http://ctep.cancer.gov/branches/pmb/agent_order_processing.htm IBCoordinator@mail.nih.gov
Specimen Tracking System (STS) Amendments, Errors, Connectivity Issues and Technical issues with the SWOG CRA Workbench:	technicalquestion@crab.org
Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM)	To review CTEP-IAM account (new requests, reset passwords): https://ctepcore.nci.nih.gov/iam/index.jsp
Access to iMedidata Rave or Delegation of Task Log (DTL)	See Protocol Section 14.X or contact CTSU Help Desk: Phone: 1-888-823-5923 or Email: ctsucontact@westat.com
Questions related to: Oncology Participant Enrollment Network (OPEN)	See Protocol Section 13.3 or contact CTSU Help Desk: Phone: 1-888-823-5923 or Email: ctsucontact@westat.com
TRIAD installations:	https://triadinstall.acr.org/triadclient/ Questions: TRIAD-Support@acr.org
Participant Transfers:	patienttransfer@crab.org
Serious Adverse Event Reporting questions:	See Protocol Section 8.5 Email: adr@swog.org

Source Documentation Portal – Central Monitoring	centralmonitorquestion@crab.org

CANCER TRIALS SUPPORT UNIT (CTSU) ADDRESS AND CONTACT INFORMATION

CONTACT INFORMATION		
For regulatory requirements:	**For participant enrollments:**	**For study data submission:**
Regulatory documentation must be submitted to the CTSU via the Regulatory Submission Portal. (Sign in at www.ctsu.org, and select the Regulatory > Regulatory Submission.) Institutions with participants waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 1-866-651-2878 to receive further instruction and support. Contact the CTSU Regulatory Help Desk at 1-866-651-2878 for regulatory assistance.	*If study is in OPEN for direct site use:* Refer to the participant enrollment section of the protocol for instructions on using the Oncology Participant Enrollment Network (OPEN). OPEN can be accessed at https://www.ctsu.org/OPEN_SYSTEM/ or https://OPEN.ctsu.org. Contact the CTSU Help Desk with any OPEN-related questions at ctsucontact@westat.com. *If the study is not in OPEN:* Refer to the participant enrollment section of the protocol for detailed instructions.	*If study is in Rave:* Data collection for this study will be done exclusively through Medidata Rave. Refer to the data submission section of the protocol for further instructions. **OR** *if study is not in Rave: Insert lead Group's mail address, phone, fax, and email address (include preferred method of submission, e.g. hard copy, email, fax#). Then add the following text:* Do not submit study data or forms to CTSU Data Operations. Do not copy the CTSU on data submissions. Other Tools and Reports: Institutions participating through the CTSU continue to have access to other tools and reports available on the SWOG CRA Workbench via the SWOG website (www.swog.org).
The most current version of the **study protocol and all supporting documents** must be downloaded from the protocol-specific Web page of the CTSU Member Web site located at https://www.ctsu.org. Access to the CTSU members' website is managed through the Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM) registration system and requires user log on with CTEP-IAM username and password. *Include this statement if applicable:* Permission to view and download this protocol and its supporting documents is restricted and is based on person and site roster assignment housed in the CTSU RSS. *Include this statement and list of item(s) here and in relevant section of the protocol if applicable:* Note: Non-lead group institutions will order the following supplies from the CTSU Operations Office: *<include list of item(s)>*. Supplies can be ordered by downloading and completing the CTSU Supply Request Form (available on the protocol-specific page on the CTSU website) and submitting it as specified on the form.		
For participant eligibility or data submission questions contact the SWOG Statistics and Data Management Center (SDMC) by phone or email: 206/652-2267 XXXXquestion@crab.org *(insert correct email address)* **For treatment or toxicity related questions** contact the Study Chair by phone or email: *(insert contact information)*		
For non-clinical questions (i.e. unrelated to participant eligibility, treatment, or clinical data submission) contact the CTSU Help Desk by phone or e-mail: CTSU General Information Line – 1-888-823-5923, or ctsucontact@westat.com. All calls and correspondence will be triaged to the appropriate CTSU representative.		
The CTSU Website is located at https://www.ctsu.org.		

SCHEMA

Schemas are necessary for all randomized trials and complicated single arm. Schemas should be a concise summary of the treatment plan. These should not include treatment details, such as dose (unless dose is the defining difference between treatment arms).

1.0 OBJECTIVES

1.1 Primary Objective(s) ***(insert from Capsule Summary / TM Proposal / etc)***

a. Insert primary objective(s)

b. Second primary

c. Etc.

1.2 Secondary Objective(s)

a. Insert secondary objective(s)

b. Etc.

c. Etc.

1.3 Additional Objective(s)

a. Insert additional objective(s)

b. Etc.

c. Etc.

Please include as needed

1.4 Translational Medicine Objectives

1.5 QOL Objectives

1.6 Imaging Objectives

1.7 Economic Objectives

1.8 PRO-CTCAE Objective

To compare participant-reported symptoms using selected PRO-CTCAE items between arms

1.9 Banking Objectives

a. To bank specimens for future correlative studies.

b. To bank PET-CT images for future correlative studies.

2.0 BACKGROUND

2.1 Background / Rationale

Break up the background section into second level sub-sections and title each accordingly

The background generally should be about 2 pages for Phase IIs and about 3 pages for Phase IIIs. Each aspect of protocol treatment should be addressed and justified. If previous experience with an agent or approach has been unpromising or non-existent for the proposed disease site, a convincing justification for proceeding should be given. Truncated

rationale for laboratory/imaging/QOL should be included, but detailed laboratory/imaging/QOL methods should be placed at the end of the protocol in an appendix instead. If necessary, include rationale for exclusion of HIV/Hep+ participants or other specific participant population.

Use endnotes for references throughout (1)

Enter estimates, whole numbers only (percentages, fractions, or decimals are not acceptable).

2.2 Inclusion of Women and Minorities and Planned Enrollment Report

This study was designed to include women and minorities, but was not designed to measure differences of intervention effects. The anticipated accrual in the ethnicity/race and sex categories is shown in the table below.

DOMESTIC PLANNED ENROLLMENT REPORT					
Racial Categories	**Ethnic Categories**				**Total**
	Not Hispanic or Latino		**Hispanic or Latino**		
	Female	**Male**	**Female**	**Male**	
American Indian/ Alaska Native					
Asian					
Native Hawaiian or Other Pacific Islander					
Black or African American					
White					
More Than One Race					
Total					

INTERNATIONAL (including Canadian participants) PLANNED ENROLLMENT REPORT					
Racial Categories	**Ethnic Categories**				**Total**
	Not Hispanic or Latino		**Hispanic or Latino**		
	Female	**Male**	**Female**	**Male**	
American Indian/ Alaska Native					
Asian					
Native Hawaiian or Other Pacific Islander					
Black or African American					
White					
More Than One Race					
Total					

3.0 DRUG INFORMATION

Investigator Brochures ***(choose from the following)***

For information regarding Investigator Brochures, please refer to SWOG Policy 15.

For this study, *(drug name[s] OR all drugs)* are commercially available; therefore, Investigator Brochures are not applicable to this/these drug/s. Information about commercial drugs is publicly available in the prescribing information and other resources.

For this study, *(drug name[s])* is/are investigational and is/are being provided under an IND held by the National Cancer Institute (NCI). The current version/s of the Investigator Brochure/s for the agent/s will be accessible to site investigators and research staff through the PMB Online Agent Ordering Processing (OAOP) application: (http://ctep.cancer.gov/branches/pmb/agent_order_processing.htm). Access to OAOP requires the establishment of a CTEP Identity and Access Management (IAM) account and the maintenance of an "active" account status and a "current" password. Questions about IB access may be directed to the PMB IB coordinator via e-mail (IBCoordinator@mail.nih.gov).

For this study, *(drug name[s])* is/are investigational and is/are being provided under an IND held by SWOG. For INDs filed by SWOG, the protocol serves as the Investigator Brochure for the performance of the protocol. In such instances submission of the protocol to the IRB should suffice for providing the IRB with information about the drug. However, in cases where the IRB insists on having the official Investigator's Brochure from the company, further information may be requested by contacting the SWOG Operations Office at 210/614-8808.

For studies with specific IND exemption:

IND Exemption

(Drug name[s]/placebo) is/are IND exempt as used in this trial. This exemption has been determined by attestation that neither the investigator nor sponsor intend to seek a new indication for use or to support any other significant change in the labeling or product advertising for *(drug name[s])*. This investigation will use an approved route of administration and dosage of *(drug name[s]* and has no factors that increase the risk of the product. This investigation will be in compliance with 21CFR parts 56, 50, and 312.7 and neither the investigator nor the sponsor will promote or represent that *(drug name[s]* is/are safe or effective for the context that is under investigation in this study. This investigation will not commercially distribute or test market the study agent and will not unnecessarily prolong an investigation.

3.1 Enter drug info here

a. Sub-info

Standard drug sections will be inserted by the Operations Office.
****PC considerations for SWOG held INDs: Is company distributing? If not, who will (do we want to get third party or do they want to subcontract directly)? Who do sites ask questions? How to order? Temperature excursion or other special shipping information? Labeling? Review to see if there's extra info for the consent (e.g., avoid grapefruit). Is drug only supplied for 12 months or will we supply until progression?***

For studies with multiple PMB-supplied agents, the last section of 3.0 will appear as below, and this section will be referenced from the drug supply and accountability subsection of each drug. This information will appear as the last subsection of the drug information subsection for studies with only one PMB-supplied agent.

3.2 NCI-Supplied Agent Ordering and Agent Accountability

NCI-supplied agents may be requested by eligible participating Investigators (or their authorized designee) at each participating institution. The CTEP assigned protocol number (**SXXXX**) must be used for ordering all CTEP supplied investigational agents. The eligible participating investigators at each participating institution must be registered with CTEP, DCTD through an annual submission of FDA Form 1572 (Statement of Investigator), NCI Biosketch, Agent Shipment Form, and Financial Disclosure Form (FDF). If there are several participating investigators at one institution, CTEP-supplied investigational agents for the study should be ordered under the name of one lead participating investigator at that institution.

Order Processing (OAOP) application. Access to OAOP requires the establishment of a CTEP Identity and Access Management (IAM) account and the maintenance of an "active" account status, a "current" password, and active person registration status. For questions about drug orders, transfers, returns, or accountability, call or email PMB any time. Refer to the PMB's website for specific policies and guidelines related to agent management.

Agent Inventory Records – The investigator, or a responsible party designated by the investigator, must maintain a careful record of the receipt, dispensing and final disposition of all agents received from PMB using the appropriate NCI Investigational Agent (Drug) Accountability Record (DARF) available on the CTEP forms page. Store and maintain separate NCI Investigational Agent Accountability Records for each agent, strength, formulation and ordering investigator in this protocol.

Useful Links and Contacts

- CTEP Forms, Templates, Documents: http://ctep.cancer.gov/forms/
- NCI CTEP Investigator Registration (RCR) Help Desk: RCRHelpDes@nih.gov
- PMB policies and guidelines: http://ctep.cancer.gov/branches/pmb/agent_management.htm
- PMB Online Agent Order Processing (OAOP) application: https://eapps-ctep.nci.nih.gov/OAOP/pages/login.jspx
- CTEP Identity and Access Management (IAM) account: https://ctepcore.nci.nih.gov/iam/index.jsp
- CTEP IAM account help: ctepreghelp@ctep.nci.nih.gov
- PMB IB Coordinator: IBCoordinator@mail.nih.gov
- PMB e-mail: PMBAfterHours@mail.nih.gov

PMB phone and hours of service: 240/276-6575 Monday through Friday between 8:30 am and 4:30 pm (ET)

Drug Information Section under Supplier: ***(for each drug)***

for CTEP-supplied drugs:

Supplier: DRUG is an investigational agent supplied to investigators by the Division of Cancer Treatment and Diagnosis (DCTD), NCI. NCI-supplied agents may be requested by the Principal Investigator (or their authorized designees) at each participating institution. Pharmaceutical Management Branch (PMB) policy requires that the agent be shipped directly to the institution where the participant is to be treated. PMB does not permit the transfer of agents between institutions (unless prior approval from PMB is obtained). The CTEP assigned protocol number must be used for ordering all CTEP supplied investigational agents. The responsible investigator at each participating institution must be registered with CTEP, DCTD through an annual submission of FDA form 1572 and a CV. If there are several participating investigators at one institution, CTEP supplied investigational agents for the study should be ordered under the name of one lead investigator at that institution. Active CTEP-registered investigators and investigator-designated shipping designees and ordering designees can submit agent requests through

the PMB Online Agent Order Processing (OAOP) application https://eapps-ctep.nci.nih.gov/OAOP/. Access to OAOP requires the establishment of a CTEP Identity and Access Management (IAM) account https://eapps-ctep.nci.nih.gov/iam/ and the maintenance of an "active" account status and a "current" password. For questions about drug orders, transfers returns or accountability, call 240/276-6575 Monday through Friday between 8:30 am and 4:30 pm (ET) or e-mail PMBAfterHours@mail.nih.gov any time.

for commercial drugs:

DRUG is commercially available and should therefore be purchased by a third party. This drug will not be supplied by the NCI."

Drug Accountability: ***Choose from the following. If none seem to be quite applicable, update per discussions with company (or other applicable entity) and then let Dana and Elaine review and approve.***

Non-Blinded Supplied by Industry

Drug Returns: Unused drug supplies must NOT be returned. Unused drug must be disposed of per local institutional guidelines.

OR

Drug Returns: All unused drug supplies must be returned to <company> for destruction. Returned drug must be sent with the <company> Return Drug for Destruction Form, which can be found on the SWOG protocol abstract page (swog.org).

Drug Accountability: The investigator, or a responsible party designated by the investigator, must maintain a careful record of the receipt, disposition, and return or disposal of all drugs received from the supplier using the NCI Drug Accountability Record Form (DARF) available at http://ctep.cancer.gov. Some drug suppliers will identify their drug shipments as participant-specific; however, there is no requirement to maintain participant-specific DARFs for non-blinded drug and drug may be dispensed to any participant on this study without receiving prior approval.

Questions about drug orders, transfers, returns, or accountability should be addressed to <company contact>.

Non-Blinded Supplied by PMB

Drug Returns: All unused drug supplies must be returned to the PMB. When it is necessary to return study drug (e.g., sealed vials remaining when expired vials are recalled by the PMB), investigators should return the study drug to the PMB using the NCI Return Agent Form available on the NCI home page (http://ctep.cancer.gov).

Drug Accountability: The investigator, or a responsible party designated by the investigator, must maintain a careful record of the receipt, disposition, and return of all drugs received from the PMB using the Drug Accountability Record Form available on the NCI home page (http://ctep.cancer.gov).

Questions about drug orders, transfers, returns or accountability should be addressed to the PMB by calling 240/276-6575 Monday through Friday between 8:30 am and 4:30 pm Eastern Time.

Blinded drug supplied by DCTD

Commented [RCJ1]: This seems inconsistent with the two categories below. Should this be DCTD instead of PMB? The following three categories just don't seem quite consistent.

Drug Transfers: Bottles **MAY NOT** be transferred from one participant to another participant or from one protocol to another protocol. All other transfers (e.g., a participant moves from one participating institution to another participating institution) must be approved in advance by the PMB. To obtain an approval for transfer, investigators should complete and submit to the PMB (fax number 240/276-6575) a Transfer Investigational Agent Form available on the CTEP home page (http://ctep.cancer.gov). The participant ID number and the participant initials must be entered in the "Received on NCI Protocol No." and the "Transferred to NCI Protocol No." fields in addition to the protocol number.

Drug Returns: Only undispensed clinical supplies should be returned to the PMB. When it is necessary to return study drug (e.g., sealed bottles remaining when a participant permanently discontinues protocol treatment, expired bottles recalled by the PMB), investigators must return the study drug to the PMB using the NCI Return Agent Form available on the CTEP home page (http://ctep.cancer.gov). The participant ID number and the participant initials should be entered in the "Lot Number" field. A separate line item is required for each participant ID number being returned. Dispensed bottles with remaining tablets should be documented in the participant-specific NCI Investigational Agent Accountability Record (i.e., logged is as “returned by participant” and logged out as “destroyed on site”) and destroyed on site in accordance with institutional policy.

Drug Accountability: The investigator, or a responsible party designated by the investigator, must maintain a careful record of the receipt, disposition, and return of all drugs received from the PMB using the NCI Investigational Agent Accountability Record available on the CTEP home page (http://ctep.cancer.gov). A separate NCI Investigational Agent Accountability Record must be maintained for each participant ID number on this protocol.

Questions about drug orders, transfers, returns or accountability should be addressed to the PMB by calling 240/276-6575 Monday through Friday between 8:30 am and 4:30 pm Eastern Time.

Blinded drug NOT supplied by DCTD

Drug transfer: Bottles **MAY NOT** be transferred from one participant to another participant or from one protocol to another protocol. All other transfers (e.g., a participant moves from one participating institution to another participating institution) must be approved **in advance** by calling <company>.

Drug Returns**:** All unused drug (unopened and unused vials remaining when a subject goes off protocol treatment, and expired vials) must be destroyed on-site in accordance with institutional policy. Opened bottles with remaining tablets should be documented in the participant-specific accountability record (i.e., logged in as "# of tablets returned") and destroyed on-site in accordance with institutional policy.

Drug accountability**:** The investigator, or a responsible party designated by the investigator, must maintain a careful record of the receipt, dispensing, and return of all study drugs received from the distributor using the **SWOG** <protocol> **Drug Accountability Record Form,** available at www.swog.org. A separate record must be maintained for each participant on this protocol.

Questions about drug orders, transfers, returns or accountability should be addressed to <company>.

4.0 STAGING CRITERIA

4.1 Diagnostic Criteria

4.2 Staging Criteria

Standard diagnostic/staging criteria will be inserted by the Operations Office.
< S:\AJCC Staging Manual>

Refer to recent similar disease site study(ies) but be sure that all relevant staging/diagnostic info is included and anything irrelevant is removed.

Pay attention to what is not needed and can be removed for eligibility determination. No need to keep any extra staging criteria here if not relevant towards eligibility determination, unless something is needed for determining stratification, etc.

SC and Stats/DCs must approve. If no diagnostic/staging criteria are to be used, remove 4.1 and 4.2 and use statement:

Staging criteria are not applicable to this study.

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a participant to be considered eligible for registration in OPEN. Section 5 may be printed and used to by the site, but is not to be uploaded in RAVE (unless specially stated).For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the SWOG SDMC in Seattle at 206/652-2267 or XXXXquestion@crab.org prior to registration. ***(insert disease site)*** **NCI policy does not allow for waiver of any eligibility criterion (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm).**

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient participant scheduling without exceeding the guidelines. **If Day X or XX falls on a weekend or holiday, the limit may be extended to the next working day.** ***(This is the only place "working day" is relevant)***

Insert eligibility criteria to define the participant population, acceptable disease and performance status, and prior and concurrent therapy. There should be a sound scientific basis for every requirement. Indicate whether measurable disease is required. Typically, eligibility is worded as "Participant must (or must not) have…" It is not appropriate to say participants are eligible within a single criterion. If we say participants with xxx are eligible, they may be by this particular criterion, but could easily be ineligible by a different criteria.

Guideline - not to be inserted in protocol

To be completed within 14 or 28 days prior to registration (depending on committee):

Bloodwork or other body fluid analyses (urinalysis, creatinine clearance) required for determination of eligibility; x-rays, scans or physical examination used for tumor measurement.

To be completed within 42 days prior to registration:

Exams used for screening (e.g., audiogram, PFT) other than blood or body analyses; x-rays, scans or ultrasound of non-measurable disease or uninvolved organs.

To be completed within 56 days prior to registration:

X-rays, scans, ultrasounds, etc., used to establish disease free status on adjuvant studies.

- **Criteria that involve logical statements ("and", "or", "unless") should be consistent with the intention of the statement. For example, if the protocol says that a participant needs a "CT or MRI and Bone Scan", is that "(CT or MRI) and Bone Scan", or is that "CT or (MRI and Bone Scan)"?**
- **Being as explicit as possible in what is *required in Section 5 vs 9*. Sites have a hard time determining if some scans or labs, for example, are required.**

- **Some criteria contain extra-long sentences and phrases and some site staff don't/can't read completely. Suggest including bullet points to ensure that critical points are clear for the audience and staff. This will help with the "add" and "or".**

In September 2018, the NCI circulated recommendations for broadening eligibility criteria on the following topics: 1) Brain Metastases, 2) HIV/AIDS, 3) Organ Dysfunction and Prior and Concurrent Malignancies, and 4) Minimum Age for Enrollment. NCI is extremely supportive of broadening eligibility criteria to make clinical trials more representative. For investigators that submit protocols to NCI's Cancer Therapy Evaluation Program (CTEP) in DCTD, the CTEP Protocol Review Committee will require new protocols being reviewed as of November 1, 2018, to use these criteria. When investigational agents and combinations of treatments might pose safety concerns with specific criteria, investigators should include the medical and scientific rationale for why the template eligibility criteria language needs modification for participant safety.

5.1 Disease Related Criteria

a. ***disease type/stage, measurable/non-measurable, etc.***

Related to the section outlining disease measurement - the last sentence of that section should be as follows). All disease must be assessed and documented on the Baseline Tumor Assessment Form.
Note for PC: Diagnosis date eligibility requirements for registration: Would be helpful to specify if diagnosis date is clinical or pathologic diagnosis date, if appropriate.

b. Participants with treated brain metastases must have no evidence of progression on the follow-up brain imaging after CNS-directed therapy.
Note from SDMC: This new section may make it very difficult to follow disease progression or response, unless imaging of the brain mets can be done at the schedule put forth in the protocol. This must be considered by the study team as they determine what is / is not applicable to each trial. If response or progression is an endpoint, we must have all disease assessed at the stated timepoints as all other disease.

(Note: in specific trials, it may be necessary to add a time factor regarding the follow-up brain imaging, but this should be as lenient as medically indicated.)
NCI Guidelines for treated/stable brain metastases:
These recommendations do not apply to:

- **Trials designed specifically for primary brain cancers, e.g., GBM.**
- **Trials designed specifically for brain metastases**
  - **Radiation**
  - **Systemic agent for a specific disease with the specified trial objective of evaluating brain metastases response to treatment (lung, melanoma, breast)**

c. Participants with active brain metastases (defined as new or progressive brain metastases) or leptomeningeal disease must not require immediate CNS-specific treatment, including through the first cycle of protocol therapy, in the opinion of the treating investigator.
NCI Guidelines for new or progressive brain metastases:
Consider inclusion of a leptomeningeal disease (LMD) cohort in early phase trials of drugs with anticipated CNS activity when relevant in the specific disease type under study.

Consideration of cerebrospinal fluid (CSF) pharmacokinetic measurements is encouraged in this context.

Guidance for inclusion in early-phase trials
Participants with active brain metastases should be included early in clinical development when there is strong scientific rationale for likelihood of benefit based on molecular pathways or histology as well as preclinical data.

- **For drugs/modalities with less robust preclinical information on potential CNS activity, inclusion of participants with active brain metastases should still be considered, particularly if brain metastases are common in the intended-use population.**
- **The inclusion of a CNS-specific cohort can provide valuable dosing and preliminary efficacy data to either support or refute inclusion in later phase trials.**

The mechanism of action of the drug or predicted blood-brain barrier (BBB) penetration should not necessarily influence a decision to include such participants. In addition, preclinical studies of intact BBB penetration are not necessarily reflective of blood-tumor barrier penetration.

Guidance for inclusion in later-phase trials:
- **Ideally, data from earlier-phase trials, in concert with the strength of the scientific rationale and preclinical data, can inform decisions on inclusion of participants with active brain metastases in later-phase trials.**

When such data are not available, a few potential trial designs could allow participants with active brain metastases to enroll, either as a parallel cohort or as a defined subset within the larger clinical trial.

d. Participants with known human immunodeficiency virus (HIV)-infection are eligible providing they are on effective anti-retroviral therapy and have undetectable viral load at their most recent viral load test and within 6 months prior to registration.
NCI Guidelines for participants with an HIV infection:
HIV-related eligibility criteria should be straightforward and focus on:
- **Current and past CD4 and T-cell counts**
- **History (if any) of AIDS-defining conditions**
- **Status of HIV treatment**

Participants with HIV infection should be treated using the same standards as other participants with co-morbidities. Anti-retroviral therapy should be considered a concomitant medication.

e. Participants with evidence of chronic hepatitis B virus (HBV) infection must have undetectable HBV viral load on suppressive therapy within in XX prior to registration.
Note from SDMC: Presumably there is an allowed timeframe for the viral load testing. Previous undetectable levels do mean it remains undetectable.

f. Participants with a history of hepatitis C virus (HCV) infection must have been treated and cured. For participants with HCV infection who are currently on treatment must have an undetectable HCV viral load within in XX prior to registration.

Note from SDMC: Presumably there is an allowed timeframe for the viral load testing. Previous undetectable levels do mean it remains undetectable.

5.2 Prior/Concurrent Therapy Criteria

a. ***any limitations on types/durations of prior therapies included or excluded or exclusions for concurrent therapies***

This section should address whether participants are allowed to be co-enrolled on other studies (including non-treatment studies that may or may not include investigational drugs) or receive concurrent therapy with any investigational agents or agents aimed at treating the cancer in question.

5.3 Clinical/Laboratory Criteria

PC Notes:

- **These are guidelines that may or should be modified based on protocol-specific or drug development-specific needs.**
- **Specify specific tests that are required, rather than general terms. Ex: Rather than saying pulmonary function tests, specify that sites should order DLCO, VO2 max, FEV1, etc. Not all sites have the same standard of care, so it's better to spell everything out that way sites aren't scrambling to bring participants back for additional testing prior to registration.**
- **For ECG evaluations of the QTc interval, do not specify any calculation or correction).**
- **If measurements are needed on Day 1/Cycle 1 within a limit, it should be documented in Section 7 and Section 9 of the protocol. The participant could be eligible, but not treated on anticipated D1/C1 due to elevated BP. In Section 5.0, SDMC cannot judge eligibility based on something that takes place after the registration.**

a. **TEMPLATE LANGUAGE** Participants must have adequate organ and marrow function as defined below:

– leukocytes	≥3,000/mcL
– absolute neutrophil count	≥1,500/mcL
– platelets	≥100,000/mcL
– total bilirubin	≤ institutional upper limit of normal (ULN)
– AST/ALT	≤3 × institutional ULN
– creatinine	≤ institutional ULN

OR

– estimated creatinine clearance *(see below)*

NCI Guidelines:

- **Liver function tests used to determine eligibility should be assessed relative to institutional normal ranges, not a universal cutoff point.**
- **Kidney functions - For agents for which renal excretion is not a major route of clearance and for which renal toxicity is not an issue, the threshold for creatinine clearance should be >30 mL/min.**

b. **TEMPLATE LANGUAGE** Participants must have adequate cardiac function. Participants with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, must have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification (see Appendix 18.X). To be eligible for this trial, participants must be class 2B or better.
NCI Guidelines:
Investigator assessment of a potential participant's risk for heart failure should use a validated clinical classification system (e.g., the New York Heart Association Functional Classification). Participants with active cardiac disease may be eligible after assessment of cardiac function by a cardiologist.

c. **TEMPLATE LANGUAGE** Participants must have a serum creatinine ≤ the IULN OR measured OR calculated creatinine clearance ≥ 50 mL/min using the following Cockroft-Gault Formula. This specimen must have been drawn and processed within xx days prior to registration:

$$\text{Calculated Creatinine Clearance} = \frac{(140 - \text{age}) \times (\text{weight in kg})\ \dagger}{72 \times \text{serum creatinine}\ *}$$

Multiply this number by 0.85 if the participant is a female.

† The kilogram weight is the participant weight with an upper limit of 140% of the IBW.
* Actual lab serum creatinine value with a minimum of 0.8 mg/dL.

d. **TEMPLATE LANGUAGE** Participants must not have uncontrolled diabetes within xx days prior to registration.
Uncontrolled diabetes: An HgA1C > 7% within 14 days prior to registration. The same criterion will be used in participants with confirmed diagnosis of diabetes mellitus who have been on a stable dietary or therapeutic regimen for this condition in the last three months.
Diabetes Definition is to be included in the protocol

e. **TEMPLATE LANGUAGE** Participants must not have uncontrolled blood pressure and hypertension within xx days prior to registration.
Uncontrolled blood pressure and hypertension: SBP > 140 mmHg or DBP > 90 mmHg within 14 days prior to registration. Participants are permitted to be receiving multiple anti-hypertensive medications (unless otherwise indicated in the study). All blood pressure measurements within the 14 days prior to registration must be SBP ≤ 140 and DBP ≤ 90. An exception can be made by a healthcare provider for a participant with a single blood pressure elevation who upon rechecking has a normal blood pressure.
Blood pressure and hypertension Definition is to be included in the protocol

f. ***Choose one of the following 2 options:***

Participants with a prior or concurrent malignancy whose natural history or treatment (in the opinion of the treating physician) does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.
NCI Guidelines for prior or concurrent malignancies:
Participants with prior or concurrent malignancies should be eligible, especially when the risk of the malignancy interfering with either safety or efficacy endpoints is very low

OR

No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, *in situ* cervical cancer, adequately treated Stage I or II cancer from which the participant is currently in complete remission, or any other cancer from which the participant has been disease free for five years.

g. Participants must not be pregnant or nursing *(add required rationale)*. Women/men of reproductive potential must have agreed to use an effective contraceptive method. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate participant chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

5.4 Specimen Submission Criteria

Any required submissions or requirements for offering participants participation in TM/banking. Please pick the appropriate criterion.

a. Participants must be offered the opportunity to participate in specimen banking as outlined in Section 15.X. With participant consent, specimens must be collected and submitted via the SWOG Specimen Tracking System as outlined in Section 15.X.

b. Participants must agree to have <blood, tissue, etc.> specimens submitted for <name of test> as outlined in Section 15.X.

c. Participants who can complete <PRO, QOL, questionnaires, etc.> forms in <language, English> must participate in the quality of life study(ies) as outlined in Section 15.X.

5.5 Regulatory Criteria

a. Participants ***must*** be informed of the investigational nature of this study and must sign and give informed consent in accordance with institutional and federal guidelines.

b. As a part of the OPEN registration process (see Section 13.X for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

For CTP studies:

As part of the registration process the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

6.0 STRATIFICATION FACTORS

Stratification factors will be inserted by the stat center.

7.0 TREATMENT PLAN

For treatment or dose modification questions, please contact ***insert 2 names and phone numbers.*** For dosing principles or questions, please consult the SWOG Policy #38 "Dosing Principles for Participants on Clinical Trials" at https://www.swog.org/sites/default/files/docs/2017-11/Policy38.pdf.

Initiation of treatment must be planned to start no more than ***x*** calendars days after registration. ***(This should be edited to fit the study as needed. Please use "calendar" days rather than "working" days.)***

7.1 Pre-Medication

a. ***Insert details of pre-medication, if applicable.***

7.2 Treatment

Insert treatment information (from Capsule Summary). When possible, use the following table format.
Note to PC: When all agents for a regimen are taken daily by mouth, please indicated that a cycle=xx days (regardless of dose delays).

For treatment or dose modification questions, please contact ***insert 2 names and phone numbers.***

a. Arm A

Agent	Dose	Route	Day	Schedule

* Note: One cycle = ***XX*** days

b. Arm B

Agent	Dose	Route	Day	Schedule

* Note: One cycle = ***XX*** days

For studies using drug administered PO include the following section:

7.1 Disease/Recurrence Assessment <if applicable>

See Section 9.0 for disease assessment time points (approximately every XX weeks). Disease assessment timing is to be based on calendar timing counted as weeks after registration, not based on cycles or drug administration.
NOTE to PC: Additional details of the disease assessment may be included here.

7.2 Drug Compliance Documentation

Drug compliance will be recorded by participants in the Intake Calendar (see Appendix 18._). Institutional CRAs will review and ascertain participant adherence with protocol therapy at the end of treatment for each cycle. Calendar should be kept in the participant's research chart. Sites utilizing the CIRB must use the Intake Calendar provided.

7.3 Full CDUS Reporting Requirement

This study falls under CTEP requirements for full CDUS reporting. This involves required submission of cycle-specific toxicity and dose information (see Section 14.X, the **SXXXX** Treatment Form, and the **SXXXX** Adverse Event Form). A cycle is defined as ***XX*** days (regardless of dose delays **<to be used only if the regimen is all daily oral treatment>**).

NOTE TO PC: CTEP requires full CDUS reporting for all Phase I and II studies under CTEP-held INDs. Phase III studies under CTEP-held INDs and studies not under CTEP-held INDs (studies under SWOG-held INDs or without an IND) only require abbreviated reporting. This section should be removed if full CDUS reporting is not required.
(https://ctep.cancer.gov/protocoldevelopment/electronic_applications/cdus.htm)

7.4 Criteria for Removal from Protocol Treatment
NOTE to PC: Add appropriate details for multi-regstep studies so that it is clear which registration step is referred to for the items delineated here.

a. Progression of disease or symptomatic deterioration (as defined in Section 10.X).
Example text for participants that are allowed to remain on treatment due to clinical benefit:

However, the participant may continue protocol treatment as long as the participant is continuing to clinically benefit from treatment in the opinion of the treating investigator. Participants should still be removed from protocol treatment for criteria below.

b. Unacceptable toxicity.

c. Treatment delay for any reason > ***X*** weeks ***(insert number of weeks)***

d. The participants may withdraw from the protocol treatment at any time for any reason.

7.5 Discontinuation of Treatment

All reasons for discontinuation of treatment must be documented in the Off Protocol Treatment Notice.

7.6 Follow-Up Period

All participants will be followed until death or ***X*** years after registration, whichever occurs first. ***(insert number of years)***

8.0 TOXICITIES TO BE MONITORED AND DOSE MODIFICATIONS

8.1 NCI Common Terminology Criteria for Adverse Events

This study will utilize the CTCAE (NCI Common Terminology Criteria for Adverse Events) Version 5.0 for toxicity and Serious Adverse Event reporting. A copy of the CTCAE Version 5.0 can be downloaded from the CTEP home page (http://ctep.cancer.gov). All appropriate treatment areas should have access to a copy of the CTCAE Version 5.0.

8.1 General Considerations
If appropriate indicate 1) whether dose re-escalations are allowed after a decrease 2) what actions to take when the participant has multiple toxicities requiring treatment modifications, 3) maximum treatment delay. Maximum dose delays should be consistent/follow similar timelines with dose modifications and disease

assessments, 4) Con-medications that should be avoided, 5) general guidelines for all AEs.

Examples below.

a. No dose reductions are allowed on <drug name(s)>.

b. The maximum dose delay for any reason is XX days.

c. Missed doses will not be made up.

d. Dose interruptions and discontinuations are allowed to manage toxicity. <specific to no dose reductions.>

e. If multiple toxicities are experienced, dose modifications will be based on the toxicity requiring the largest dose reduction.

f. Reductions are based on the dose being given at the end of the preceding cycle and are based on toxicities observed since the prior toxicity evaluation.

g. If a drug must be permanently discontinued, the participant must be removed from protocol therapy (see Section 7.X).

h. <Can one treatment with continue if the other treatment is discontinued? Consult with the Study Chairs, Drs. XX at xx@email.

8.2 Dose Modifications

a. Arm A

b. Arm B

If appropriate, include a section for recommended management of side effects, such as antibiotics or antiemetics, or a section indicating what treatments are contraindicated, such as NSAIDs or corticosteroids.

Insert dose modification information. Points to consider:

Will G-CSF be allowed? If so, standard language will be inserted by Ops Office.

Which toxicity levels result in changes? Only current CTCAE grade definitions should be used.

What is the modification based on? Indicate whether modification is based on day of treatment, most severe toxicity experienced during the previous interval, or both.

Dose change: If a dose change is required, indicate: what dose the change is calculated from (starting dose or previous dose); what further dose changes are required if toxicity persists after dose modification; what the dose levels are for each decrease; when the dose becomes 0, i.e., permanently discontinued; when no further reductions are made regardless of persistent toxicity; whether dose increase is permitted in the absence of further toxicity.

Use of ancillary treatment: If instructions are to use ancillary treatments instead of decreasing dose, e.g., antiemetics or growth factors, indicate what measures are taken when the ancillary treatment is not effective.

Dose delay: Indicate what should be done if toxicity has not resolved at the end of the delay; how long treatment should be delayed before permanently discontinuing the treatment; to what grade of toxicity the participant must recover; what the minimum duration of the recovery is prior to restarting treatment; what dose level

should be used after the delay; whether the study calendar is stopped during the delay (i.e., doses are made up) or whether it continues (i.e., missed doses are omitted). After a hold, the next dose should be scheduled based on the planned date.

Instructions concerning dose increases after a decrease: Indicate to what grade of toxicity the participant must recover; how large the increase should be; and how many increases are allowed. Occasionally dose re-escalations are not allowed except for participants receiving G-CSF support. In this case the item should be along the lines of: "No dose re-escalations are allowed, except for participants receiving G-CSF support per sections 7.__ and 8.__. If the participant maintains an ANC of >= 1,000 throughout the initial cycle of G-CSF supported chemotherapy, then the next cycle of chemotherapy may be increased to the next higher dose level with continued support of G-CSF. No dose escalations above the original dose level should be performed on participants taking G-CSF."

Dose modification information will be put into standard table format by Ops Office.

8.3 White blood Cell Growth Factors

If used, white blood cell growth factors, including biosimilars, must be used per ASCO guidelines (http://jco.ascopubs.org/content/24/19/3187.full) and NCCN Guidelines® Myeloid Growth Factors (http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf).

8.4 Dose Modification Contacts

For treatment or dose modification questions, please contact ***insert 2 names and phone numbers.***

8.5 Adverse Event Reporting Requirements

Notes to the PC: For Protocols that utilize the Rave® / CTEP-AERS integration:
Please Note: This protocol utilizes Rave® / Cancer Therapy Evaluation Program Adverse Event Reporting System (CTEP-AERS) integration for expedited reporting of serious adverse events. The CTEP-AERS integration enables evaluation of post-baseline Adverse Events (AE) entered in Rave to determine whether they require expedited reporting.

All AEs that occur after baseline are collected in Medidata Rave using the Adverse Event form, which is available for entry at each treatment or reporting period, and used to collect AEs that start during the period or persist from the previous reporting period. The Clinical Research Associate (CRA) will enter AEs that occur prior to the start of treatment on a baseline form that is not included in the Rave-CTEP-AERS integration. AEs that occur prior to enrollment must begin and end on the baseline Adverse Events form and should not be included on the standard Adverse Events form that is available at treatment unless there has been an increase in grade.

Prior to sending AEs through the rules evaluation process, site staff should verify the following on the Adverse Event form in Rave:

- The reporting period (course/cycle) is correct; and
- AEs are recorded and complete (no missing fields) and the form is query free (fields
  added to the form during study build do not need to be query free for the integration call with CTEP-AERS to be a success).

The CRA reports AEs in Rave at the time the Investigator learns of the event. If the CRA modifies an AE, it must be re-submitted for rules evaluation.

Upon completion of AE entry in Medidata Rave, the CRA submits the AE for rules evaluation by completing the Expedited Reporting Evaluation form. Both NCI and protocol-specific reporting rules evaluate the AEs submitted for expedited reporting. A report is initiated in CTEP-AERS using information entered in Medidata Rave for AEs that meet reporting requirements. The CRA completes the report by accessing CTEP-AERS via a direct link on the Medidata Rave Expedited Reporting Evaluation form.

In the rare occurrence, that Internet connectivity is lost; a 24-hour notification is to be made to CTEP by telephone at 301-897-7497. Once Internet connectivity is restored, the 24-hour notification that was phoned in must be entered immediately into CTEP-AERS using the deep link from Medidata Rave.

Additional information about the CTEP-AERS integration is available on the CTSU website:

- Study specific documents: Protocols > Documents> Education and Promotion; and
- Expedited Safety Reporting Rules Evaluation user guide: Resources > CTSU Operations Information> User Guides.

NCI requirements for SAE reporting are available on the CTEP website:

- NCI Guidelines for Investigators: Adverse Event Reporting Requirements is available at https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/aeguidelines.pdf.

If you have questions about this process, please contact the SAE Program Manager 210-614-8808 or email adr@swog.org.

The CTEP-AERS electronic reporting system “Help” feature has detailed instructions in the section "Submitting Reports for RAVE Users".

Current standard language will be inserted by the Ops Office
Note to PCs: add from S:\PROTOCOL COORDINATION\PC STANDARDS\SAE REPORTING

9.0 STUDY CALENDAR

Calendar examples:


S1826 Example Calendar.docx


S1900A Calendar Example.docx

9.1 Arm A **<Arms with the same cycle length maybe on the same calendar. This will reduce inconsistences between attempting to maintain multiple calendars.>**

9.2 Arm B

Which laboratory tests and scans must be performed while on treatment, and how often should these be done? Which laboratory tests and scans must be performed during follow-up, and how often should these be done? How to "adjust" the calendar if treatment is delayed or held? Based on this information and that contained in other sections of the protocol, the Ops Office will create the study calendar.

Notes to the PC:

Please include in the template standard language about methods of assessing disease needing to be the consistent and confirmation of response when best response is an endpoint.

First column = "pre-registration Step 1"

Second column (if needed) = "pre-registration Step 2"

An "X" in a column means that item is to be done at the BEGINNING of that column's timeframe unless… Should this be put in Best Practices?

A footnote is not needed if the Xs in the calendar are self-explanatory

Shouldn't have to refer to section 7 to know the length of cycle

Combine lines as much as possible (H&P and Wt&PS)

Specify specific tests that are required, rather than general terms. Ex: Rather than saying pulmonary function tests, specify that sites should order DLCO, VO2 max, FEV1, etc. Not all sites have the same standard of care, so it's better to spell everything out that way sites aren't scrambling to bring participants back for additional testing prior to registration.

Instead of symbols, use capital letters

"End of treatment assessment" column – Might not need all the time. Include information about when this should take place.

"Follow up prior to progression"

"Follow up after progression" – Anything that is supposed to take place at progression should go in this column.

If submission of images, say "submit scans to Triad/AGMednet" (to emphasize)

Footnotes – put on the left or at the top as often as possible (not in the body of the calendar unless the footnote is specific to that particular occurrence)

Do not include information in a footnote that can be found else where in the protocol. Instead, reference the section.

Copy Elaine on CTEP submission. This will be her trigger for QA review.

(below each calendar)
NOTE: the study calendar is a good tool for a general snapshot of study requirements but does not replace details provided in the relevant sections of the protocol. Use the study calendar in conjunction with the detailed procedures and information in the protocol but not as the sole or primary source for managing this trial.

NOTE: Forms are found on the protocol abstract page on the SWOG website (www.swog.org) and on the CTSU website (www.ctsu.org). Forms submission guidelines are found in Section 14.0.
(remove CTSU if not on CTSU menu)

NOTE: Unless indicated otherwise in the protocol, scheduled procedures and assessments (treatment administration, toxicity assessment for continuous treatment, disease assessment, specimen collection and follow-up activities) must follow the established SWOG guidelines as outlined in
https://www.swog.org/sites/default/files/docs/2017-10/Best%20Practices%20upddate.pdf.

For FDA studies, please include windows around each visit/assessment. For all studies refer to Best Good Practice document

(for footnotes of each calendar, as necessary)
Results of these tests do not determine eligibility but are performed prior to registration.

If these tests are also recommended during treatment, add "and during treatment" *directly after "registration".*

If these tests are also recommended both during treatment and through follow up (after completion of treatment), add ", during treatment and throughout follow up" *directly after "registration"*

If you need a landscape oriented calendar, put it here, otherwise remove

10.0 CRITERIA FOR EVALUATION AND ENDPOINT ANALYSIS

10.1 Insert criteria

a.
Standard language will be inserted by the Ops Office. Must be reviewed/approved by SC and Stats/Data. S:\PROTOCOL COORDINATION\PC STANDARDS\SECTION 10.0

11.0 STATISTICAL CONSIDERATIONS

11.1 Insert considerations

a.
This section will be written by the stat center.

Phase I studies

"There is no formal Data and Safety Monitoring committee for Phase I studies. Adverse events and accrual monitoring are done routinely by the Study Chairs and Study Statisticians. Accrual and adverse event listings are posted real time. A conference call between the study team and participating investigators takes place *<<<insert frequency here>>>* to discuss enrollment, participant progress, adverse events, dose limiting toxicities, and dose escalation/de-escalation decisions. Formal toxicity reports are published Group-wide every 6 months. In addition, the study team at the SWOG Statistics and Data Management Center, Serious Adverse Event Coordinator at the Operations Office, SAE Physician Reviewer, and Study Chair monitor serious adverse events on an ongoing basis."

Phase II studies (single arm)

There is no formal Data and Safety Monitoring Committee for this study. Accrual reports are generated weekly and study-specific accrual is monitored by the Study Chair, Study Statistician and the Disease Committee Chair. Reports summarizing adverse events, serious adverse events (SAEs), and treatment administration are provided monthly to the Study Chair and Study Statistician for monitoring. In addition, all SAEs which by definition require expeditious reporting are reviewed and processed by the Adverse Event Coordinator at the SWOG Operations Office and a physician reviewer based on data provided via the NCI CTEP-AERS system. Cumulative study-specific SAE reports are provided to the Study Chair and Study Statistician upon occurrence of an event. Formal reports summarizing the study are prepared for all SWOG members every 6 months.

Randomized Phase II and Phase III studies

A Data and Safety Monitoring Committee will oversee the conduct of the study. The Committee consists of four members from outside of the SWOG Cancer Research Network, three SWOG members, three non-voting representatives from the National Cancer Institute (NCI), and the Group Statistician (non-voting). The members of this Committee will receive confidential reports every six months from the SWOG Statistics and Data Management Center, and will meet at the Group's bi-annual meetings as necessary. The Committee will be responsible for decisions regarding possible termination and/or early reporting of the study.

12.0 DISCIPLINE REVIEW

Commented [RCJ2]: Since this is used so infrequently any more, we would ask that the reason for the pathology submission is put here, but that all of the specimen submission details is included in Section 15.0. Some have been confused when 15.0 does not include all of the specimen details.

12.1

The reason for the pathology submission: (submission details go into Section 15) Does this study require central pathology review, central radiation therapy review, or central surgery review? (NOTE: In diseases for which there is general agreement among pathologists regarding essential aspects of diagnosis [tumor grade, histologic subtype, etc.], central pathology review may not be necessary.)

If so, what is the purpose of the review?

For path review: Be specific about the type, number and size of specimens to be submitted. What is the procedure from which these specimens will be obtained, and when will this procedure be performed? How must the specimens be packed (i.e., dry ice, etc.)? To whom should they be sent? What will happen to the specimens after path review is complete: will they be banked, destroyed, returned to the sending institution or used for molecular tests? (NOTE: Details of molecular tests are NOT included in this section. Specimens for testing are submitted per instructions in Section 15.)

For surgery review: What should be submitted and to whom?

For radiation therapy review: What is the level of review (i.e., rapid review, final review)? Obtain standard language from QARC.

13.0 REGISTRATION GUIDELINES

13.1 Registration Timing

Initiation of treatment must be planned to start no more than ***x*** calendars days after registration. ***(This should be edited to fit the study as needed. Please use "calendar" days rather than "working" days.)***

Note to PC: this language is also contained in Section 7. SDMC would like it in both spots.

REMOVE SLOT RESERVATION INFO IF THE STUDY IS NOT UTILIZING THE SWOG SLOT RESERVATION SYSTEM

13.2 Slot Reservation

Participant enrollment for this study will be facilitated using the Slot-Reservation System in conjunction with the Registration system in the Oncology Participant Enrollment Network (OPEN). Prior to discussing protocol entry with the participant, all site staff must use the CTSU OPEN Slot Reservation System to ensure that a slot on the protocol is available to the participant. Once a slot- reservation confirmation is obtained, site staff may then proceed to enroll the participant to this study.

Participants planning to enroll on this study must first have a slot reserved in advance of the registration, even if the site plans to enroll right away.

All site staff will use OPEN to create a slot reservation. OPEN is a web-based application and can be accessed at https://open.ctsu.org, or from the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org, or from the OPEN Participant Registration link on the SWOG CRA Workbench. Please refer to the 'Slot Reservation

Quick Reference Site User Guide' within the OPEN tab on the CTSU members' website under 'Training and Demonstration Materials' for detailed instructions.

The individual making the slot reservation for the participant must be prepared to provide answers to the following questions:

a. Institution CTEP ID

b. Protocol Number

c. Registration Step

d. Participant Initials

e. Participant's Date of Birth

f. ZIP Code

g. Gender (select one):
- Female Gender
- Male Gender

Slot reservations expire within 7 calendar days. A warning e-mail will be sent 48 hours before the expiration date. The reservation can be renewed any time before it expires as long as at least 1 slot is still available. After it expires, a new slot reservation must be created for the participant before they can be enrolled to this trial. Reservations may also be withdrawn at any time. If you withdraw a reservation, please notify the SWOG Statistics and Data Management Center at XXXXquestion@crab.org ***(insert relevant committee).***

13.3 Investigator/Site Registration

Prior to the recruitment of a participant for this study, investigators must be registered members of a Cooperative Group. Each investigator must have an NCI investigator number and must maintain an "active" investigator registration status through the annual submission of a complete investigator registration packet to CTEP.

13.4 CTEP Registration Procedures

Food and Drug Administration (FDA) regulations and National Cancer Institute (NCI) policy require all individuals contributing to NCI-sponsored trials to register and to renew their registration annually. To register, all individuals must obtain a Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) account at https://ctepcore.nci.nih.gov/iam. In addition, persons with a registration type of Investigator (IVR), Non-Physician Investigator (NPIVR), or Associate Plus (AP) (i.e., clinical site staff requiring write access to OPEN, Rave, or acting as a primary site contact) must complete their annual registration using CTEP's web-based Registration and Credential Repository (RCR) at https://ctepcore.nci.nih.gov/rcr.

RCR utilizes five-person registration types.
- IVR — MD, DO, or international equivalent;
- NPIVR — advanced practice providers (e.g., NP or PA) or graduate level researchers (e.g., PhD);
- AP — clinical site staff (e.g., RN or CRA) with data entry access to CTSU applications (e.g., Roster Update Management System (RUMS), OPEN, Rave,);
- Associate (A) — other clinical site staff involved in the conduct of NCI-sponsored trials; and

- Associate Basic (AB) — individuals (e.g., pharmaceutical company employees) with limited access to NCI-supported systems.

RCR requires the following registration documents:

Documentation Required	IVR	NPIVR	AP	A	AB
FDA Form 1572	✔	✔			
Financial Disclosure Form	✔	✔	✔		
NCI Biosketch (education, training, employment, license, and certification)	✔	✔	✔		
GCP training	✔	✔	✔		
Agent Shipment Form (if applicable)	✔				
CV (optional)	✔	✔	✔		

An active CTEP-IAM user account and appropriate RCR registration is required to access all CTEP and Cancer Trials Support Unit (CTSU) websites and applications. In addition, IVRs and NPIVRs must list all clinical practice sites and Institutional Review Boards (IRBs) covering their practice sites on the FDA Form 1572 in RCR to allow the following:

- Addition to a site roster;
- Assign the treating, credit, consenting, or drug shipment (IVR only) tasks in OPEN;
- Act as the site-protocol Principal Investigator (PI) on the IRB approval; and
- Assign the Clinical Investigator (CI) role on the Delegation of Tasks Log (DTL).

In addition, all investigators act as the Site-Protocol PI, consenting/treating/drug shipment, or as the CI on the DTL must be rostered at the enrolling site with a participating organization (i.e., Alliance).

Additional information is located on the CTEP website at https://ctep.cancer.gov/investigatorResources/default.htm. For questions, please contact the **RCR Help Desk** by email at RCRHelpDesk@nih.gov.

TEXT FOR REGISTRATION PROCEDURES <IF APPLICABLE>

- *Include the following text/sub-sections within the Registration section of the protocol.*
- *If this study is using one of the CTSU services, but will **not** be posted to the CTSU website because of limited participation to the LPO (i.e. not a Central Institutional Review Board (CIRB) reviewed trial that is open to the LPO or sites within the LPO), add a note under this section to clarify that protocol-specific regulatory documents are found on the LPO website.*
- *If this is a CIRB reviewed study with participation limited to the LPO, add a note under this section to clarify that protocol documents are found on the CTSU website, but supplemental documents will be available on the LPO website.*

13.5 CTSU Registration Procedures

This study is supported by the NCI Cancer Trials Support Unit (CTSU).

a. **IRB Approval:**

For CTEP and Division of Cancer Prevention (DCP) studies open to the National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP) Research Bases after March 1, 2019, all U.S.-based sites must be members of the NCI Central Institutional Review Board (NCI CIRB). In addition, U.S.-based sites must accept the NCI CIRB review to activate new studies at the site after March 1, 2019. Local IRB review will continue to be accepted for studies that are not reviewed by the CIRB, or if the study was previously open at the site under the local IRB. International sites should continue to submit Research Ethics

Board (REB) approval to the CTSU Regulatory Office following country-specific regulations.

Sites participating with the NCI CIRB must submit the Study Specific Worksheet for Local Context (SSW) to the CIRB using IRBManager to indicate their intent to open the study locally. In order for the SSW approval to be processed, the Signatory Institution must inform the CTSU which CIRB-approved institutions aligned with the Signatory Institution are participating in the study. The NCI CIRB's approval of the SSW is automatically communicated to the CTSU Regulatory Office, but sites are required to contact the CTSU Regulatory Office at CTSURegPref@ctsu.coccg.org to establish site preferences for applying NCI CIRB approvals across their Signatory Network. Site preferences can be set at the network or protocol level. Questions about establishing site preferences can be addressed to the CTSU Regulatory Office by emailing the email address above or calling 1-888-651-CTSU (2878).

Include the following (highlighted) paragraph for trials that will include sites using their local IRB or REB as well as for trial with non U.S.-based NCTN and NCORP sites.

Sites using their local IRB or REB, must submit their approval to the CTSU Regulatory Office using the Regulatory Submission Portal located in the Regulatory section of the CTSU website. Acceptable documentation of local IRB/REB approval includes:

- Local IRB documentation;
- IRB-signed CTSU IRB Certification Form; and/or
- Protocol of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption Form.

In addition, the Site-Protocol Principal Investigator (PI) (i.e. the investigator on the IRB/REB approval) must meet the following criteria to complete processing of the IRB/REB approval record:

- Holds an Active CTEP status;
- Rostered at the site on the IRB/REB approval (*applies to US and Canadian sites only*) and on at least one participating roster;
- If using NCI CIRB, rostered on the NCI CIRB Signatory record;
- Includes the IRB number of the IRB providing approval in the Form FDA 1572 in the RCR profile; and
- Holds the appropriate CTEP registration type for the protocol.

Additional Requirements
Assignment of site registration status in the CTSU Regulatory Support System (RSS) uses extensive data to make a determination of whether a site has fulfilled all regulatory criteria including but not limited to: the following:

- An active Federal Wide Assurance (FWA) number;
- An active roster affiliation with the Lead Protocol Organization (LPO) or a Participating Organization (PO); and
- Compliance with all protocol-specific requirements (PSRs).

b. **Protocol Specific Requirements (PSR) for *<INSERT PROTOCOL NUMBER>* Site Registration**

If this is a study with a radiation and/or imaging (RTI) component, add the following to the protocol if applicable.

1. PSR for Radiation and/or Imaging (RTI) Component

   This is a study with a radiation and/or imaging (RTI) component and the enrolling site must be aligned to an RTI provider. To manage provider associations or to add or remove associated providers, access the Provider Association page from the Regulatory section on the CTSU members' website at https://www.ctsu.org/RSS/RTFProviderAssociation. Sites must be linked to at least one Imaging and Radiation Oncology Core (IROC) provider to participate on trials with an RTI component. Enrolling sites are responsible for ensuring that the appropriate agreements and IRB approvals are in place with their RTI provider. A primary role on any roster is required to update provider associations, though all individuals at a site may view provider associations. To find who holds primary roles at your site, please view the Person Roster Browser under the RUMS link on the CTSU website.

If IROC-Houston will conduct RT modality credentialing, add the following to the protocol:

2. PSR for RT Modality Credentialing (IROC-Houston)

   IROC Credentialing Status Inquiry (CSI) Form – this form is submitted to IROC Houston to verify credentialing status or to begin a new modality credentialing process.

If this study uses the IROC integration suite to document that the enrolling site is associated with a radiation or imaging (RT/I) provider credentialed for the study modalities, add the following to the protocol:

3. PSR for Radiation or Imaging (RT/I) Provider Credentialed (IROC Integration suite)

   To complete protocol-specific credentialing the RTI provider or enrolling site should follow instructions in the protocol to submit documentation or other materials to the designated IROC Quality Assurance (QA) center. Upon the IROC QA center approving the RTI provider for the study modality, IROC will automatically send the approval to the Regulatory Support System (RSS) to comply the protocol specific requirement. IROC will continue to copy the provider and/or enrolling site on modality approvals.

   Upon site registration approval in RSS, the enrolling site may access OPEN to complete enrollments. The enrolling site will select their credentialed provider treating the subject in the OPEN credentialing screen and may need to answer additional questions related to treatment in the eligibility checklist.

If applicable, add any other protocol-specific documents or requirements (e.g., site or investigator specialized credentialing; evidence of training; study-specific regulatory forms) needed for site registration. Include any processing instructions, or reference the location in the protocol or appendices where further instructions can be found.

4. PSR for xxx *(e.g., site or investigator specialized credentialing; evidence of training; study-specific regulatory forms)* <if applicable, required for FDA studies>

   A member of each institution (CRA or investigator, etc.) must complete the Protocol Specific Requirements (PSR) prior to participant registration. The PSR can be satisfied by completing the training online and submitting the verification form to the CTSU Regulatory Office via the Regulatory Submission Portal on the CTSU website.

Include only if study will use a Delegation of Tasks Log (DTL) – This is limited to registration studies.

c. **Delegation of Task Log (DTL)**

Each site must complete a protocol-specific Delegation of Tasks Log (DTL) using the DTL application in the Delegation Log section on the CTSU members' website. The Clinical Investigator (CI) is required to review and electronically sign the DTL prior to the site receiving an Approved site registration status and enrolling participants to the study. To maintain an approved site registration status the CI must re-sign the DTL at least annually and when a new version of the DTL is released; and activate new task assignments requiring CI sign-off. Any individual at the enrolling site on a participating roster may initiate the site DTL. Once the DTL is submitted for CI approval, only the designated DTL Administrators or the CI may update the DTL. Instructions on completing the DTL are available in the Help Topics button in the DTL application and include a Master Task List, which describes DTL task assignments, CI signature, and CTEP registration requirements.

Include this section if the DTL has training requirements.

The DTL for this study has training requirements as follows:

{Add description of training requirement for this study and the task it is linked to}

In addition, the following task assignment restrictions apply to this protocol:

{Add description of task assignment restrictions (i.e., persons assigned the Unblinded Study Personnel task may not be assigned other tasks except Investigational Agent Accountability. There must be at least two persons assigned to the Unblinded Study Personnel task.)}

The individual initiating the DTL for the site should upload the above listed training documentation when making the task assignment. The designated reviewer will accept or reject the documentation. A note regarding rejection of any training documents will display on the Site DTL Browser next to the task assignment. The DTL cannot be submitted for CI sign-off until the minimum number of individuals is assigned to the task and have met the training requirements.

Include this section if CCTG is a participant and holds the Clinical Trials Agreement with Health Canada.

Canadian sites participating under Canadian Cancer Trials Group (CCTG), when CCTG hold the Clinical Trials Agreement with Health Canada, should complete the DTL in CCTG's Ripple application. Ripple is integrated with the CTSU DTL application for this trial.

Include this sub-section for trials that will have supplemental protocol documents posted on the CTSU website.

d. **Downloading Site Registration Documents:**

Download the site registration forms from the protocol-specific page located on the CTSU members' website. Permission to view and download this protocol and its

supporting documents is restricted and is based on person and site roster assignment. To participate, the institution and its associated investigators and staff must be associated with the LPO or a PO on the protocol.

- Log on to the CTSU members' website (https://www.ctsu.org) using your CTEP-IAM username and password;
- Click on *Protocols* in the upper left of your screen
  - Enter the protocol number in the search field at the top of the protocol tree, or
  - Click on the By Lead Organization folder to expand, then select *[Corresponding Organization]*, and protocol number *[NCI Protocol #]*;
- Click on *Documents*, select *Site Registration*, and download and complete the forms provided. (Note: For sites under the CIRB initiative, IRB data will load automatically to the CTSU as described above.)

Add additional protocol specific details in this section as needed.

e. **Submitting Regulatory Documents:**
Submit required forms and documents to the CTSU Regulatory Office via the Regulatory Submission Portal on the CTSU website.

To access the Regulatory Submission Portal log on to the CTSU members' website → Regulatory → Regulatory Submission.

Institutions with participants waiting that are unable to use the Regulatory Submission Portal should alert the CTSU Regulatory Office immediately at 1-866-651-2878 in order to receive further instruction and support.

f. **Checking Your Site's Registration Status:**
You can verify your site's registration status on the members' side of the CTSU website.

- Log on to the CTSU members' website;
- Click on *Regulatory* at the top of your screen;
- Click on *Site Registration;*
- Enter your 5-character CTEP Institution Code and click on Go.

Note: The status shown only reflects institutional compliance with site registration requirements as outlined above. It does not reflect compliance with protocol requirements for individuals participating on the protocol or the enrolling investigator's status with the NCI or their affiliated networks.

13.6 Oncology Participant Enrollment Network (OPEN) Registration Requirements

The individual registering the participant must have completed the appropriate SWOG Registration Worksheet. The completed form must be referred to during the registration but should not be submitted as part of the participant data.

The Oncology Participant Enrollment Network (OPEN) is a web-based registration system available on a 24/7 basis. OPEN is integrated with CTSU regulatory and roster data and with the Lead Protocol Organization (LPOs) registration/randomization systems or Theradex Interactive Web Response System (IWRS) for retrieval of participant registration/randomization assignment. OPEN will populate the participant enrollment data in NCI's clinical data management system, Medidata Rave.
Requirements for OPEN access:

- A valid CTEP-IAM account;
- To perform enrollments or request slot reservations: Be on a LPO roster, ETCTN Corresponding roster, or PO roster with the role of Registrar. Registrars must hold a minimum of an AP registration type;
- If a Delegation of Tasks Log (DTL) is required for the study, the registrar(s) must hold the OPEN Registrar task on the DTL for the site; and
- Have an approved site registration for a protocol prior to participant enrollment.

To assign an Investigator (IVR) or Non-Physician Investigator (NPIVR) as the treating, crediting, consenting, drug shipment (IVR only), or receiving investigator for a participant transfer in OPEN, the IVR or NPIVR must list the IRB number used on the site's IRB approval on their Form FDA 1572 in RCR. If a DTL is required for the study, the IVR or NPIVR must be assigned the appropriate OPEN-related tasks on the DTL.
Prior to accessing OPEN, site staff should verify the following:

- Participant has met all eligibility criteria within the protocol stated timeframes and the affirmation of eligibility on the Registration Worksheet has been signed by the registering investigator or another investigator designate. Site staff should refer to Section 5.0 to verify eligibility.
- All participants have signed an appropriate consent form and HIPAA authorization form (if applicable).

Note: The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

OPEN will also ask additional questions that are not present on the SWOG Registration Worksheet. The individual registering the participant must be prepared to provide answers to the following questions:

a. Institution CTEP ID

b. Protocol Number

c. Registration Step

d. Treating Investigator

e. Credit Investigator

f. Participant Initials

g. Participant's Date of Birth

h. Participant SSN (SSN is desired, but optional. Do not enter invalid numbers.)

i. Country of Residence

j. ZIP Code

k. Gender (select one):
   - Female Gender
   - Male Gender

l. Ethnicity (select one):
   - Hispanic or Latino
   - Not Hispanic or Latino
   - Unknown

m. Method of Payment (select one):
- Private Insurance
- Medicare
- Medicare and Private Insurance
- Medicaid
- Medicaid and Medicare
- Military or Veterans Sponsored NOS
- Military Sponsored (Including Champus & Tricare)
- Veterans Sponsored
- Self Pay (No Insurance)
- No Means of Payment (No Insurance)
- Other
- Unknown

n. Race (select all that apply):
- American Indian or Alaska Native
- Asian
- Black or African American
- Native Hawaiian or other Pacific Islander
- White
- Unknown

All site staff will use OPEN to enroll participants to this study. Access OPEN at https://open.ctsu.org or from the OPEN link on the CTSU members' website. Further instructional information is in the OPEN section of the CTSU website at https://www.ctsu.org, https://open.ctsu.org, or from the OPEN Participant Registration link on the SWOG CRA Workbench. For any additional questions, contact the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com.

If the study is using the OPEN Slot Reservation System, include the following in the protocol:

Participant enrollment for this study will be facilitated using the Slot Reservation System in conjunction with the registration system in OPEN. Prior to discussing protocol entry with the participant, all site staff must use the CTSU OPEN Slot Reservation System to ensure that a slot on the protocol is available to the participant. Once a slot reservation confirmation is obtained, site staff may then proceed to enroll the participant to this study.

If specific person-level attributes (e.g., neurocognitive certification, surgical credentialing) are required for site staff before enrollment, add to bulleted list above.

a. The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

b. Further instructional information is provided on the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org or at https://open.ctsu.org. For any additional questions contact the CTSU Help Desk at 888/823-5923 or ctsucontact@westat.com.

If applicable, add language to describe site reimbursements for specific tests and/or bio-specimen submissions that may trigger additional funding.

c. *For example, site submission of optional or conditional blood draws:* To receive site reimbursement for specific tests and/or bio-specimen submissions, completion dates must be entered in the OPEN Funding screen post registration. Refer to the protocol-specific funding page on the CTSU members' website for additional information *(Protocol xxx >Funding Information).* Timely entry of completion dates is recommended as this will trigger site reimbursement.

13.7 Exceptions to SWOG registration policies will not be permitted.

a. Participants must meet all eligibility requirements.

b. Institutions must be identified as approved for registration.

c. Registrations may not be cancelled.

d. Late registrations (after initiation of treatment) will not be accepted.

14.0 DATA SUBMISSION SCHEDULE

Data submission schedule will be created by the stat center using the format below.

14.1 Data Submission Requirement

Data must be submitted according to the protocol requirements for ALL participants registered, whether or not assigned treatment is administered, including participants deemed to be ineligible. Participants for whom documentation is inadequate to determine eligibility will generally be deemed ineligible

14.2 Master Forms

Master forms can be found on the protocol abstract page on the SWOG website (www.swog.org) and the CTSU website (www.ctsu.org) and (with the exception of the sample consent form and the Registration Worksheet) must be submitted on-line via the Web; see below for details.

14.3 Data Submission Procedures

a. Data collection for this study will be done exclusively through the Medidata Rave® clinical data management system. Medidata Rave is a clinical data management system being used for data collection for this trial/study. Access to the trial in Rave is controlled through the CTEP-IAM system and role assignments. To access Rave via iMedidata:

- Site staff will need to be registered with CTEP and have a valid and active CTEP-IAM account; and
- Assigned one of the following Rave roles on the relevant Lead Protocol Organization (LPO) or Participating Organization roster at the enrolling site: Rave CRA, Rave Read Only, Rave CRA (LabAdmin), Rave SLA, or Rave Investigator. Refer to https://ctep.cancer.gov/investigatorResources/default.htm for registration types and documentation required.
    - To hold Rave CRA or Rave CRA (Lab Admin) role, site staff must hold a minimum of an AP registration type;
    - To hold Rave Investigator role, the individual must be registered as an NPIVR or IVR; and
    - To hold Rave Read Only role, site staff must hold an Associates (A) registration type.

If the study has a Delegation of Tasks Log (DTL), individuals requiring write access to Rave must also be assigned the appropriate Rave tasks on the DTL.

Upon initial site registration approval for the study in Regulatory Support System (RSS), all persons with Rave roles assigned on the appropriate roster will be sent a study invitation e-mail from iMedidata. To accept the invitation, site staff must log into the Select Login (https://login.imedidata.com/selectlogin) using their CTEP-IAM user name and password, and click on the "accept" link in the upper right-corner of the iMedidata page. Site staff will not be able to access the study in Rave until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learnings (eLearnings), and can be accessed by clicking on the link in the upper right pane of the iMedidata screen. If an eLearning is required and has not yet been taken, the link to the eLearning will appear under the study name in iMedidata instead of the Rave EDC link; once the successful completion of the eLearning has been recorded, access to the study in Rave will be granted, and a Rave EDC link will display under the study name.

Site staff that have not previously activated their iMedidata/Rave account at the time of initial registration approval for the study in RSS will also receive a separate invitation from iMedidata to activate their account. Account activation instructions are located on the CTSU website, Rave tab under the Rave resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on iMedidata/Rave is available on the CTSU members' website in the Data Management > Rave section at www.ctsu.org/RAVE/ or by contacting the CTSU Help Desk at 1-888-823-5923 or by e-mail at ctsucontact@westat.com.

b. You may also access Rave® via the SWOG CRA Workbench via the SWOG website (www.swog.org).

For difficulties with the CRA Workbench, please email technicalquestion@crab.org.

(For studies using CTSU)

c. Institutions participating through the Cancer Trials Support Unit (CTSU), please refer to the CTSU Participation Table.

(For studies using Central Monitoring Review using the CTSU Source Document Portal– This is limited to registration studies.)

d. Central Monitoring Review using the CTSU Source Document Portal

Central Monitoring (CM) Review is required for this protocol. CM allows Lead Protocol Organizations (LPOs) to remotely compare data entered in Rave to source documentation to ensure that sites are adhering to the protocol and central monitoring plan as well as accurately transcribing data from participants' charts (i.e., source data verification).

Sites can upload source documents required for CM Review as documented in the central monitoring plan using the Source Document Portal (SDP). This application is available on the CTSU members' website under Auditing & Monitoring and may also be accessed using a direct link within Rave on the CM Alert form. Site staff with the CRA or Investigator roles in Rave can view and upload source documents. Prior to saving source documents on the SDP, each site is responsible for removing or redacting any Personally Identifiable Information (PII) (note that functionality to do this redaction exists within the SDP itself). Designated LPO staff will review each document after it has been loaded on the SDP to ensure the appropriate documents have been uploaded and to ensure PII is redacted.

Additional information on the SDP is available on the CTSU members' website under Auditing & Monitoring > Source Document Portal in the Help Topics button

or by contacting the CTSU Help Desk (1-888-823-5923 or ctsucontact@westat.com).

- *Include CM requirements determined by the LPO or Lead Academic Organization (LAO) and NCI in this section.*
- *Note to LPO: All LPOs have access to view information related to source document submissions for their associated protocols on the Source Document Portal (SDP) located in the Auditing & Monitoring section of the CTSU website. LPO staff with roles of CM Triage and CM Review on the CTSU roster in RSS can view uploaded source documents to perform triage and review for central monitoring. LPOs are responsible for completing the OPEN-Rave checklist for the study and submitting it to the CTSU. Identifying the study as requiring central monitoring on the OPEN-Rave checklist alerts the CTSU to set the Central Monitoring flag in RSS. LPOs must set up all data points requiring CM Review in Rave prior to submitting the OPEN-Rave checklist to the CTSU. Once the Central Monitoring flag in RSS is set, the SDP will start pulling data from Rave.*

14.4 Data Submission Overview and Timepoints

Commented [RCJ3]: Need to have Vital Status form included every time a form is to be submitted in Rave.

(include the following statements/forms as applicable)

a. WITHIN 15 DAYS OF REGISTRATION: ***(Insert pre-registration /baseline forms)***

Submit the following:

Onstudy Forms

Pre-Registration/Baseline Abnormalities Form (for full CDUS studies only)

Commented [MC4]: Should all the "baseline" text be updated to "pre-registration"?

Pre-Registration/Baseline Tumor Assessment Form

Pathology Report

Submit radiology reports from all scans performed to assess disease at baseline.

Specimens as outlined in Section 15.0

b. WITHIN XX DAYS AFTER REGISTRATION:

Submit the following:

Additional Study Specific Forms/Scan Images /Specimen submission

c. WITHIN 15 DAYS AFTER EACH CYCLE OF TREATMENT

Submit the following:

Vital Status Form

Treatment Form

Adverse Event Form

Follow Up Tumor Assessment Form

d. WITHIN 15 DAYS AFTER EACH DISEASE ASSESSMENT UNTIL PROGRESSION:

Submit the following:

Vital Status Form
Disease Assessment<<put in appropriate name of disease assessment form>>
Form documenting results of assessment

Pathology Report <if applicable>

Submit radiology reports from all scans performed to assess disease.

Additional study specific reports/forms

e. WITHIN 15 DAYS OF DISCONTINUATION OF TREATMENT:

Submit the following:

Vital Status Form

Off Protocol Treatment Notice

Final Treatment Form

Final Adverse Event Form

WITHIN 15 DAYS OF PROGRESSION/RELAPSE:

Submit Vital Status Form and ***(Insert form name)*** (if the participant was still on protocol treatment) or Follow-Up Form (if the participant was off protocol treatment) documenting date, site and method for determining progression/relapse.

f. Within 30 days of EVERY Follow-up *TIMEFRAME (e.g. every 3 months for first year, every 6 months for second and third years, then annually until 5 years from registration)*

Submit the following:

Vital Status Form
Follow Up Form

Late Adverse Events (if prior to treatment for progression or relapse or a second primary, and prior to non-protocol treatment, the participant experiences any severe [Grade ≥ 3] adverse event that is possibly, probably, or definitely related to protocol treatment, or a Serious Adverse Event [SAE] of any grade/attribution, that has not been previously reported).

g. WITHIN 30 DAYS OF DECLARATION OF LOST TO FOLLOW-UP, REFUSAL OF ANY FOLLOW-UP, OR A MAXIMUM FOLLOW-UP OF **X** YEARS".

Vital Status Form
End of Study Form

Note: this is for registrational intent studies to indicate
The last statement in this section is:

h. WITHIN 4 WEEKS OF KNOWLEDGE OF DEATH:

Submit the Notice of Death **and a final** ***(Insert form name)*** (if the participant was still on protocol treatment) or Follow-Up Form (if the participant was off protocol treatment) documenting death information.

15.0 SPECIAL INSTRUCTIONS

15.1 Title for Non-Standard Registration Requirements

If site is required to meet any non-standard requirements prior to registering a participant, include those instructions in Section 15.1. Examples: training, submitting CDA, credentialing, etc. Throughout the protocol, refer the reader to this section as often as possible.

15.2 SHIPPING SAMPLES

a. SWOG Specimen Tracking System (STS)

All specimen submissions for this study must be entered and tracked using the SWOG online Specimen Tracking system. SWOG members may log on the online system via the CRA Workbench. To access the CRA Workbench, go to the SWOG Web site (http://swog.org) Non- SWOG users may log into SpecTrack using their CTSU UserID and password on the SpecTrack login page located at https://spectrack.crab.org (select the option "SWOG – SWOG – CTSU"). SpecTrack start-up instructions (both written and demo) are available after signing in to SpecTrack.

A copy of the Shipment Packing List produced by the online Specimen Tracking system should be printed and placed in the pocket of the specimen bag if it has one, or in a separate resealable bag.

ALL SPECIMENS MUST BE LOGGED VIA THIS SYSTEM; THERE ARE NO EXCEPTIONS.

(NOTE: If a specimen had an incomplete submission, this must be documented in the Specimen Tracking System under "Special Instructions" at time of specimen submission. If no specimen was available, this must be documented in the Specimen Tracking System by choosing "Notify that Specimen Cannot be Submitted"). **<additional language should be included if lack of specimen will deem the participant ineligible or if they can continue with the study>**

To report technical problems with Specimen Tracking, such as database errors or connectivity issues, please send an email to technicalquestion@crab.org. For procedural help with logging and shipping specimens, there is an introduction to the system on the Specimen Tracking main page (https://spectrack.crab.org/Instructions); or contact the SWOG Statistics and Data Management Center at 206/652-2267 to be routed to the Data Coordinator for further assistance.

In the online specimen tracking system, the appropriate SWOG laboratory for submission of ***type of specimens*** samples for SWOG Repository Submission and ***type of testing*** testing is identified as follows:

Lab #XXX: LAB NAME (DO NOT INCLUDE ADDRESS)
Phone: XXX/XXX-XXXX
Contact: CONTACT PERSON

b. Federal guidelines for the shipment of blood products:

a. The tube must be wrapped in an absorbent material.

b. The tube must then be placed in an AIRTIGHT container (like a resealable bag).

c. Pack the resealable bag and tube in a Styrofoam shipping container.

d. Pack the Styrofoam shipping container in a cardboard box.

e. Mark the box "Biohazard".

15.3 Translational Medicine and Banking (***REQUIRED*** or ***REQUIRED*** IF PARTICIPANT CONSENTS*) choose*

This section is optional. It is usually used to give instructions for submitting specimens for correlative studies. The Ops Office will write this section AFTER a translational medicine plan has been approved by the SWOG Executive Committee.

Option #1: For specimens being sent to or routed through the repository using standard collection/submission instructions for all specimens being submitted (i.e. there is no deviation from the standard website instructions in quantity or specimen type) use the following:

Specimens for translational medicine and banking (submitted to the SWOG Specimen Repository – Solid Tissue, Myeloma and Lymphoma Division, Lab #201 *OR* SWOG Specimen Repository – Leukemia Division, Lab #200) (*include either* required *or* optional for participant):

a. (*If optional include* "With participant's consent") Specimens must be submitted at the following times (see Section(s) 9.0)

1. INSERT SPECIMEN TYPE(S)/TIMEPOINTS

b. Specimen Collection and Submission Instructions

All specimen submissions for this study must be entered and tracked using the SWOG online Specimen Tracking system. Complete specimen collection and submission instructions can be accessed on the SWOG Specimen Submission webpage (https://www.swog.org/member-resources/biospecimen-resources). If collection/submission instructions differ from those in the protocol, the protocol instructions should be followed; otherwise, the website instructions should be followed.

If specimen collection kits are being supplied insert the following:

c. Specimen collection kits may be ordered by using the SWOG Specimen Repository Management Application at http://ricapps.nationwidechildrens.org/BPCKitManagement.

If specimen collection kits are NOT being supplied insert the following:

d. Specimen collection kits are not being provided for this submission; sites will use institutional supplies.

Option #2: ***For protocols that use non-standard specimens or specimen submission (i.e. collection and/or submission deviate from standard website instructions) include the following:***

15.4 Specimens for TM STUDY NAME (***REQUIRED*** or ***REQUIRED IF PARTICIPANT CONSENTS***) *choose*:

a. (*If optional include* "With participant's consent") Specimens must be submitted at the time points listed below. Collection instructions are outlined in Section 15. and submission instructions are outlined in Section 15._.

b. (*If optional include* "With participant's consent") Specimens must be submitted at the following times (see Section(s) 9.):

1. INSERT SPECIMEN TYPE(S)/TIMEPOINTS

c. INSERT PROTOCOL SPECIFIC SPECIMEN COLLECTION INSTRUCTIONS

If specimen collection kits are being supplied insert the following:

d. Specimen collection kits may be ordered by INSERT INSTRUCTIONS.

If specimen collection kits are NOT being supplied insert the following:

d. Specimen collection kits are not being provided for this submission; sites will use institutional supplies.

15.5 Imaging Submission Requirements (***REQUIRED*** or ***REQUIRED IF PARTICIPANT CONSENTS***) *choose*:

(include if appropriate): Type of images must be locally read and interpreted by the local site radiology service. ***Type of images*** must then be submitted to the Imaging and Radiation Oncology Core (IROC) at Ohio via TRIAD Imaging Submission procedures for central data collection and quality control (QC) check as well as central review.

a. Image Submission Time Points:

Digital image submission is required at the following time points ***(± insert appropriate window of allowable submission if different from best practices)***:

- ***Timepoints***

b. TRIAD Digital Image Submission

Transfer of Images and Data (TRIAD) is the American College of Radiology's (ACR) image exchange application. TRIAD provides sites participating in clinical trials a secure method to transmit DICOM RT and other objects. TRIAD anonymizes and validates the images as they are transferred.

1. TRIAD Access Requirements:

TRIAD will be the sole means of image transfer to the IROC Ohio. TRIAD should be installed prior to study participant enrollment to ensure prompt secure, electronic submission of imaging.

- Site staff who submit images via TRIAD will need to register with CTEP and have a valid and active CTEP-IAM account (see ***Section 13.X***).
  - Must be registered as an Associate, Associate Plus, Non-Physician Investigator, or Investigator registration type. Refer to the CTEP Registration Procedures section for instructions on how

to request a CTEP-IAM account and complete registration in Registration and Credential Repository (RCR).

- To submit images, site staff must hold the 'TRIAD Site User' role on the NCTN or ETCTN roster. All individuals on the Imaging and Radiation Oncology Core provider roster have access to TRIAD, and may submit images for credentialing purposes, or for enrollments to which the provider is linked in OPEN.

2. TRIAD Installations:

To submit images, the individual holding the TRIAD Site User role will need to install the TRIAD application on their workstation. TRIAD installation documentation is available at: https://triadinstall.acr.org/triadclient/.

This process can be done in parallel to obtaining your CTEP-IAM account username and password and RCR registration.

For questions, contact TRIAD Technical Support staff via email TRIAD-Support@acr.org or 1-703-390-9858.

Example of Image Submission Section: (may be customized to fit the study, but TRIAD information should remain if using TRIAD; note that AG Mednet information should replace TRIAD information if AG Mednet will be used).

15.6 Quality of Life Submission Requirements (**REQUIRED or REQUIRED IF *PARTICIPANT CONSENTS***)

This section is optional. It is usually used to give instructions for submitting questionnaires for QOL studies. The Ops Office will write this section AFTER a quality of life plan has been approved by the SWOG Executive Committee (Triage). QOL study chairs, objectives, background, rational, eligibility, endpoints, statistical plan, and analysis should be included in the appendix.

<Include title, if applicable>

a. Timepoints

b. Site Directions for Administering Questionnaires

16.0 ETHICAL AND REGULATORY CONSIDERATIONS

Current standard language will be inserted by the Ops Office
PCs, add from S:\PROTOCOL COORDINATION\PC STANDARDS\SECTION 16.0

17.0 BIBLIOGRAPHY

1. ***This is where endnotes will start***

18.0 APPENDIX

Insert appendices as necessary

18.1 Translational Medicine if TM appendix is used, also include banking logistics

The Ops Office will write this section AFTER a TM plan has been approved by the SWOG Executive Committee (Triage). TM study chairs, objectives, background, rational, eligibility, endpoints, statistical plan, and analysis should be included in the appendix.

18.2 Quality of Life if *QOL will be included*
The Ops Office will write this section AFTER a quality of life plan has been approved by the SWOG Executive Committee (Triage). QOL study chairs, objectives, background, rational, eligibility, endpoints, statistical plan, and analysis should be included in the appendix

18.3 Central Monitoring ***(if registrational intent study)***

18.4 APPENDIX D PARTICIPANT DRUG INFORMATION HANDOUT AND WALLET CARD

[need instructions for when it is appropriate – CTEP will supply for CTEP -Held INDs]

Commented [MC5]: Need instructions

Information for Participants, Their Caregivers, and Non-Study Healthcare Team on Possible Interactions with Other Drugs and Herbal Supplements

[Note to authors: This appendix consists of an "information sheet" to be handed to the participant at the time of enrollment. Use or modify the text as appropriate for the study agent, so that the participant is aware of the risks and can communicate with their regular prescriber(s) and pharmacist. A convenient wallet-sized information card is also included for the participant to clip out and retain at all times. If you choose to use them, please note that the information sheet and wallet card will require IRB approval before distribution to participants.]

The participant _____ is enrolled on a clinical trial using the experimental study drug, *[insert study drug name]*. This clinical trial is sponsored by the [SWOG/National Cancer Institute]. This form is addressed to the participant, but includes important information for others who care for this participant.

These are the things that you as a healthcare provider need to know:

[Use or delete sections below as appropriate.]

[Insert study drug name] interacts with *[(a) certain specific enzyme(s) in your liver*, certain transport proteins that help move drugs in and out of cells**, the heart's electrical activity (QTc prolongation)***]* .

- *The enzyme(s) in question is/are ***[name(s) of CYP isoenzyme(s)]***, and *[insert brief, easy explanation of the nature of the interaction,* i.e., *for substrates: "[insert study drug name] is broken down by this enzyme and may be affected by other drugs that inhibit or induce this enzyme."]*
- **The protein(s) in question is/are ***[name of transporter(s)]*** and *[insert brief, easy explanation of the nature of the interaction,* i.e., *for substrates: "[insert study drug name] is moved in and out of cells/organs by this transport protein."]*
- ***The heart's electrical activity may be affected by *[insert study drug name]*. The study doctor may be concerned about QTc prolongation and any other medicine that is associated with greater risk for having QTc prolongation.

To the participant: Take this paper with you to your medical appointments and keep the attached information card in your wallet.

[Insert study drug name] may interact with other drugs which can cause side effects. For this reason, it is very important to tell your study doctors of any medicines you are taking before you enroll onto this clinical trial. It is also very important to tell your doctors if you stop taking any regular medicines, or if you start taking a new medicine while you take part in this study. When you talk about your current medications with your doctors, include medicine you buy without a prescription (over-the-counter remedy), or any herbal supplements such as St. John's Wort. It is

helpful to bring your medication bottles or an updated medication list with you.

Many health care providers can write prescriptions. You must tell all of your health care providers (doctors, physician assistants, nurse practitioners, pharmacists) you are taking part in a clinical trial.

These are the things that you and they need to know:

[Insert study drug name] must be used very carefully with other medicines that use certain ***[liver enzymes or transport proteins to be effective or to be cleared from your system or that may affect your heart's electrical activity]***. Before you enroll onto the clinical trial, your study doctor will work with your regular health care providers to review any medicines and herbal supplements that are considered ***["strong inducers/inhibitors or substrates]*** of ***[name(s) of CYP isoenzyme(s)], [transport protein(s), or any medicine associated with greater risk for having QTc prolongation."]***

- Please be very careful! Over-the-counter drugs (including herbal supplements) may contain ingredients that could interact with your study drug. Speak to your doctors or pharmacist to determine if there could be any side effects.
- *[Add other specific medications here, if necessary. Examples include acid suppressing drugs, anticoagulants, NSAIDS, digoxin.]*
- Your regular health care provider should check a frequently updated medical reference or call your study doctor before prescribing any new medicine or discontinuing any medicine. Your study doctor's name is

  _____ and he or she can be contacted at

  _____.

STUDY DRUG INFORMATION WALLET CARD

You are enrolled on a clinical trial using the experimental study drug _____. This clinical trial is sponsored by the [SWOG or NCI]. _____ may interact with drugs that are ***[processed by your liver, or use certain transport proteins in your body or affects the electrical activity of your heart]***. Because of this, it is very important to:

- Tell your doctors if you stop taking any medicines or if you start taking any new medicines.
- Tell all of your health care providers (doctors, physician assistants, nurse practitioners, or pharmacists) that you are taking part in a clinical trial.
- Check with your doctor or pharmacist whenever you need to use an over-the-counter medicine or herbal supplement.

_____ interacts with a ***[specific liver enzyme called CYP_____, transport protein, heart's electrical activity (QTc prolongation]***, and must be used very carefully with other medicines that interact with ***[this enzyme, transporter, or agent]***.

- Before you enroll onto the clinical trial, your study doctor will work with your regular health care providers to review any medicines and herbal supplements that are considered ***"[strong inducers/inhibitors or substrates of CYP_____, or transporter; or affect the heart's electrical activity.]***"
- Before prescribing new medicines, your regular health care providers should go to a frequently-updated medical reference for a list of drugs to avoid, or contact your study doctor.
- Your study doctor's name is _____

  and can be contacted at _____.

MODEL CONSENT FORM (S:\PROTOCOL COORDINATION\PC STANDARDS\ NCI_Informed_Consent_Template)

The Model Informed Consent Form is separate from the protocol but will be submitted to CTEP/DCP in conjunction with the protocol. The MCF is preceded by "Notes for Local Institution Consent Form Authors" and "Notes for Local Investigators." The study - as well as the local consent form meeting the guidelines noted in these documents - must be reviewed and approved by the Institutional Review Board prior to registration and treatment of participants on this study.

Using the following information provided by the Study Coordinator, the Ops Office will write the informed consent document:

- ***Please provide a list of options that the participant has, other than being on this study.***
- ***Please provide a list of the risks for each treatment regimen in layman's terms. Categorize each risk as either "likely", "less likely" or "rare but serious". Also, in the "likely" and "less likely" categories, please identify those side effects that may be serious.***
- ***Please classify all tests and procedures as one of the following: (1) part of regular cancer care, (2) part of regular cancer care, but being done more frequently because the participant is on this study, or (3) being tested or being done to see how the study is affecting the participant.***

Placebo: These capsules do not contain any medication. These capsules will look just like the capsules containing _____, however, there should not be any side effects.