**GUIDANCE/INSTRUCTIONS**

**Remove this page before finalizing and distributing the clinical trial protocol.**

This template was designed using the following guidances:

* + ICH E6(R3) Good Clinical Practice
  + ICH E9 Statistical Principles for Clinical Trials
  + Grants.nih.gov/policy/clinical-trials/protocol-template.htm – IND/IDE Protocol Word Template
  + https://ctep.cancer.gov/protocolDevelopment/templates\_applications.htm#policiesAndGuidelines

Protocol template instructions:

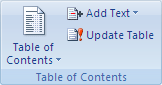
1. This template has been created to assist in the development of an interventional investigator-initiated trial (IIT) protocol. It is not mandatory that you follow the exact order presented in this template (although this is the preferred format for studies that will utilize the Clinical Trials Office (CTO). However, all the information contained in this template must be present, in some format, in your final protocol.
2. *Red italicized font describes what should be written in a given section. Delete the red-italicized verbiage from your final version of the protocol.*
3. Black plain font indicates boilerplate or example text that can be used if appropriate.
4. Sections are organized into Headings, Heading 1, Heading 2, and Heading 3. We recommend not editing or changing Heading 1, but subsequent headings can be edited as you see fit. The Heading formatting can be found under *Microsoft Word Applying Styles.* **Please retain this formatting** as it will create and automatically update the Table of Contents (TOC) and convert to Bookmarks in final PDF*.*

|  |
| --- |
| **MS Word Style Features** |
| word-style-word-document-style-ribbon-1 |

1. To update the TOC in your protocol document:

MS Word 2007 or later

1. Under the **References** tab, in the **Table of Contents** group, click **Update Table**.



Click **Update entire table**.

MS Word 2003

1. Click the table of contents.
2. Press F9.

**Please do not edit the TOC manually.**

1. Please Ensure that the **Title Page** is page 1.

|  |  |
| --- | --- |
| **Title:** |  |
| **Protocol Number:** | <Unique identification Number> *(Assigned by IRB)* |
| **IND #:** | <Number if applicable> |
| **National Clinical Trials (NCT)#:** | <Number if available> |
| **Principal Investigator:** | <Name/Credentials> *(One person only – may not be a resident/fellow)*  Institute/Department or division  Address  City, state, Zip  Phone:  Fax:  Email: |
| **Sponsor/ Research Coordinating Center:** | University of Arizona Cancer Center  1515 N. Campbell  Tucson, AZ 85719 |
| **Funded by: *(if applicable) or***  **Source of Support: *(for instances where only study drug is provided)*** |  |
| **Study Agent (if applicable):** |  |
| **Version (s) and Dates(s)** | V. X.X, <MM/DD/YYYY> |

|  |  |
| --- | --- |
| Study Synopsis | |
| Title | *Full Title* |
| Version | *Current protocol version number* |
| Funder | *Grant agency, pharmaceutical company, or departmental funds* |
| Study Center(s) | *If multicenter, list all projected centers to be involved & indicate who the lead site will be.* |
| Patient population | *Specify the sample size, gender, age, demographic group, general health status, geographic location, and number of patients.* |
| Rationale for Study | *Provide a brief description of the rationale for the study; this should only be a few sentences in length.* |
| Primary Objective | *Include the primary objective(s). The objective(s) should be the same as the objectives contained in the body of the protocol. These align with Primary Purpose in clinicaltrials.gov.* |
| Secondary Objective | *Include the secondary objective(s). The objective(s) should be the same as the objectives contained in the body of the protocol.* |
| Exploratory Objectives | *Include exploratory objectives (if applicable). See instructional text in Section 2.3 below for recommendations regarding exploratory objectives.* |
| Study Design | *Indicate the phase, if single site or multi-site, type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design, adaptive design, platform/umbrella/basket, trials with decentralized elements)* |
| Study Drug, Dose, and route of administration | *If the study intervention is a drug or biologic, Include name of study drug, dose and route of administration.* |
| Duration of study | *Estimated time (in months) from when the study opens to enrollment until completion of data analyses.* |
| Participant Duration | *Time (e.g., in months) it will take for each individual participant to complete all participant visits.* |

# Investigator Agreement

I have read, understand, and will adhere to the protocol as written. The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form will be obtained before any participant is enrolled. Any changes to the protocol will be approved by the study Principal Investigator and the IRB, except changes to eliminate an immediate hazard to study subjects. All changes to the consent form will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

I agree to conduct this study in accordance with the current International Conference on Harmonization (ICH) guidance, the Good Clinical Practice (GCP) guidance, the Declaration of Helsinki, FDA regulations, local IRB and legal requirements.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature Date (MM/DD/YY)

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Name of Principal Investigator

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# Background and Rationale

*No text is to be entered in this section; rather, it should be included under the relevant subheadings below.*

*The following subsections should include relevant background information and rationale for the clinical trial. This should be a brief overview (e.g., approximately 3-7 pages). Referring to the Investigator’s Brochure (IB) for more detail is also appropriate. The information should be written at manuscript or close to manuscript quality.*

## Background

* *Summary of findings from non-clinical studies that are potentially clinically significant.*
* *Summary of finding from clinical studies that are relevant to the trial.*
* *Reference to literature and data that are relevant to the trial and that provide background for the trial.*
* *Description of Investigational Product (IP) (if applicable)*
* *Description of and justification for the route of administration, dosage, dosage regimen and treatment period(s).*

<Insert Text>

## Study Rationale

*State the problem or question (e.g., describe the population, disease, current standard of care, if one exists, and limitations of knowledge or available therapy) and the reason for conducting the clinical trial.*

<Insert Text>

## Description of Population

<Insert Text>

## Potential Risks and Benefits

### Known Potential Risks

* *Refer to package insert/ investigator brochure for known potential risks in humans from both pre-clinical and clinical studies.*
* *If risk information cannot be described from the package insert, relevant published literature can also provide relevant risk information.*
* *In addition to the above describe any physical, psychological, social, legal, economic or other risks that may be associated with the study.*

<Insert Text>

### Known Potential Benefits

* *Refer to package insert/ investigator brochure for known potential benefits in humans from both pre-clinical and clinical studies.*
* *In addition, relevant literature can also provide potential relevant benefit information*
* *Describe any physical, psychological, social, legal, or any other potential benefits to individual participants or society in general, as a result of participating in the study.*
* *Provide justification as to why the risks of participation in the study outweigh the value of the information to be gained.*

<Insert Text>

# Objectives and Endpoints

*For purposes of registration and reporting to ClinicalTrials.gov, the terms Objectives and Endpoints as used in this template align with the terms Primary Purpose and Outcome Measures in ClinicalTrials.gov, respectively.*

*An objective is the purpose for performing the study in terms of the scientific question to be answered. Express each objective as a statement of purpose (e.g., to assess, to determine, to compare, to evaluate) and include the general purpose (e.g., efficacy, effectiveness, safety) and/or specific purpose (e.g., dose-response, superiority to placebo, effect of an intervention on disease incidence, disease severity, or health behavior).*

*A study endpoint is a specific measurement or observation to assess the effect of the study variable (study intervention). Study endpoints should be prioritized and should correspond to the study objectives and hypotheses being tested.*

*When writing endpoints think SMART:*

* ***Specific*** *– should be complete and accurate*
* ***Measurable*** *– Can you tell what unit of measure will be used for a given outcome measure. If not, it's probably unclear or multiple measures.*
* ***Achievable***
* ***Relevant***
* ***Time bound*** *– Should be a specific time point rather than calendar dates at which the endpoint measure will be assessed from the participant's perspective. All time points should include a standard unit of time (e.g., days, months, weeks). For time-to event (e.g., disease progression, death) the time frame should at minimum include criteria for the event and the estimated period over which the event is assessed (e.g., "date of randomization until the first documented progression or date of death from any cause, whichever came first, assessed up to 100 months").*

## Primary Objectives and Endpoints

|  |  |  |
| --- | --- | --- |
| Objectives | Endpoints | Justification for primary endpoint |
| *The primary objective is the main question. This objective drives statistical planning for the trial (e.g., calculating the sample size to provide appropriate power for statistical testing). It is strongly recommended that you have only one primary objective. For Phase II trials, this will likely be related to efficacy but may also be safety/tolerability.*  <Insert Text> | *The primary endpoint should be the variable capable of providing the most clinically relevant and convincing evidence directly related to the primary objective. This will usually be an efficacy variable but may also be related to safety/tolerability.*  <Insert Text> | *The clinical relevance of the primary endpoint and the validity of the associated measurement procedures should be addressed here.*  <Insert Text> |

## Secondary Objectives and Endpoints

*Note: Results of primary and secondary objectives need to be reported to clinicaltrials.gov 1 year after the primary completion date. Exploratory objectives do not need to be reported.*

|  |  |
| --- | --- |
| Objectives | Endpoints |
| The secondary objective(s) are goals that will provide further information on the use of the intervention.  <Insert Text> | Secondary endpoints should be clearly specified and may include, for example, endpoints related to efficacy, safety, or both. Secondary endpoints are those that may provide supportive information about the study intervention’s effect on the primary endpoint or demonstrate additional effects on the disease or condition. It is recommended that the list of secondary endpoints be short, because the chance of demonstrating an effect on any secondary endpoint after appropriate correction for multiplicity becomes increasingly small as the number of endpoints increases.  <Insert Text> |
| <Insert Text; add/remove rows as needed> | <Insert Text> |

## Exploratory Objectives and Endpoints

*It is strongly recommended to label objectives that are not associated with health outcomes as exploratory.*

|  |  |
| --- | --- |
| Objectives | Endpoints |
| <Insert Text; add/remove rows as needed> | <Insert Text> |
| <Insert Text; add/remove rows as needed> | <Insert Text> |

# Trial Design

*No text is to be entered in this section; rather it should be included under the relevant subheadings below.*

## Overall Design

### Study Characteristics

*This section should include the study Phase, design type, and measures to minimize bias.*

* *Design type e.g., double-blind, placebo-controlled, parallel design, adaptive design, platform/umbrella/basket, trials with decentralized elements)*
* *Measures to minimize bias = randomization and/or blinding*
* *Define criterion for patients to be evaluable.*

<Insert Text>

### Study Arms

*Provide a detailed description of the study arms/groups and intervention assigned to each arm/group.*

<Insert Text>

### Patient Population

*The study population should be appropriate for clinical trial phase and the development stage of the study intervention. Given the continuing challenges in achieving clinically relevant demographic inclusion in clinical trials, it is important to focus on clinically relevant potential participants at the earliest stages of protocol development.*

<Insert Text>

### Number of subjects

*If applicable, provide # of participants per center.*

<Insert Text>

## Subject participation period

### Duration of therapy

*Provide a description of how long subjects should anticipate being on study therapy/intervention.*

<Insert Text>

### Duration of follow-up

*Provide a description of how long subjects should anticipate being on follow-up after completing study therapy/intervention.*

<Insert Text>

## End of study Definition

*A clinical trial is considered completed when participants are no longer being examined or the last participant’s last study visit has occurred.*

Example text provided as a guide, customize as needed:

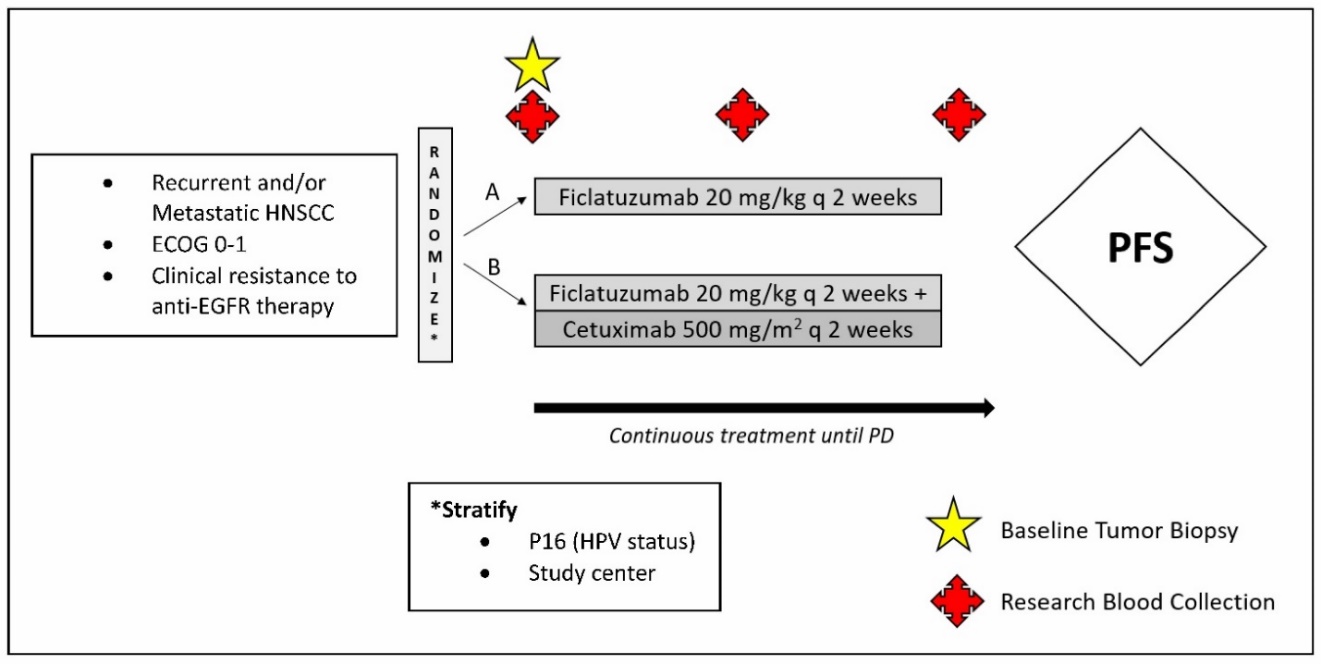
[A participant is considered to have completed the study if he or she has completed all phases of the study including the last visit or the last scheduled procedure shown in the Schedule of Events (SoE), section 8.

The end of the study is defined as completion of the last visit or procedure shown in the SoE in the trial.]

## Study Schema

*This section should include a diagram that provides a quick “snapshot” of the study and ideally be limited to 1 page. Below are examples of schematics that show the level of detail needed to convey an overview of the study design. For assistance with formatting, please reach out to the IIT managers at* [*UACC-IIT@uacc.arizona.edu*](mailto:UACC-IIT@uacc.arizona.edu)*.*

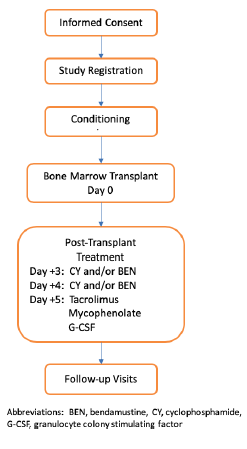
*Example 1:*

****

A screenshot of a cell phone

Description automatically generated*Example 2:*

*Example 3:*



# Eligibility Criteria

Investigators will maintain an electronic subject log (in the UACC OnCore system) of all potential (i.e., consented) study subjects, which will include as applicable (demographics, informed consent, eligibility, treatment assignment, on treatment, off treatment, follow up and off study dates). The target population for this study is patients with [*insert detail*].

*For assistance with drafting the inclusion/exclusion criteria below, the following reference is recommended: CTEP recommendations on eligibility,* [*broadened inclusion/exclusion criteria document released 9/26/2018*](https://ctep.cancer.gov/protocolDevelopment/templates_applications.htm#policiesAndGuidelines)

## Inclusion Criteria

<Insert Text>

## Exclusion Criteria

<Insert Text>

## Enrollment

*Keep the below language:*

Screening of patients’ medical records prior to obtaining informed consent is acceptable if the IRB has approved a waiver of PHI authorization. HIPAA authorization will be obtained from all patients through the informed consent form. Eligibility criteria will be confirmed by the principal investigator ensuring all criteria listed above are met.

All subjects who complete the screening period of the study will be <registered *and/or* randomized *(edit accordingly)*> and assigned a unique sequential subject identification number. This number will be used to identify the subject throughout the clinical study and will be used on all applicable study documentation related to that subject. The subject identification number will remain constant throughout the study.

The written informed consent document(s) must be signed and personally dated by the subject or by the subject’s legally authorized representative and completed to a fully executed informed consent document and processed per the institution standard operating procedures.

Before subjects may be entered into the study, a copy of the written institutional review board (IRB) approval of the protocol, informed consent form (ICF), and all other applicable subject information and/or recruitment material must be on file at the institution.

## Screen Failures

Participants who are consented to participate in the clinical trial, who do not meet one or more criteria required for participation in the trial during the screening procedures, are considered screen failures. Indicate how screen failures will be handled in the trial, including conditions and criteria upon which re-screening is acceptable, when applicable.

Example text provided as a guide, customize as needed:

[Screen failures are defined as participants who consent to participate in the clinical trial but are not subsequently randomly assigned to the study intervention or entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

Individuals who do not meet the criteria for participation in this trial (screen failure) because of a <specify modifiable factor> may be rescreened. Rescreened participants should be assigned the same participant number as for the initial screening.]

# Withdrawal of Consent or Discontinuation of Participation

## Discontinuation of study intervention

Example text provided as a guide, customize as needed:

[Discontinuation from <study intervention> does not mean discontinuation from the study, and remaining study procedures should be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

* <Describe the procedures and data to be collected, as well as any follow-up evaluations>]

## Participant discontinuation/withdrawal from the study

Describe the type and timing of data to be collected for withdrawn/discontinued participants, including the process by which the data are handled, in accordance with applicable regulatory requirements. Also, describe any required follow-up procedures for participants who have discontinued the intervention, i.e., will patients still be assessed for adverse events and how long; will they still need to complete the follow-up/ final study visits; etc.

Example text provided as a guide, customize as needed:

[Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

* Pregnancy
* Significant study intervention non-compliance
* If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
* Disease progression which requires discontinuation of the study intervention
* If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
* Participant unable to receive <study intervention> for [x] days/weeks.

The reason for participant discontinuation or withdrawal from the study will be recorded on the <specify> Case Report Form (CRF). Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, <will> *or* <will not> be replaced.]

## Lost to Follow-up

The protocol should describe the nature and duration of study follow-up. Validity of the study is a potential issue when participants are lost to follow-up, as information that is important to the endpoint evaluation is then lost. Participants are considered lost to follow-up when they stop reporting to scheduled study visits and cannot be reached to complete all protocol-required study procedures. Describe the plans to minimize loss to follow-up and missing data.

Example text provided as a guide, customize as needed:

[A participant will be considered lost to follow-up if he or she fails to return for <specify number of visits> scheduled visits and is unable to be contacted by the study site staff.

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

* The site will attempt to contact the participant and reschedule the missed visit <specify time frame> and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
* Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant’s last known mailing address or local equivalent methods). These contact attempts should be documented in the participant’s medical record or study file.
* Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.]

# Study Drug (if applicable)

*This language can usually be obtained from the drug/agent manufacturer. If the study drug will be supplied commercially, the IDS Pharmacy team can provide/confirm the appropriate language for drug supply, receipt, storage, accountability, and destruction.*

NOTE: For current information, please see the FDA package insert *and/or* the Investigator’s Brochure.

## Potential Risks

<Insert Text>

## Reproductive Safety

<Insert Text>

## Description, Supply, and Storage

### Classification

<Insert Text>

### Description

<Insert Text>

### Mechanism of Action

<Insert Text>

### Metabolism

<Insert Text>

### Supply, receipt, and storage

<Insert Text>

### Drug compliance and accountability

<Insert Text>

### Disposal and destruction

<Insert Text>

### Drug ordering

*This section can be deleted if this information is given under section 6.3.5.*

<Insert Text>

### Packaging and labeling of study drug

<Insert Text>

# Treatment Plan or Study Plan

## Study intervention description

***Give a brief (1-2 paragraphs at most) summary of the trial treatment(s) and the dosage and dosage regimen of the IP, including a description of the dosage form, packaging, and labeling. IP information can usually be obtained from the IB for an investigational drug or biologic and the Package insert for a licensed or approved drug or biologic.***

**<Insert Text>**

## Treatment/intervention administration

* *Instructions for treatment/intervention administration*
* *Dose, route, and schedule including information on what should be done if a dose is missed.*
* *Include in this section any pre-medications and supportive care therapies that may need to be taken prior to the investigational treatment/intervention.*
* *It may be useful to summarize this all in a table format prior to giving details.*

<Insert Text>

## Dose Delays/Dose Modifications

* *If more than one drug/agent is administered, provide a detailed description of dose delays/modifications separately for each agent. This information can usually be obtained from the drug/agent manufacturer.*
* *Example of Dose Modification Table:*

| ***Event*** | **Management/Next Dose for *[Agent Name]*** | **Management/Next Dose for *[Agent Name]*** |
| --- | --- | --- |
| ≤ Grade 1 | *Insert appropriate management guidelines in this column.* | *Insert appropriate management guidelines in this column.* |
| Grade 2 |  |  |
| Grade 3 |  |  |
| Grade 4 |  |  |
| \**Footnote any relevant guidelines regarding how long a delay in therapy is allowed before patients should go off protocol therapy*  \*\**Footnote any relevant guidelines regarding how many dose reductions are allowed before patients should go off protocol therapy.* | | |
| *Insert any recommended management guidelines, if appropriate.* | | |

## Concomitant Medications

### Acceptable Concomitant Medications

<Insert Text>

### Prohibited Concomitant Medications

<Insert Text>

## Rescue Medications & Supportive care

*Example*:

<Insert drug name> will be administered at <insert dose and route> for <insert reason, i.e., grade 2 adverse events>.

## Study intervention compliance

<Insert Text>

# Schedule of Events

*Please keep this layout and edit accordingly. For assistance with formatting, please reach out to the IIT managers at* [*UACC-IIT@uacc.arizona.edu*](mailto:UACC-IIT@uacc.arizona.edu)*. The schedule of activities must capture the procedures that will be accomplished at each study visit, and all contact, with study participants e.g., telephone contacts. This includes any tests that are used for eligibility, participant randomization or stratification, or decisions on study intervention discontinuation. Only include procedures that contribute to participant eligibility and study objectives and endpoints. Other procedures should be done sparingly and with consideration, as they may add unnecessary complexity and detract from recruitment.*

*Allowable windows should be stated for all visits. To determine the appropriate windows, consider feasibility and relevance of the visit time points to study endpoints (e.g., pharmacokinetic (PK) studies may allow little or no variation, with required time points measured in minutes or hours, whereas a 6-month follow-up visit might have a window of several weeks).*

| **Procedures** | Screening  Day -7 to -1 | Enrollment/Baseline  Visit 1, Day 1 | Study Visit 2  Day 7 +/-1 day | Study Visit 3  Day 14 +/- 1 day | Study Visit 4  Day 21 +/-1 day | Study Visit 5  Day 28 +/-1 day | Study Visit 6  Day 35 +/-1 day | Study Visit 7  Day 42 +/-1 day | Study Visit 8  Day 49 +/-1 day | Study Visit 9  Day 56 +/-1 day | Study Visit 10  Day 63 +/-1 day | Study Visit 11  Day 70 +/- 1 day | Study Visit 12  Day 77 +/-1day | Final Study Visit 13 Day 84 +/-1 day |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Informed consent | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Demographics | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Medical history | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Randomization | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Administer study intervention |  | X |  |  | X |  |  | X |  |  | X |  |  |  |
| Concomitant medication review | X | X---------------------------------------------------------------------------------------------X | | | | | | | | | | | |  |
| Physical exam (including height and weight) | X | X |  |  | X |  |  | X |  |  | X |  |  | X |
| Vital signs | X | X |  |  | X |  |  | X |  |  | X |  |  | X |
| Height | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Weight | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| Performance status | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| Hematology | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| serum chemistry a | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Pregnancy test b | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EKG (as indicated) | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Adverse event review and evaluation | X | X---------------------------------------------------------------------------------------------X | | | | | | | | | | | | X |
| Radiologic/Imaging assessment | X |  |  |  | X |  |  |  | X |  |  |  |  | X |
| Other assessments (e.g., immunology assays, pharmacokinetic) | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Complete Case Report Forms (CRFs) | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| a: Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, AST, ALT, sodium.  b: Serum pregnancy test (women of childbearing potential). | | | | | | | | | | | | | | |

# Study Procedures and Assessments

*No text is to be entered in this section; rather, it should be included under the relevant subheadings below.*

*This section should be a detailed discussion of each study visit and all assessments needed to assess efficacy and safety.*

## Screening period & pre-treatment procedures

### Screening evaluations

<Insert Text>

### Registration/Randomization

<Insert Text>

### Mandatory baseline assessments

<Insert Text>

## Treatment/intervention Period

<Insert Text>

## End of treatment/intervention

<Insert Text>

## Follow-up Visits

<Insert Text>

## Early treatment termination

*Example text provided as a guide, customize as needed:*

[Termination is defined as a subject being taken off study treatment for reasons other than treatment completion. Follow up/end of study evaluation procedures will be conducted as described above in section 9.4 for subjects who are terminated early. Subjects who end treatment due to an AE determined to be at least possibly related to the study must be followed up weekly for AE assessment until the AE is resolved, returns to baseline grade, or stabilizes, whichever occurs first.]

## Off study

*Example text provided as a guide, customize as needed:*

[Subjects will be considered off study when all planned treatment, early termination, and follow-up visits have been completed, unless death or withdrawal of consent to continue participation occurs.]

# Correlative/ Special studies

*If the trial does not include correlative studies, this section should be marked as “N/A”.*

<Insert Text>

# Data and Safety Monitoring Plan

***Contact the UACC DSMB Coordinator, Linda Maynard (***[***uacc-dsmb@uacc.arizona.edu***](mailto:uacc-dsmb@uacc.arizona.edu)***) for assistance’ with this section.*** *She will provide the standard language based on the DSM Plan risk level. The risk level will be determined by the DSMB Chair.*

# Statistical Considerations

## Study Endpoints

*For each endpoint clearly state which patients will be considered evaluable.*

### Primary Endpoint

<Insert Text>

### Secondary Endpoint(s)

<Insert Text>

### Exploratory Endpoint(s)

<Insert Text>

## Sample Size

<Insert Text>

## Randomization and Stratification (if applicable)

<Insert Text>

## Protocol Early Stopping Rules/ Safety analysis

<Insert Text>

# Quality control and quality assurance

# Administrative and Regulatory obligations

*No text is to be entered in this section; rather, it should be included under the relevant subheadings below.*

## Institutional Review Board (IRB) Approval and Consent

It is expected that the IRB will have the proper representation and function in accordance with federally mandated regulations. The IRB should approve the consent form and protocol.

In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s) and should adhere to Good Clinical Practice (GCP) and to ethical principles that have their origin in the Declaration of Helsinki.

Before recruitment and enrollment onto this study, the patient will be given a full explanation of the study and will be given the opportunity to review the consent form. Each consent form must include all the relevant elements currently required by the FDA Regulations and local or state regulations. Once this essential information has been provided to the patient and the investigator is assured that the patient understands the implications of participating in the study, the patient will be asked to give consent to participate in the study by signing an IRB approved consent form.

Prior to a patient’s participation in the trial, the written informed consent form should be signed and personally dated by the patient and by the person who conducted the informed consent discussion.

## Changes to the protocol

Amendments to the protocol will be initiated and maintained by the Principal Investigator or protocol writer designee. Requests for revisions may come from multiple sources, including but not limited to the Principal Investigator, study team, drug company, or FDA (if applicable). All amendments will be subject to the review and approval of the University of Arizona (UA) Human Subjects Protection Program and governmental regulatory bodies (if applicable), as well as by [*insert funding Sponsor name if applicable*]. Amendments will be distributed upon approval by the UA Human Subjects Protection Program.

## Deviations

The investigator will conduct the study in conformance with this protocol, generally accepted standards of Good Clinical Practice and all applicable federal, state and local laws, rules, and regulations.

The investigator should not implement any deviation from, or changes of, the protocol without prior review and documented IRB approval of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g. change of monitor(s), change of telephone number(s). A waiver of inclusion/exclusion criteria granted by the sponsor-investigator must be documented and IRB approved prior to implementation.

## Future Use of Stored Specimen and Data

*The information in this section will be study dependent. Common repositories used in UACC IIT research are: Tissue Acquisition and Cellular/Molecular Analysis (TACMASR), Human Immune Monitoring Facility (HIMF), Clinical and Translational Sciences Research Center (CATS), and Tissue Acquisition and Repository for Gastrointestinal and Hepatic Systems (TARGHETS).*

*Example text provided as a guide, customize as needed:*

Data collected for this study will be analyzed and stored at the UACC. After the study is completed, the de-identified, archived data will be transmitted to and stored at <specify name of Biospecimen Repository>, for use by other researchers including those outside of the study.

With the participant’s approval and as approved by local Institutional Review Boards (IRBs), de-identified biological samples will be stored at the <specify name of Biospecimen Repository>. These samples could be used to research the causes of <specify condition(s)>, its complications and other conditions for which individuals with < specify condition(s)> are at increased risk, and to improve treatment.

During the conduct of the study, an individual participant can choose to withdraw consent to have biological specimens stored for future research. However, withdrawal of consent with regard to biospecimen storage may not be possible after the study is completed.  When the study is completed, access to study data and/or samples will be provided through the <specify name of Repository>.]

## Study Discontinuation and Closure

*Example text provided as a guide, customize as needed:*

[This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause.  Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to <study participants, investigator, funding agency, the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor and regulatory authorities>.  If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and funding agency and will provide the reason(s) for the termination or suspension.  Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

* Determination of unexpected, significant, or unacceptable risk to participants
* Demonstration of efficacy that would warrant stopping
* Insufficient compliance to protocol requirements
* Data that are not sufficiently complete and/or evaluable
* Determination that the primary endpoint has been met
* Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB and/or Food and Drug Administration (FDA).]

## Data handling and record keeping

### Case Report Forms

Data Collection for this study will be done through <OnCore Clinical Trial Management system or RedCap>. Access to the trial in <OnCore or RedCap> is granted to appropriate roles identified at the time of study activation, or upon request. Site users will not be able to access the study in <OnCore or RedCap> until all required and study specific trainings are completed.

Once a patient is confirmed and registered to the study, eCRFs should be submitted according to the schedule of events (section 8). Generally, all data are due within 7 business days of a visit or end of cycle. A set amount of data may also be requested for any screen failures, as is defined by the study (section 4.4). In most instances, this will include baseline data from the time of registration to the date of screen failure.

### Record keeping and Record Retention

Study documentation includes all Case Report Forms, data correction forms or queries, source documents, Sponsor-Investigator correspondence, monitoring logs/letters, and regulatory documents (e.g., protocol and amendments, IRB correspondence and approval, signed patient consent forms).

Source documents include all recordings of observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical research study.

Retention and/or destruction of essential paper and electronic documents at the conclusion of the trial is done in accordance with local institution/IRB/IEC policies and procedures as established in U.S. Federal regulations. Government agency regulations and directives require that the study investigator must retain all study documentation pertaining to the conduct of a clinical trial. In the case of a study with a drug seeking regulatory approval and marketing, these documents shall be retained for at least two years after the last approval of marketing application in an International Conference on Harmonization (ICH) region. Per the UA Human Subjects Protection Program, research records will be maintained for 6 years after completion of the research. All paper records will be transferred to UA Records & Archives for archiving 6 months after study completion. IRB records are retained for 6 years following completion of the research for all research studies, whether or not participants are enrolled.

## Investigator responsibilities

The investigator will conduct the study in conformance with this protocol, generally accepted standards of Good Clinical Practice and all applicable federal, state and local laws, rules, and regulations.

The investigator should not implement any deviation from, or changes of, the protocol without prior review and documented IRB approval of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change of monitor(s), change of telephone number(s). A waiver of inclusion/exclusion criteria granted by the sponsor-investigator must be documented and IRB approved prior to implementation.

## Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the sponsor (UACC), and funding agency (if applicable). This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies or pharmaceutical company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant’s contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by UACC requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at UACC Biostatistical & Bioinformatics Shared Resource (BBSR). This will not include the participant’s contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by UACC research staff are secured and password protected.

# ABBREVIATIONS

*The abbreviations are listed in table format; delete and/or add rows as needed.*

*The following abbreviations are used in the protocol template:*

|  |  |
| --- | --- |
| AE | Adverse Event |
| CRF | Case Report Form |
| CTCAE | Common Toxicity Criteria for Adverse Events |
| DLT | Dose Limiting Toxicity |
| DSMB | Data and Safety Monitoring Board |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practice |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonization |
| IND | Investigational New Drug |
| IRB | Institutional Review Board |
| QA/QC | Quality Assurance/Quality Control |
| SAE | Serious Adverse Event |
| SRC | Scientific Review Committee |
| UACC | University of Arizona Cancer Center |

# References

*We recommend using* ***Endnote*** *to insert and format references. If assistance is needed, contact the IIT Managers at* [*UACC-IIT@uacc.arizona.edu*](mailto:UACC-IIT@uacc.arizona.edu)*.*

# Appendices

## Appendix A. Performance Status Criteria

|  |  |  |  |
| --- | --- | --- | --- |
| **ECOG Performance Status Scale** | | **Karnofsky Performance Scale** | |
| Grade | Descriptions | Percent | Description |
| 0 | Normal activity.  Fully active, able to carry on all pre-disease performance without restriction. | 100  90 | Normal, no complaints, not evidence of disease.  Able to carry on normal activity; minor signs or symptoms of disease |
|
| 1 | Symptoms, but ambulatory.  Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (*e.g.*, light housework, office work). | 80  70 | Normal activity with effort; some signs or symptoms of disease  Cares for self, unable to carry on normal activity or to do active work |
|
| 2 | In bed < 50% of the time.  Ambulatory and capable of all self-care, but unable to carry out any work activities.  Up and about more than 50% of waking hours. | 60  50 | Requires occasional assistance but is able to care for most of his/her needs.  Requires considerable assistance and frequent medical care |
|
| 3 | In bed > 50% of the time.  Capable of only limited self-care, confined to bed or chair more than 50% of waking hours. | 40  30 | Disabled, requires special care and assistance.  Severely disabled, hospitalization indicated. Death not imminent. |
|
| 4 | 100% bedridden.  Completely disabled.  Cannot carry on any self-care.  Totally confined to bed or chair. | 20  10 | Very sick, hospitalization indicated. Death not imminent  Moribund, fatal processes, progressing rapidly. |
|
| 5 | Dead. | 0 | Dead. |

## Appendix B. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0

Toxicity will be scored using CTCAE Version 5.0 for toxicity and adverse event reporting. A copy of the CTCAE Version 5.0 can be downloaded from the CTEP homepage (<http://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5X7.pdf>). All appropriate treatment areas should have access to a copy of the CTCAE Version 5.0. All adverse clinical experiences, whether observed by the investigator or reported by the patient, must be recorded, with details about the duration and intensity of each episode, the action taken with respect to the test drug, and the patient’s outcome. The investigator must evaluate each adverse experience for its relationship to the test drug and for its seriousness.

The investigator must appraise all abnormal laboratory results for their clinical significance. If any abnormal laboratory result is considered clinically significant, the investigator must provide details about the action taken with respect to the test drug and about the patient’s outcome.