Document Coversheet

Study Title: Priming Immunotherapy in Advanced Disease With Radiation

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	2/6/2025
NCT Number:	NCT03313804
IRB Number	45336
Coversheet created:	3/18/2025

IMPORTANT NOTE:

If you accidentally select the wrong IRB type or "Protocol Process Type" while your Initial Review (IR) application is in draft form (unsubmitted), you may change your selections. Please contact the Office of Research Integrity (ORI) at 859-257-9428, IRBsubmission@uky.edu, or request a consult to resolve any questions regarding your selections *prior* to submitting your Initial Review application.

If your **submitted IR application has been returned to you for requested revisions or additional information,** to streamline the review process **do not make changes** to your selections here **unless instructed to do so by the ORI/IRB.**

Changes to this section cannot be made after initial approval has been issued (the option is not available for MR or CR).

For guidance, see:

- Which IRB?
- Which Protocol Process Type?
- "Getting Started"

Which IRB

- (•) Medical ( ) NonMedical

Protocol Process Type

- ( ) Exemption
- (•) Expedited (Must be risk level 1)
- ( ) Full

The revised Common Rule expanded exemption certification category 4 for certain secondary research with identifiable information or biospecimens. The regulations no longer require the information or biospecimens to be existing. For more information see the Exemption Categories Tool.

EXPEDITED CERTIFICATION

0 unresolved comment(s)

To Be Completed Only If Protocol is to Receive Expedited Review

Applicability

A. Research activities that (1) present no more than *minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
B. The categories in this list apply regardless of the age of subjects, except as noted.
C. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
D. The expedited review procedure may not be used for classified research involving human subjects.
E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

**"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. 45 CFR 46.102(i)*

Check the appropriate categories that apply to your research project:

☑ Study was originally approved by the full IRB at a convened meeting.

☐ 1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

A. Research on drugs for which an investigational new drug application is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
B. Research on medical devices for which (i) an investigational device exemption application is not required*; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.**

* Study must meet one of the IDE Exempt categories listed on the Device Form Attachment.
** An approved Device used in research according to its approved labeling is considered Exempt from IDE requirements.
NOTE: Select Category 1 for compassionate use medical device applications or individual patient expanded access investigational drug applications for which FDA has waived the requirement for full review.

☐ 2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

A. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
B. From other adults and children* considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

NOTE: Intravenous (IV), Port, Central, or any other lines are NOT eligible under this category even if the research involves "minimal risk".

*In Kentucky, "child/children" refers to all individuals less than 18 years of age unless the individual(s) is/are legally emancipated. (See Informed Consent SOP for discussion of "Emancipated Individuals" under Kentucky state law.) Individuals less than 18 years of age who are not emancipated meet the federal definition for "child" (e.g., DHHS, FDA, and U.S. Department of Education). Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." If conducting research outside the state of Kentucky, you are responsible for complying with applicable state law.

☐ 3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

A. Hair and nail clippings in a nondisfiguring manner;
B. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
C. Permanent teeth if routine patient care indicates a need for extraction;
D. Excreta and external secretions (including sweat);
E. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
F. placenta removed at delivery;
G. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
H. Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
I. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
J. Sputum collected after saline mist nebulization.

☐ 4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

A. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
B. Weighing or testing sensory acuity;
C. Magnetic resonance imaging;
D. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
E. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

☐ 5) Research involving materials (data, documents, records, or specimens) that have been or will be collected solely for non-research purposes (such as medical treatment or diagnosis) as well as research involving existing information or specimens that were previously collected for research purposes, provided they were not collected for the currently proposed research. (Note: Some research in this category may qualify for Exempt review. This listing refers only to research that is not exempt.)
(Note: If submission includes materials previously collected for either non-research or research purposes in a protocol for which IRB approval expired, you may check Category 5. However, a separate category must also be selected for prospective collection of data/specimens obtained solely for research purposes)

☐ 6) Collection of data from voice, video, digital, or image recordings made for research purposes.

☐ 7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.)

CONTINUATION REVIEW/FINAL REVIEW

0 unresolved comment(s)

In accordance with federal regulations and/or local policies, the IRB conducts periodic review of all currently approved projects. If you need your IRB approval to continue and you do not complete and submit the required materials in a timely manner, IRB approval will expire at the end of your current approval period.

If you have any questions, please contact the Office of Research Integrity at 859-257-9428 or email IRBsubmission@uky.edu.

To initiate your continuation review (CR)/annual administrative review (AAR), or properly close your study, complete this section and update/correct all other sections of your IRB application as applicable.
*****IMPORTANT*** Before leaving this page to update other sections of your application, be sure to SAVE this section first.**

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1. Status of the Research

Check the statement(s) that best describe(s) the current status of your research:

- ☐ No subjects have enrolled to date.
- ☐ Recruitment and/or enrollment of new subjects or review of records/specimens continue.
- ☐ Study is closed to enrollment, but subjects still receive research-related interventions (e.g., treatment, blood draws).
- ☑ Study enrollment is permanently closed; subjects have completed all research-related interventions; and the study remains active only for long-term follow-up of subjects (see Tool Tip above for info on long-term follow-up of subjects).*
- ☐ Research has progressed to the point that it involves 1) Data analysis, including analysis of identifiable private information or identifiable biospecimens; and/or 2) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.*
- ☐ The remaining research activities are limited only to data analysis. There is access to records or specimens either directly or through codes or links to the data.*
- ☐ The remaining research activities are limited only to data analysis. There is no subject/record/specimen identifying codes or links to the data; the researcher or research team cannot readily ascertain the subject's identity.*
- ☐ All study activities are complete. IRB approval can be inactivated.

*Possibility that review will move from Full to Expedited.

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2. If subjects have been enrolled within the last year, and the IRB approved a consent/assent form for your study:

Please attach a complete, signed copy for the last two subjects enrolled with **each** consent/assent form/HIPAA form since the last annual review.
(Example: If 3 different approved consent forms were used since the last annual review, please provide the two most recent signed copies of each version for a total of six.)

Attachments

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3. Informed Consent

If the study is **open to subject enrollment, please go to the Informed Consent section of the E-IRB Application and verify attachment(s) include:**

- One clean copy in PDF (without the IRB Approval stamp) of the currently approved consent/assent document(s), or,
- If requesting changes to the consent/assent document(s), submit one copy with the changes highlighted (and designate Document Type as "Highlighted"), and one clean copy in PDF (without the changes highlighted).

If the study is **open to subject enrollment and the IRB has waived the requirement to document informed consent, please go to the Informed Consent section of the E-IRB Application and verify attachment(s) include:**

- One clean copy in PDF of the currently approved document used for the informed consent process (e.g., cover letter, phone script), or,
- If requesting changes to the consent/assent document(s), submit one copy with the changes highlighted (and designate Document Type as "Highlighted"), and one clean copy in PDF (without the changes highlighted).

If the study is **closed to subject enrollment, please go to the Informed Consent section of the E-IRB Application and remove Informed Consent Documents designated to get an IRB approval stamp to avoid having them appear valid for enrollment.**

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4. Unanticipated Problems Involving Risk to Subjects or Others/Adverse Events Summary & Assessment

Did any **problems/adverse events** occur during the last 12 months?

○ Yes ◉ No

In the space below, provide a written summary of both unanticipated problems* and available information regarding adverse events since the last review (e.g., initial review or annual/continuing review). The amount of detail provided in such a summary will vary depending on the type of research being conducted; in many cases, such a summary could be a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and investigator's brochure (if applicable). **The summary must include the PI's assessment whether the problems/adverse events warrant changes to the protocol, consent process, or risk/benefit ratio.**

Note: It is the IRB's expectation that all unanticipated problems involving risk to subjects or others or related deaths requiring prompt reporting are submitted in the appropriate time frame (See Policy [PDF]). Your response to this Annual/Continuing Review is considered assurance that all prompt reportable problems/adverse events have been submitted for IRB review.

*For multisite studies, the written summary should describe external events determined to be unanticipated problems involving risk to subjects or others.

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5. Subject Info To-Date

Our records for the previously approved IRB application indicate the **IRB approved estimate** of subjects to be enrolled (or records/specimens reviewed) is:

100

Enter the number of enrolled subjects (or records/specimens reviewed) that **have not been previously reported** to the IRB

0

Our records for the previously approved IRB application indicate the previous total # of subjects enrolled (or records/specimens reviewed) since activation of the study is:

97

The new total number of subjects enrolled (or records/specimens reviewed) since activation of the study:

97

Please review the Project Info section for the IRB approved estimate of subjects to be enrolled (or records/specimens reviewed). If this new total exceeds your approved estimate of subjects to be enrolled (or records/specimens reviewed), please update the number in the field for Number of Human Subjects in the Project Info section.

6. Data and Safety Monitoring Board (DSMB)/Plan (DSMP)

If your study is monitored by a DSMB or under a DSMP, attach all documentation (i.e. summary report; meeting minutes) representing Data and Safety Monitoring activities that have not been previously reported to the IRB.

Attachments

Attach Type	File Name
CR Data Safety Monitoring Doc	16_MCC-17-MULTI-20-PMC_DSMC Memo_17Jan2025 (TB).pdf
CR Data Safety Monitoring Doc	s1_MCC-17-MULTI-20-PMC_DSMC Findings Memo_17Jan2025 (TB).pdf
CR Data Safety Monitoring Doc	20_MCC-17-MULTI-20-PMC_DSMC Memo_19Apr2024.pdf
CR Data Safety Monitoring Doc	s1-3_MCC-17-MULTI-20-PMC_DSMC Findings Memo_19Apr2024.pdf
CR Data Safety Monitoring Doc	22_MCC-17-MULTI-20-PMC_DSMC Memo_10May2024 - TB (1).pdf
CR Data Safety Monitoring Doc	s4_MCC-17-MULTI-20-PMC_DSMC Findings Memo_10May2024 - TB.pdf
CR Data Safety Monitoring Doc	20_MCC-17-MULTI-20-PMC_DSMC Memo_21Jun2024 - TB.pdf
CR Data Safety Monitoring Doc	ers3_MCC-17-MULTI-20-PMC_DSMC Findings Memo_21Jun2024 - TB.pdf
CR Data Safety Monitoring Doc	17_MCC-17-MULTI-20-PMC_DSMC Memo_26Jul2024.pdf
CR Data Safety Monitoring Doc	20_MCC-17-MULTI-20-PMC_DSMC Memo_16Aug2024.pdf
CR Data Safety Monitoring Doc	MCC-17-MULTI-20-PMC_DSMC Audit Findings Memo_10Sep2024 - MCC (TB).pdf

CR Data Safety Monitoring Doc	min11_MCC-17-MULTI-20-PMC_DSMC Findings Memo_20Sep2024 (TB).pdf
CR Data Safety Monitoring Doc	21_MCC-17-MULTI-20-PMC_DSMC Memo_18Oct2024 (TB).pdf
CR Data Safety Monitoring Doc	s2_MCC-17-MULTI-20-PMC_DSMC Findings Memo_18Oct2024 (TB).pdf
CR Data Safety Monitoring Doc	20_MCC-17-MULTI-20-PMC_DSMC Memo_13Dec2024 (BS).pdf
CR Data Safety Monitoring Doc	s5_MCC-17-MULTI-20-PMC_DSMC Findings Memo_13Dec2024 deferred (BS).pdf

7. Since the most recent IRB Initial/Continuation Review Approval:

Have there been any **participant complaints** regarding the research?

○ Yes ◉ No

If yes, in the field below, provide a summary describing the complaints.

Have any **subjects withdrawn** from the research voluntarily or by you as the PI for reasons related to safety, welfare, or problems related to the conduct of the research? If a participant does not meet the screening criteria for a study even if they signed a screening consent it is NOT considered a withdrawal.

○ Yes ◉ No

If yes, in the field below, provide a detailed explanation to the withdrawal(s) including if participants were lost to contact.

Has any **new and relevant literature** been published since the last IRB review, especially literature relating to risks associated with the research?

○ Yes ◉ No

If yes, attach a copy of the literature as well as a brief summary of the literature including, if pertinent, the impact of the findings on the protection of human subjects.

Attachments

Have there been any **interim findings?**

○ Yes ◉ No

If yes, attach a copy of **Interim Findings**.

Attachments

Have **subjects experienced any benefits?**

○ Yes ◉ No

If yes, in the field below, provide a description of benefits subjects have experienced.

Have there been any **inspections/audits/quality improvement reviews** of your research protocol resulting in the need for corrective action in order to protect the safety and welfare of subjects?

○ Yes ◉ No

If yes, please attach documentation evidencing the outcome(s) and any corrective action(s) taken as a result.

Attachments

Was an FDA 483 issued as a result of any inspections/audits?

○ Yes ◉ No

If yes, submit documentation using attachment button above.

8. Risk Level:

Our records for the previously approved IRB application show your research is:

Risk Level: 2

Has something during the course of your research changed the level of risk?

◉ Yes ○ No

If yes, go to the Risk Level section, mark the appropriate risk level, and in the field below, describe why the risk level has changed:

Study enrollment is permanently closed; subjects have completed all research-related interventions; and the study remains active only for long-term follow-up of subjects- study had been previously reviewed by full committee

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9. Funding/Support:

Our records for the **previously approved** IRB application indicate your research is being submitted to, supported by, or conducted in cooperation with the following external or internal agency(ies) or funding program(s):

- ☐ Grant application pending
- ☐ (HHS) Dept. of Health & Human Services
  - ☐ (NIH) National Institutes of Health
  - ☐ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☐ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☑ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Other:

Please **update the Funding/Support section of your IRB application** if needed, including the following attachments if they contain changes not previously reported to the IRB:

- A current copy of your **protocol if you are conducting industry/pharmaceutical research;**
- A current **Investigator Brochure** (submit a copy with all changes underlined).
- A **new or revised grant application** for this project.

Did your project receive extramural funding?

○ Yes ◉ No

If yes, please review and correct if necessary, the OSPA Account # information under the **Funding/Support section** of your IRB application.

If the project is externally funded, has the sponsor offered any of the research team enrollment incentives or other personal benefit bonuses? (e.g., cash/check, travel reimbursements, gift checks, etc.)

○ Yes ○ No ◉ N/A

Note: It is University of Kentucky policy that personal benefit bonuses are not allowed. If these conditions change during the course of the study, please notify the IRB.

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10. Project Information

Our records for the previously approved IRB application indicate your estimated project end date is:

06/30/2028

If you have a new estimated project end date, please go to the Project Info section and change the date in the field for Anticipated Ending Date of Research Project.

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11. Study Personnel

Our records for the previously approved IRB application indicate the following individuals are study personnel on this project (if applicable):

Last Name	First Name
Adams	Val
Arnold	Susanne
Bramel	April
Childs	Jefferson
Comer	Elisha
England	Shawn
Faul	Leigh Anne
Fernand	Anthony
Fischer	Brianna
Hallahan	Brent
Hao	Zhonglin
Heath	Heather
Land	Jennifer
Martin	Sarah
Mattingly	Alfred
McGarry	Ronald
Morgan	Rachael
Murphy	Sharon
Myint	Zin
Napier	Dana
Reusch	Ellen
Reynolds	Jeri
Sirrine	Matthew
Temple	Stephanie
Young	Jared
Zinner	Ralph

Please review the individuals listed above and update your records as needed in the Study Personnel section of the E-IRB application, being sure that each individual listed has completed or is up-to-date on the mandatory human research protection training [see the policy on Mandatory Human Subject Protection Training FAQs (required every three years)].

12. Progress of the Research

To meet federal requirements the IRB is relying on your RESEARCH DESCRIPTION as a protocol summary and their expectation is that it is up-to-date. If the currently approved protocol (or research description) in your E-IRB application is outdated, please make applicable changes, and describe in the field below any substantive changes and explain why they are essential. If none, insert "N/A" in the text field below. If you are closing your study, you may use the space below to summarize the final status of the research.

n/a

Note: No changes in the research procedures should have occurred without previous IRB review. Approval from the IRB must be obtained before implementing any changes.

Provide a brief **summary** of any **modifications that affect subject safety and/or welfare** approved by the IRB since the last initial or continuation review (If none, insert "N/A" in the text field below.):

n/a

Attach one copy of the most recent progress report sent to the FDA, if available. All PI-sponsored IND/IDE studies are required to submit a copy of the FDA progress report.

Attachments

13. Confidentiality/Security

Review your Research Description section and update the Confidentiality portion, if necessary, to describe measures for security of electronic and physical research records (e.g., informed consent document(s), HIPAA Authorization forms, sensitive or private data).

14. Subject Demographics

Our records for the previously approved IRB application indicate the following categories of subjects and controls are included in your research:

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☐ Non-English Speaking
- ☐ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☑ Patients
- ☐ Appalachian Population

Please review the Subject Demographics section of your IRB application for accuracy, and note the following:

If during the course of your research 1) any prisoners have been enrolled, OR 2) subjects have been enrolled that became involuntarily confined/detained in a penal institution that have not been previously reported to the IRB, go to Subject Demographic section in your E-IRB application and mark “prisoners” in the categories of subjects to be included in the study, if it is not already marked.

Note: If either 1 or 2 above apply, and you have received funding from the Department of Health and Human Services (HHS), a Certification Letter should have been submitted to the Office for Human Research Protections (OHRP); prisoners and individuals who

have become involuntarily confined/detained in a penal institution cannot continue participation in the research until OHRP issues approval. If the Certification has not been submitted, contact the Office of Research Integrity.

Based on the **total # of subjects** who have enrolled, complete the subject demographic section below:

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native				
Asian	1			
Black or African American	4	6		
Latinx				
Native Hawaiian or Other Pacific Islander				
White	52	33		
American Arab/Middle Eastern/North African				
Indigenous People Around the World				
More than One Race				
Unknown or Not Reported	1			

If unknown, please explain why:

no information given

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15. Research Sites

Our records for the previously approved IRB application indicate that you are conducting research at the following sites:

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☑ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☑ UK Hospital

Schools/Education Institutions Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Other Hospitals and Med. Centers

- ☐ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Other:

If the above listed sites are not accurate, go to the Research Sites section of the E-IRB application to update the facilities at which research procedures have been or will be conducted.

If you are adding a new off-site facility, you may also need to update your E-IRB application Research Description, Research Sites, Informed Consent, and other affected sections as well as any documents which will list the off-site facility. Documents needing updating may include, but not limited to:

- Consent forms (attachment under Informed Consent section)
- Brochures (attachment under Additional Info section)
- Advertisements (attachment under Research Description section) ;
- Letter of support (attachment under Research Sites section)).

Please revise applicable sections and attachments as necessary.

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16. Disclosure of Significant Financial Interest

Disclosure of Significant Financial Interest:

Our records for the previously approved IRB application indicate that you, your investigators, and/or key personnel (KP) have a significant financial interest (SFI) related to your/their responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2):

○ Yes ◉ No

If you need to update your records, please go to the PI Contact Information section and/or Details for individuals listed in the Study Personnel section to change your response to the applicable question(s).

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17. Supplementals

To ensure the IRB has the most accurate information for your protocol you are expected to re-visit the E-IRB application sections and make corrections or updates as needed. At a minimum you are being asked to review the following sections for accuracy:

STUDY DRUG INFORMATION—Please review for accuracy.
STUDY DEVICE INFORMATION—Please review for accuracy.
RESEARCH ATTRIBUTES—Please review for accuracy.
OTHER REVIEW COMMITTEES -- Please review for accuracy.

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (Use the exact title listed in the grant/contract application, if applicable).
If your research investigates any aspect of COVID-19, please include "COVID19" at the beginning of your Project Title and Short Title

MCC-17-MULTI-20 (2017-033): Priming Immunotherapy in Advanced Disease with Radiation

Short Title Description
Please use a few key words to easily identify your study - this text will be displayed in the Dashboard listing for your study.

MULTI-20: Immunotherapy in Adv + Radiation

Anticipated Ending Date of Research Project: 6/30/2028

Maximum number of human subjects (or records/specimens to be reviewed) 97

After approval, will the study be open to enrollment of new subjects or new data/specimen collection? ○ Yes ◉ No

Are you requesting that the UK IRB serve as the lead IRB for a multi-site study, **OR** that the UK IRB defer review to another IRB? [Click here for "IRB Reliance" help]
○ Yes ◉ No
If "Yes," before completing your IRB application, fill out the Reliance Request Form and submit it to irbreliance@uky.edu.

PI CONTACT INFORMATION

0 unresolved comment(s)

Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be listed as PI here.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

The Principal Investigator's (PI) contact information is filled in automatically based on who logged in to create the application.

If you are not the Principal Investigator, do NOT add yourself as study personnel.
To change the PI contact information on an application in Researcher edit status:

- click "Change Principal Investigator";
- search for the PI's name using the search feature;
- click "Select" by the name of the Principal Investigator, then "Save Contact Information".

You will automatically be added as study personnel with editing permissions to continue editing the application.

Change Principal Investigator:

First Name:	John	Room# & Bldg:	CC401B, Roach Building
Last Name:	Villano	Speed Sort#:	405360093
Middle Name			
Department:	Internal Medicine - 7H350	Dept Code:	7H350
PI's Employee/Student ID#:	10877051	Rank:	Professor
PI's Telephone #:	8593230405	Degree:	MD
PI's e-mail address:	jlvillano@uky.edu	PI's FAX Number:	8592577715
PI is R.N.	○ Yes ◉ No	HSP Trained:	Yes
		HSP Trained Date:	11/22/2022
		RCR Trained:	Yes

Do you, the PI, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ Yes ◉ No

RISK LEVEL

0 unresolved comment(s)

Indicate which of the categories listed below accurately describes this protocol

- (●) (Risk Level 1) Not greater than minimal risk
- ( ) (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
- ( ) (Risk Level 3) Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- ( ) (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

*"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

*****For Expedited and Exempt Applications, the research activities must be Risk Level 1 (no more than minimal risk to human subjects).*****

Refer to UK's guidance document on assessing the research risk for additional information.

SUBJECT DEMOGRAPHICS **0 unresolved comment(s)**

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc.) 18 to 99

Study Population:

Describe the characteristics of the subject population, including age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion.

Provide the following information:

- A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
- Justification for the inclusion of vulnerable groups such as children, prisoners, adults with impaired consent capacity, or others who may be vulnerable to coercion or undue influence.

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

Subjects must be 18 years of age or older. The expected M:F ratio will be approximately 1:1.9. The racial composition will reflect the population of Central Kentucky and the patients seen at the Markey Cancer Center: Caucasian: African American: Hispanic: Asian: Native American: 70:20:10:<1:<1 %. No groups are excluded from this study. We expect to enroll 76 patients in 48 months.

Attachments

Attach Type	File Name
StudyPopulation	Full eligibility from current protocol.pdf

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations. Possible demographic sources: Census Regional Analyst Edition, Kentucky Race/Ethnic Table, Kentucky Population Data.
(Please note: The IRB will expect this information to be reported at Continuation Review time for Pre-2019 FDA-regulated Expedited review and Full review applications):

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:				
Asian:				
Black/African American:	3	3		
Latinx:				
Native Hawaiian/Pacific Islander:				
White:	25	25		
American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:		1		

If unknown, please explain why:

Indicate the categories of subjects and controls to be included in the study. You may be required to complete additional forms depending on the subject categories which apply to your research. If the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check populations which the research does not specifically target. For example: a large record review of a diverse population may incidentally include a prisoner or an international citizen, but you should not check those categories if the focus of the study has nothing to do with that status.

Check All That Apply (at least one item must be selected)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☐ Non-English Speaking (translated long or short form)
- ☐ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☑ Patients
- ☐ Appalachian Population

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults
- Economically or Educationally Disadvantaged Persons

Other Resources:

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see also the E-IRB Research Description section on this same topic]
- International Citizens [DoD SOP may apply]
- Military Personnel and/or DoD Civilian Employees

Assessment of the potential recruitment of subjects with impaired consent capacity (or likelihood):

☐ Check this box if your study does NOT involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). If there is no direct intervention/interaction you will not need to answer the impaired consent capacity questions.

Does this study focus on adult subjects with any conditions that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes and you are not filing for exemption certification, go to "Form T", complete the form, and attach it using the button below.

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For creating your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and edit to match your research project.

Additional Resources:

- Informed Consent/Assent Website
- Waiver of Consent vs. Waiver of Signatures
- Sample Repository/Registry/Bank Consent Template

Consent/Assent Tips:

- If you have multiple consent documents, be sure to upload each individually (not all in a combined file).
- If another site is serving as the IRB for the project, attach the form as a "Reliance Consent Form" so the document will not receive a UK IRB approval stamp; the reviewing IRB will need to stamp the consent forms.
- Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".
- It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously *approved* versions will still be available in Protocol History.
- Attachments that are assigned a Document Type to which an IRB approval stamp applies will be considered the version(s) to be used for enrolling subjects once IRB approval has been issued.
  Document Types that do NOT get an IRB approval stamp are:
  - "Highlighted Changes",
  - "Phone Script", and
  - "Reliance Consent Form",
  - "Sponsor's Sample Consent Form".

How to Get the Section Check Mark

1. You must:

   a) provide a response in the text box below describing how investigators will obtain consent/assent, and
   b) check the box for at least one of the consent items and/or check mark one of the waivers

2. If applicable attach each corresponding document(s) **as a read-only PDF.**
3. If you no longer need a consent document approved (e.g., closed to enrollment), or, the consent document submitted does not need a stamp for enrolling subjects (e.g., umbrella study, or sub-study), only select "Stamped Consent Doc(s) Not Needed".
4. After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

Check All That Apply

- ☐ Informed Consent Form (and/or Parental Permission Form and/or translated short form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☐ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Reliance Consent Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☑ Stamped Consent Doc(s) Not Needed

Attachments

Informed Consent Process:

Using active voice, in the text box below, describe how investigators will obtain consent/assent. Include:

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)

- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

Will electronic consent form/process be utilized on-site or remotely for this study?

○ Yes ◉ No

If yes, in addition to addressing the above bullet points, describe the e-consent method and platform, including any hyperlinks, videos, or enhancements used to convey information, if applicable. Attach a representation of the e-consent with signature fields. For guidance, see the ORI E-Consent web page.

Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Special considerations may include:

- Obtaining consent/assent for special populations such as children, prisoners, or people with impaired decisional capacity
- *Research Involving Emancipated Individuals*
  If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **prior to submitting this application to the IRB**. Include research legal counsel's recommendations in the "Additional Information" section as a separate document.
- *Research Involving Non-English Speaking Subjects*
  For information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see IRB Application Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.
- *Research Repositories*
  If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the Sample Repository/Registry/Bank Consent Template.

Once a subject is referred for consideration in the study, the subject's history and status will be completely evaluated and treatment recommendations will be discussed thoroughly with the subject. Any alternative forms of therapy will be presented as objectively as possible. The risks and hazards of the study drug will be explained to the subject. The Investigator shall seek consent only under circumstances that provide the subject sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or under influence. The subject will be given ample time to review the consent and ask any questions before making a decision. The subject will then receive a signed copy of the consent form.
Requests for information about the research or complaints will be addressed to the PI, research staff, Ombudsman or Office of Research Integrity as appropriate. All requests or complaints will be handled in a timely, courteous, and confidential manner following University policies.

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval to waive the requirement for the informed consent process, or to alter some or all of the elements of informed consent, complete, Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting a waiver of the requirement for the informed consent process.

☐ I am requesting an alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered and/or omitted, and justify the alteration.

SECTION 2.

Explain how each condition applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.

☐ Request for Waiver of Signatures

If you are requesting IRB approval to waive the requirement for signatures on informed consent forms, **your research activities must fit into one of three regulatory options**:

1. The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., a study that involves participants who use illegal drugs).
2. The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (e.g., a cover letter on a survey, or a phone script).
3. The participant (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk to the subject, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

Select the option below that best fits your study.

If the IRB approves a waiver of signatures, participants must still be provided oral or written information about the study. To ensure you include required elements in your consent document, use the ***Cover Letter Template*** *as a guide. There is an English and a Spanish version.*

○ **Option 1**

Describe how your study meets these criteria:

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant (or legally authorized representative) must be asked whether (s)he wants to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.

○ **Option 2**

Describe how your study meets these criteria:

a) The research presents no more than minimal risk to the participant:

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

○ **Option 3**

Describe how your study meets these criteria:

a) The subject (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm.

b) The research presents no more than minimal risk to the subject.

c) There is an appropriate alternative mechanism for documenting that informed consent was obtained.

STUDY PERSONNEL **0 unresolved comment(s)**

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must click the 'Save Study Personnel Information' button.

◉ Yes ○ No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is required for a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed below. ***Residents and students who are PI's are encouraged to designate the faculty advisor or at least one other individual as a contact with an editor role (DP).***
- Role: DP = Editor (individual can view, navigate, and edit the application for any review phase (IR, CR/FR, MR) or 'Other Review", and submit Other Reviews on behalf of the PI.)
- Role: SP = Reader (individual can view and navigate through the currently approved application only.)

To add an individual via the below feature:

- Search for personnel;
- Click "select" by the listing for the person you want to add;
- For each person, specify responsibility in the project, whether authorized to obtain informed consent, AND denote who should receive E-IRB notifications (contact status).

NOTE: Study personnel must complete human subject protection (HSP) and Responsible Conduct of Research (RCR) training before implementing any research procedures. For information about training requirements for study personnel, visit UK's HSP FAQ page, the RCR Getting Started page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (HSPTrainingSupport@uky.edu) for credit.

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI	Active
Adams	Val	Consultant/Advisor	SP	N	N	PhD	P	Y	01/15/2025	Y	N	06/27/2018	N	Y
Arnold	Susanne	Sub-Investigator	SP	Y	N	MD	P	Y	02/01/2023	Y	N	06/27/2018	N	Y
Bramel	April	Project Assistance/Support	SP	N	Y		P	Y	10/11/2024	Y	N	04/28/2022	N	Y
Childs	Jefferson	Study Coordinator	DP	N	Y		P	Y	09/27/2024	Y	N	04/28/2022	N	Y
Comer	Elisha	Data Collection	SP	N	N		P	Y	11/13/2024	Y	N	06/27/2018	N	Y
England	Shawn	Study Coordinator	DP	N	N		P	Y	12/01/2023	Y	N	06/27/2018	N	Y
Faul	Leigh Anne	Project Assistance/Support	SP	N	Y		P	Y	12/14/2023	Y	N	04/28/2022	N	Y
Fernand	Anthony	Study Coordinator	DP	N	N		P	Y	09/27/2024	Y	N	06/16/2020	N	Y
Fischer	Brianna	Study Coordinator	DP	Y	Y		P	Y	05/30/2023	Y	N	02/24/2022	N	Y
Hallahan	Brent	Data Collection	SP	N	N	PhD	P	Y	11/26/2024	Y	N	06/27/2018	N	Y
Hao	Zhonglin	Sub-Investigator	SP	Y	N	MD	P	Y	09/19/2023	Y	N	06/27/2018	N	Y
Heath	Heather	Study Coordinator	DP	Y	N		P	Y	08/01/2022	N	N	06/27/2018	N	Y
Land	Jennifer	Project Assistance/Support	SP	N	Y		P	Y	08/03/2023	Y	N	04/28/2022	N	Y
Martin	Sarah	Study Coordinator	DP	Y	N		P	Y	11/21/2023	Y	N	05/22/2021	N	Y
Mattingly	Alfred	Data Analysis/Processing	SP	N	N		P	Y	11/21/2023	Y	N	09/28/2022	N	Y
McGarry	Ronald	Sub-Investigator	SP	Y	N	MD	P	Y	06/04/2024	Y	N	06/27/2018	N	Y
Morgan	Rachael	Consultant/Advisor	SP	N	N		P	Y	10/25/2024	Y	N	06/28/2018	N	Y
Murphy	Sharon	Project Assistance/Support	DP	N	Y		P	Y	09/27/2024	Y	N	08/14/2024	N	Y
Myint	Zin	Sub-Investigator	SP	Y	N	MD	P	Y	01/05/2025	Y	N	06/27/2018	N	Y
Napier	Dana	Data Collection	SP	N	N		P	Y	08/12/2024	Y	N	06/27/2018	N	Y
Reusch	Ellen	Study Coordinator	DP	Y	Y		P	Y	02/21/2023	Y	N	05/07/2020	N	Y
Reynolds	Jeri	Study Coordinator	DP	Y	N	RN	P	Y	11/03/2023	Y	N	06/27/2018	N	Y
Sirrine	Matthew	Data Analysis/Processing	SP	N	N		P	Y	05/17/2024	Y	N	09/28/2022	N	Y
Temple	Stephanie	Study Coordinator	DP	N	N	BS	P	Y	06/04/2024	Y	N	06/12/2020	N	Y
Young	Jared	Project Assistance/Support	DP	N	Y		P	Y	02/13/2024	Y	N	08/14/2024	N	Y
Zinner	Ralph	Sub-Investigator	SP	Y	N	M.D.	P	Y	02/28/2023	Y	N	05/14/2020	N	Y
Bondada	Subbarao	Consultant/Advisor	SP	N	N	PhD	P	Y	12/18/2024	Y	Y	02/28/2024	N	Y

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI	Active
Buchanan	Mikayla	Study Coordinator	DP	Y	N		S	Y	09/26/2022	N	Y	01/30/2024	N	Y
Cohen	Donald	Consultant/Advisor	SP	N	N	PhD	P	N	11/11/2020		Y	02/28/2024	N	N
Cohn	Dianne	Data Collection	SP	N	N		P	N	08/02/2017		Y	01/07/2019	N	N
Cooper	Shelley	Study Coordinator	DP	Y	N		P	N	08/08/2021		Y	03/16/2023	N	N
Gill	Love	Study Coordinator	DP	N	Y		P	Y	10/20/2022	Y	Y	04/28/2022	N	Y
Groleau	Jonathan	Project Assistance/Support	SP	N	N			N	11/11/2021		Y	01/22/2025	N	N
Kincer	Mary	Data Collection	SP	N	N		P	N	02/19/2019		Y	04/03/2020	N	Y
Kolesar	Jill	Sub-Investigator	SP	Y	N	PharmD		Y	09/11/2022	Y	Y	01/22/2025	N	N
Maloney	Patrick	Data Analysis/Processing	SP	N	N		P	Y	10/03/2024	Y	Y	09/28/2022	N	Y
Parasramka	Saurabh	Consultant/Advisor	SP	N	N	PhD	P	N	08/31/2020		Y	02/28/2024	N	Y
Pavlik	Heather	Study Coordinator	DP	Y	Y	RN	P	Y	07/22/2024	Y	Y	05/22/2021	N	Y
Santa-Teresa	Monica	Study Coordinator	SP	N	N		P	Y	09/27/2024	Y	Y	04/03/2020	N	Y
Scowby	Alison	Data Collection	SP	N	N		P	N	12/20/2018		Y	06/16/2020	N	N
Sims	Lorrie	Data Collection	SP	N	N		P	N	05/04/2021		Y	01/30/2024	N	Y
Slone	Stacey	Consultant/Advisor	SP	N	N	PhD	P	Y	05/09/2024	Y	Y	01/07/2019	N	Y
Thind	Ravneet	Sub-Investigator	SP	Y	N	MD	P	Y	07/25/2023	N	Y	04/03/2020	N	Y
Vela	Cory	Consultant/Advisor	SP	N	N	PharmD	P	N	06/25/2018		Y	04/03/2020	N	N
Wells	Chad	Study Coordinator	DP	N	N		P	N	09/02/2020		Y	09/28/2022	N	N
Williamson	Amy	Study Coordinator	SP	N	N		P	N	03/29/2017		Y	04/03/2020	N	N
Wu	Jianrong	Consultant/Advisor	SP	N	N	PhD	P	N	11/11/2020		Y	02/28/2024	N	N

RESEARCH DESCRIPTION

0 unresolved comment(s)

You may attach a sponsor's protocol pages in the "Additional Information" section and refer to them where necessary in the Research Description. However, each prompt that applies to your study should contain at least a summary paragraph.

Pro Tips:

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section or under the Additional Information section to include supplemental information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background

Include a brief review of existing literature in the area of your research. You should identify gaps in knowledge that should be addressed and explain how your research will address those gaps or contribute to existing knowledge in this area. For interventional research, search PubMed and ClinicalTrials.gov for duplicative ongoing and completed trials with same condition and intervention(s).

see appendix -background

Objectives

List your research objectives. Please include a summary of intended research objectives in the box below.

Primary: 1.1.1 Single arm Phase II trial to assess six-month (mo) progression free survival (PFS) compared to historical control.

Study Design

Describe and explain the study design (e.g., observational, secondary analysis, single/double blind, parallel, crossover, deception, etc.).

- *Clinical Research*: Indicate whether subjects will be randomized and whether subjects will receive any placebo.
- *Community-Based Participatory Research*: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.
- *Qualitative research*: Indicate ranges where flexibility is needed, if a fixed interview transcript is not available, describe interview topics including the most sensitive potential questions.
- *Research Repositories*: If the purpose of this submission is to establish a Research Repository (bank, registry) and the material you plan to collect is already available from a commercial supplier, clinical lab, or established IRB approved research repository, provide scientific justification for establishing an additional repository collecting duplicate material. Describe the repository design and operating procedures. For relevant information to include, see the UK Research Biospecimen Bank Guidance or the UK Research Registry Guidance.

This is an open label, single group study. This study proposes to treat metastatic NSCLC and HNSCC patients who are already initiating an immune checkpoint inhibitor (such as Nivolumab, Atezolizumab or Pembrolizumab) for disease treatment as per FDA approved guidelines. In these patients, we will deliver a short-course radiation to a single systemic (non-CNS) site within 14 days of receiving the first dose of immune checkpoint inhibitors. This sequence allows radiation to release tumor antigens from immune inaccessible areas such as necrotic tumor or low perfusion to provide a robust anti-tumor immune response with immune checkpoint inhibitors.

Attachments

Attach Type	File Name
StudyDesign	objectives and background_PA 17Feb2020.pdf
StudyDesign	Schema and study design_PA 17Feb2020.pdf

Subject Recruitment Methods & Advertising

Describe how the study team will identify and recruit subjects. Please consider the following items and provide additional information as needed so that the IRB can follow each step of the recruitment process.

- How will the study team identify potential participants?
- Who will first contact the potential subjects, and how?
- Will you use advertisements? If so, how will you distribute those?
- How and where will the research team meet with potential participants?
- If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations.
- How you will minimize undue influence in recruitment?
- Attach copies of all recruiting and advertising materials (emails, verbal scripts, flyers, posts, messages, etc.).

For additional information on recruiting and advertising:

- IRB Application Instructions - Advertisements
- PI Guide to Identification and Recruitment of Human Subjects for Research

Subjects will be identified by referral from community oncologists and primary care physicians, as well as internal referrals from physicians at the University of Kentucky. Subjects will initially be evaluated by treating oncologist, and will be offered initial information about the clinical trial if appropriate. Agreeable subjects will then be invited to participate in an informed consent process as described in #6 below. The study will be posted on the website of the Markey Cancer Center in the general information list and listed in the Markey Cancer Center quarterly: Clinical Research Newsletter.
We are not doing any advertising for this study.

See attached appendix-eligibility criteria

Attachments

Attach Type	File Name
Advertising	Amend 12 dtd 29July2022-Appendix eligibility criteria.pdf

Research Procedures

Describe how the research will be conducted.

- What experience will study participants have?
- What will study participants be expected to do?
- How long will the study last?
- Outline the schedule and timing of study procedures.
- Provide visit-by-visit listing of all procedures that will take place.
- Identify all procedures that will be carried out with each group of participants.
- Describe deception and debrief procedures if deception is involved.

Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project. List medications that are explicitly forbidden or permitted during study participation.

Laboratory tests to assess normal organ and bone marrow function and radiographic studies will be done during enrollment and screening. Subjects will receive standard of care (SOC) immune checkpoint inhibitors as determined by the treatment team based on the FDA indication of the subject's cancer and their clinical judgement. Within two weeks of initiation, subjects will then receive either:
• SBRT to target to achieve Biological Equivalent Dose (BED) > 100 Gy OR
• 30 Gy fractionated radiation therapy (RT) delivered as a 3 dimensional (3-D) dose.
The lesion choice will be made by the treating radiation oncologist and will be directed to a single malignant focus. Essentially, the goals of both techniques are the same but SBRT is reserved for lesions that are readily encompassed by a single field with large RT fractions in which dose-limiting organs are within safe limits.
Patients will be treated until disease progression (PD) and followed for six months following disease progression or for a maximum of three years from registration.
Experimental procedures include the following: a) obtaining informed consent, b) evaluating for inclusion and exclusion criteria, c) assessing adverse events by infusion center nurse, research nurse, or other qualified healthcare professional, d) recording and using the clinical data outlined in flowcharts to develop the data base for this study, e) spot radiation, and f) research lab draws (correlative blood listed on study calendar).

Attachments

Attach Type	File Name
ResearchProcedures	Calendar Protocol vd 17Feb2020.pdf

Data Collection & Research Materials

In this section, please provide the following:

- Describe all sources or methods for obtaining research materials about or from living individuals (such as specimens, records, surveys, interviews, participant observation, etc.), and explain why this information is needed to conduct the study.
- For each source or method described, please list or attach all data to be collected (such as genetic information, interview scripts, survey tools, data collection forms for existing data, etc.).
- If you will conduct a record or chart review, list the beginning and end dates of the records you will view.

N/A

Attachments

Resources

Describe the availability of the resources and adequacy of the facilities that you will use to perform the research. Such resources may include:

- Staffing and personnel, in terms of availability, number, expertise, and experience;
- Computer or other technological resources, mobile or otherwise, required or created during the conduct of the research;
- Psychological, social, or medical services, including equipment needed to protect subjects, medical monitoring, ancillary care, or counseling or social support services that may be required because of research participation;
- Resources for communication with subjects, such as language translation/interpretation services.

Research staff of the Markey Cancer Center Clinical Research Organization with oncology research related experience, ranging from one to thirteen years, will assist the PI in the conduct of the study. All subjects will have study medication dispensed in the Markey Cancer Center's closely monitored clinic area, with on-site pharmacy and medical support, certified oncology nurses and ready access to emergency care. The University's social services, patient advocate, and Office of Research Integrity are readily available to provide support or services needed.
Additional Key Personnel for this study are identified on the MCC-CRO Global KP (MCC-CRO Master SP list). This allows for cross-coverage of studies managed by the MCC-CRO.

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?
- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

- Describe potential direct benefits to study participants – including diagnostic or therapeutic, physical, psychological or emotional, learning benefits. This cannot include incentives or payments.
- State if there are no direct benefits.
- Describe potential benefits to society and/or general knowledge to be gained.

Describe why potential benefits are reasonable in relation to potential risks. If applicable, justify why risks to vulnerable subjects are reasonable to potential benefits.

Possible Side Effects of Nivolumab: Common (= to or more than 20%): Tiredness /
Common (4-20%):
• Anemia which may require blood transfusion
• Swelling and redness of the eye
• Pain in belly
• Diarrhea, nausea, loss of appetite
• Dry mouth
• Fever
• Swelling and redness at the site of the medication injection
• Bruising, bleeding
• Pain or swelling of the joints
• Reaction during or following a drug infusion which may cause fever, chills, rash
Nivolumab may cause patient's immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:
• Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
• Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
• Skin: itching; rash, blisters including inside the mouth; loss of skin pigment
• Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
• Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.
Rare and serious (3% or less):
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
Nivoulmab may cause patient's immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:
• Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
• A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
• Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
• Heart problems including inflammation and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
• Problem of the muscle, including inflammation, which can cause muscle pain and severe muscle weakness sometimes with dark urine
• Inflammation of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck
• Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
• Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut), and can lead to death. If patient considers an allogeneic stem transplant after participating in this study, they should tell their doctor that they have received BMS-936558 therapy, since the risk and severity of transplant-associated complications may be increased.
Possible Side Effects of Pembrolizumab:
Pembrolizumab is an agent involved in the blockage of "immune checkpoints". This may result in severe and possibly fatal immune-mediated side effects probably due to stimulation and growth of immune cells (T-cells). Immune-mediated side effects have been reported in patients receiving pembrolizumab. In clinical trials, most immune-mediated side effects went away when pembrolizumab was stopped for a short time, steroids were taken and other supportive care given.

Pembrolizumab is a medicine that may treat patient's melanoma by working with their immune system. Pembrolizumab can cause patient immune system to attack normal organs and tissues in many areas of their body and can affect the way they work. These problems can sometimes become serious or life-threatening.

1. Lung problems (pneumonitis). Symptoms of pneumonitis may include:
• shortness of breath
• chest pain
• new or worse cough

2. Intestinal problems (colitis) that can lead to tears or holes in patient's intestine. Signs and symptoms of colitis may include:
• diarrhea or more bowel movements than usual
• stools that are black, tarry, sticky, or have blood or mucus
• severe stomach-area (abdomen) pain or tenderness
3. Liver problems (hepatitis). Signs and symptoms of hepatitis may include:
• yellowing of your skin or the whites of patient's eyes
• dark urine
• nausea or vomiting
• feeling less hungry than usual
• pain on the right side of patient's stomach area (abdomen)
• bleeding or bruising more easily than normal
4. Hormone gland problems (especially the thyroid, pituitary, and adrenal glands). Signs and symptoms that your hormone glands are not working properly may include:
• rapid heart beat
• weight loss
• increased sweating
• weight gain
• hair loss
• feeling cold
• constipation
• your voice gets deeper
• muscle aches
• dizziness or fainting
• headaches that will not go away or unusual headache
5. Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:
• change in the amount or color of your urine.
6. Problems in other organs. Signs of these problems may include:
• rash
• changes in eyesight
• severe or persistent muscle or joint pains
• severe muscle weakness
Common (= to or more than 20%): Tiredness
Common (4-20%):• Anemia which may require blood transfusion
• Pain
• Pain and swelling of thyroid
• Diarrhea, nausea
• Sores in the mouth which may cause difficulty swallowing
• Chills, fever
• Swelling of the body which may cause shortness of breath
• Infection
• Loss of appetite
• Damage to the bone which may loss of motion
• Fluid in the joints
• Joint stiffness
• Blisters on the skin, itching, acne, rash, skin changes, hives
• Swelling and redness of the skin
• The body's reaction to the drug can occur during treatment or weeks to months later: multiple organs may be involved but primarily bowels, liver, skin, nerves and glands that make hormones; symptoms may include diarrhea, rash and numbness/tingling of hands and feet
Rare and serious (3% or less):
• Heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness
• Swelling and redness of the eye
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
• Reaction during or following a drug infusion which may cause fever, chills, rash
• Weakness and paralysis
• Muscle weakness
• Feeling of "pins and needles" in arms and legs
• Kidney damage which may require dialysis
• Severe skin rash with blisters and can involve inside of mouth and other parts of the body

Risk Profile for Atezolizumab / Common (= to or more than 20%): Tiredness

Common (4-20%): • Pain
• Diarrhea, nausea, vomiting
• Difficulty swallowing
• Chills, fever
• Flu-like symptoms including body aches
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
• Loss of appetite
• Headache
• Swelling around the brain leading to headache and confusion
• Redness and swelling around the brain and spinal cord leading to headache, fever and stiff neck
• Shortness of breath, stuffy nose
• Dry skin
• Itching, acne, rash
• Rash that develops on skin, nails, scalp and inside of mouth or vagina that may be painful
Rare and serious (3% or less):
• Heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness
• Swelling of the body which may cause shortness of breath
• Reaction during or following a drug infusion which may cause fever, chills, rash
• Weakness and paralysis
• Damage to the muscles which may cause weakness
Reproductive: Patients should not get pregnant, breastfeed, or father a baby while in this study and for at least 31 weeks after the last dose of the Immune Checkpoint Inhibitor they receive (nivolumab, pembrolizumab or atezolizumab). The potential harm of these drugs to an unborn baby is not known.
Radiation Therapy:
• COMMON, SOME MAY BE SERIOUS
In 100 people receiving radiation therapy, more than 20 and up to 100 may have one or more of the following:
• Reddening, tanning, or peeling of the skin
• Mild pain
• Hair loss
• Tiredness
• Diarrhea, nausea, decreased appetite
• Anemia, which may require transfusion
• Infection, especially when white blood cell count is low
• Frequent urination
• Fatigue

• OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving radiation therapy, from 4 to 20 may have one or more of the following:
• Thickening and numbness of the skin
• Sores or ulcers on the skin or near the cancer location
• Permanent hair loss
• Bleeding from the skin
• Sores in mouth which may cause difficulty swallowing
• Cough
• Shortness of breath
• Pain in your ribs
• Belly pain
• Sexual dysfunction which may include the inability to develop or maintain a penile erection during sexual intercourse and/or pain during intercourse
• Patient may also experience the additional risks specific to the area of the body where they receive the radiation.

Possible Side Effects of Radiation Therapy to the Lung, Neck or Chest:
•
• COMMON, SOME MAY BE SERIOUS
• In 100 people receiving radiation therapy to the lung, neck or chest, more than 20 and up to 100 may have one or more of the following:
• A common effect of this treatment in previous studies was scaring of the lung tissue that can lead to cough, thick mucous (phlegm), difficulty breathing, and other symptoms of pneumonia. There can also be permanent scaring of a portion of the lung or ribs. Efforts will be made to reduce this risk and limit its effect. However, it is possible you will have shortness of breath at rest or during exercise, may need to receive oxygen, and/or may have chest wall pain. A few patients may need oxygen therapy permanently. In rare cases this can be life threatening
• Tiredness, which is temporary
• The skin in the treatment area may become reddened and/or dry, and chest hair in the treatment area may fall out and may not grow back

• OCCASIONAL, SOME MAY BE SERIOUS
• In 100 people receiving radiation therapy to the lung, neck or chest, from 4 to 20 may have one or more of the following:
• Cough
• Difficulty breathing

• Chest radiotherapy can cause changes in normal lungs. These changes can be as unimportant as small amounts of "scarring" seen on x-rays that does not cause symptoms. Sometimes chest radiotherapy can cause lung damage that leads to symptoms such as chest pain, shortness of breath, cough, or fever. Rarely, these symptoms can be severe or life threatening. Treatment for this lung damage involves pain medicines, anti-inflammatory medicines (corticosteroids), and rarely, oxygen therapy, which may be permanent. Patient should tell doctors immediately if you have any of these symptoms
• Irritation of the esophagus, which may result in heartburn or pain on swallowing
• Fever
• Chest wall discomfort or pain
• Rib fracture, which may cause pain

• RARE, AND SERIOUS
• In 100 people receiving radiation therapy to the lung, neck or chest, 3 or fewer may have one or more of the following:
• Irritation of the lining around the heart, which can cause chest pain, shortness of breath, and irregular or rapid heartbeat; rarely, this can require surgery to correct.
• Irritation and/or damage to the muscle of the heart; rarely, this can cause a heart attack, heart failure, and/or death
• Irritation and/or damage to the spinal cord (the major nerve within the spine), which can lead to weakness, tingling or numbness of the lower body and legs; very rarely, this can lead to inability to move or control the lower half of the body.
• Damage or scarring of nerves in the chest, which may result in a hoarse voice or a tingling “pins and needles” sensation, or pain in the chest and rib area, depending on the nerve affected
• Damage or scarring of nerves at the top of the lungs, which may result in a tingling “pins and needles” sensation or pain or weakness of the muscles of the arm and hand, since these nerves provide sensation and muscle control for the arm and hand
• Narrowing of the esophagus (tube to the stomach), which can result in swallowing difficulty
• Thinning of the wall of the esophagus; rarely, this can cause a hole in the esophagus and/or a hole in your lung which could result in difficulty with eating and breathing
• Irritation of the large blood vessels surrounding the heart; rarely, this can cause bleeding (coughing up blood) and/or death
• Irritation of the voice box which can cause hoarseness and/or pain
• Damage to the blood vessels in the neck
Radiation Therapy can induce tumor-cell death, an important step for eliciting an anti-tumor immune response. Reports of partial or complete resolution of tumors outside the radiation field define the abscopal effect. Preclinical models demonstrate that radiotherapy combined with immune activation, specifically PD-1 blockade, results in a specific CD8+ T-cell phenotype associated with a tumor-reactive population and having significant tumor response.

Our study proposes to treat metastatic NSCLC and HNSCC patients who are already initiating an immune checkpoint inhibitor (such as Nivolumab, Atezolizumab or Pembrolizumab) for disease treatment as per FDA approved guidelines. In these patients we will deliver a short-course radiation to a single systemic (non-CNS) site within 14 days of receiving the first dose of immune checkpoint inhibitors. This sequence allows radiation to release tumor antigens from immune inaccessible areas such as necrotic tumor or low perfusion to provide a robust anti-tumor immune response with immune checkpoint inhibitors.

In the limited studies of these drugs with concurrent radiation minimal to no increase in toxicities were observed. There is no guarantee that subjects will get any benefit from taking part in this study. Their condition may become worse or may improve. Data obtained from this study Your willingness to take part may help doctors better understand and/or treat others who have these conditions.

Available Alternative Opportunities/Treatments

Describe alternative treatments or opportunities that might be available to those who choose not to participate in the study, and which offer the subject equal or greater advantages. If applicable, this should include a discussion of the current standard of care treatment(s).

If not on study, patients could receive the standard of care at UK, which is the same treatment as in this study without the SBRT radiation. Subjects could participate in a different study, if one is available or they may decline treatment for their cancer but receive care to relieve symptoms.

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Records, Privacy, and Confidentiality

Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Specify who will have access to the data/specimens and why they need access.

Describe how data will be managed after the study is complete:

- If data/specimens will be maintained, specify whether identifiers will be removed from the maintained information/material.
- If identifiers will not be removed, provide justification for retaining them and describe how you will protect confidentiality.
- If the data/specimens will be destroyed, verify that this will not violate retention policies and will adhere to applicable facility requirements.

If this study will use de-identified data from another source, describe what measures will be taken to ensure that subject identifiers are not given to the investigator.

If applicable, describe procedures for sharing data/specimens with collaborators not affiliated with UK.

For additional considerations:
Return of Research Results or Incidental Research Findings
HIPAA policies
FERPA policies
Procedures for Transfer agreements
Information regarding multi-site studies
NIH Genomic Data Sharing (GDS) Policy
Digital Data

Specimens from subjects (fresh or archived FFPE tumor block) are reviewed to confirm diagnosis for participation in the study. Medical/Clinical information pertaining to protocol is included in the subjects' medical records. Copies are also kept in subjects' protocol chart. This ensures timely record review, and allows for collection of data points required to meet primary and secondary objectives of the study.
Confidentiality of medical information is discussed at length in the informed consent. Subjects are made aware of what data will be collected, where it is stored and who has access to the information. Study data may be published or shared with other researchers, but the identity and medical history of each study participant will remain strictly confidential. Representatives of University of Kentucky, the Food and Drug Administration (FDA), the National Cancer Institute (NCI), or representatives and the Institutional Review Board (IRB) may view study data and information.

During the study, information will be collected to assess compliance with the study requirements. These records will be used by the FDA, the IRB, and the Investigator(s) in connection with complying with their obligations relating to this study. The records will not be used for any other purposes or disclosed to any other party without the subject's permission. All records will be coded with an identification number to protect their identity. Data will be stored in a secured area for at least two years after the study is completed. All data stored is on site at Markey Cancer Center Clinical Research Organization in locked facilities, and with limited access to records by designated research staff. All research records will be held for a minimum of six years following completion of the study
Patients enrolled in this study will be evaluated clinically and with standard laboratory tests before and at regular intervals during their participation in this study. Safety assessments will consist of monitoring and recording of all Adverse Events (AEs) and all serious adverse events (SAEs); measurement of protocol-specified hematology, clinical chemistry, and urinalysis variables; measurement of protocol-specified vital signs; and other protocol-specified tests that are deemed critical to the safety evaluation of the study drug(s). Patients will be evaluated for all adverse events for the duration of their participation in the study. Patients discontinued from the treatment phase of the study for any reason will be evaluated approximately 30 days (between 30 and 37 days) after the decision to discontinue treatment.
Safety will be evaluated from the incidence of all AEs including SAEs and the severity of AEs according to the NCI CTC guidelines. Reporting guidelines for AEs will comply with the University of Kentucky's IRB requirements and are extensively described in the clinical protocol. To minimize risks, tests are performed at intervals to monitor the clinical status of the subject. Confidentiality of medical information is discussed at length in the informed consent. Subjects are made aware of what data will be collected, where it is stored and who has access to the information. To assure necessary medical intervention in the event of an adverse experience, patients are asked to notify their physician in the event of any adverse experience in the consent. The patients are interviewed at each clinic visit by the research staff and are specifically asked if they have had any adverse experiences. Adverse events from ongoing studies are reviewed as the sponsor submits them to the PI and if necessary patients are contacted concerning any new information; and the information is added to the "Risks and/or Discomforts" section of the consent form.
Patients will be examined and graded at the end of the neoadjuvant treatment cycle for subjective/objective evidence of developing toxicity according to NCI-CTCAE version 5.0 toxicity criteria.

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Check this item to confirm that you will retain all IRB-related records for a minimum of 6 years after study closure.

Payment

Describe the incentives (monetary or other) being offered to subjects for their participation. If monetary compensation is offered, indicate the amount and describe the terms and schedule of payment. Please review this guidance for more information on payments to subjects, including restrictions and expectations.

Subjects will not receive any payment for their participation in this study.

Costs to Subjects

Include a list of services and/or tests that will not be paid for by the sponsor and/or the study (e.g., MRI, HIV). Keep in mind that a subject will not know what is "standard" – and thus not covered by the sponsor/study – unless you tell them.

Subjects will be responsible for the costs of all care and treatment they receive during this study that they would normally receive for their condition. These are costs that are considered medically reasonable and necessary and will be part of the care they receive if they do not take part in this study.
The medical costs related to a patient's care and treatment because of research related harm will be their responsibility.
Neither the subjects nor their insurance company will be billed for: spot radiation or the research lab draws as these are for this study

Data and Safety Monitoring

The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research or NIH-funded/FDA-regulated clinical investigations.

- If you are conducting greater than minimal risk research, or your clinical investigation is NIH-funded, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.
- If this is a non-sponsored investigator-initiated protocol considered greater than minimal risk research, and if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

The Principal Investigator has primary responsibility for monitoring the safe conduct of this study. Additionally, the Markey Cancer Center Data Safety and Monitoring Plan outlines oversight and monitoring of all cancer clinical trials. The Committee is responsible for reviewing data to identify patient safety and protocol compliance issues. The Markey Protocol Review Committee (PRC) assigns studies a DSMC review timeline based on the phase, origination of the study and known safety issues.

The members of the MCC DSMC consist of Medical Oncologists, a Pharmacist, a Nurse Manager, a Certified Clinical Research Professional and a Reporter. These members were selected based on their experience, reputation for objectivity, and knowledge of clinical trial methodology. All members should view themselves as representing the interest of the study patients and not that of the institution.
At each meeting, the following data is reviewed by MCC DSMC: treatment issues, serious adverse events (SAEs) per FDA definitions, dose levels, dose modifications, and responses as applicable.
The DSMC reviews the protocol to assure the following: progress of the trial and safety of participants; compliance with requirements for the reporting of adverse events; any actions resulting in a temporary or permanent suspension by the sponsor; and data accuracy and protocol compliance.
The DSMC, the Protocol Review Committee (PRC), the responsible disease-specific Clinical Care and Research Team (CCART) and/or the UK IRB are empowered to immediately suspend accrual to any study under its purview for any of the following: Failure to comply with AE/SAE reporting requirements; poor study enrollment; protocol violations or issues related to patient safety
Data management will be performed by cross-team members at MCC represented by a data management group at the CRI SRF and Biostatistics and Bioinformatics (BB) SRF working closely with the MCC CRO. A protocol specific Data Management Plan (DMP) will be authored by a senior data manager in collaboration with the biostatistician and the CRO. Each team will be expected to review and sign off on the DMP prior to finalization.
To maintain best clinical practices in data management, the DMP may include, but not be limited to, CRF/eCRF design, database build and design, database training, edit check/validation specifications, study database testing/release, data and paper workflow, report, metrics, query/discrepancy management, management of external (including laboratory) data, medical coding, SAE handling/reconciliation, data transfers and database lock. The protocol specific DMP will additionally define the schedule at which data will be accessed by study statisticians to perform statistical programming for conduct of data quality, data control, data management, generation of interim reports and statistical analysis. Cross-team members will collaborate to establish procedures and timelines for quality control, audits, query resolution, interim and final data analysis.

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Future Use and Sharing of Material (e.g., Data/Specimens/Information)

If the material collected for this study will be used by members of the research team or shared with other researchers for future studies, please address the following:

- list the biological specimens and/or information that will be kept
- briefly describe the types, categories and/or purposes of the future research
- describe any risks of the additional use
- describe privacy/confidentiality protections that will be put into place
- describe the period of time specimens/information may be used
- describe procedures for sharing specimens/information with secondary researchers
- describe the process for, and limitations to, withdrawal of specimens/data

Subjects will be given the opportunity to allow for banking of specimens collected during this study. The consent form includes an opt-in check box regarding the use of their samples and the release of results to them as well as the information below.

Banking biologic material (specimens) for future use

During this study additional peripheral blood samples will be collected from you as part of the correlative study to assess immune activation. Samples will be collected, stored and managed by the University of Kentucky Bio Specimen and Tissue Procurement (BSTP) group. Once all samples for all subjects have been collected, they will be thawed and analyzed simultaneously. There may be leftover samples which could be useful to other research as part of a biospecimen bank.

WHAT IS THE PURPOSE OF THE BANK?

The purpose of the bank is to store leftover samples, along with health information for research purposes. Researchers can then use the stored materials for future research studies to learn more about cancer and other health conditions.

We intend to collect samples from about 76 patients. Having samples from many people allows the researchers to identify trends and

discover better ways to diagnose, prevent, and treat many conditions.

The researchers may use the genetic material (genes, DNA, RNA) in your sample to learn about the role genes play in heath and disease. Results of genetic studies may also reveal information about your family members.

WHERE WILL SAMPLES AND INFORMATION BE STORED AND FOR HOW LONG?

The samples and information will be stored at the University of Kentucky Markey Biospecimen and Tissue Procurement Shared Resource Facility until they are all used up.

WHAT WILL THE BANK COLLECT AND STORE FOR RESEARCH?

In addition to the blood that is drawn as part of your standard care, additional blood samples will be collected for correlative studies at the beginning of the study, on day 1 of each cycle and when you go

off treatment. We would like to keep any specimen leftover from these blood draws in the bank. No additional blood will be taken for the bank.

We also would like to have permission to look at your medical records from time to time. We would collect general information related to your health such as test results, treatments, and doctor's notes. The confidentiality section below provides details about how we will keep your information private.

WILL YOU BE CONTACTED ABOUT FUTURE RESEARCH?

The researchers who access samples or information related to them will not contact you about future research. If you wish to participate in research studies, you may find information at www.ukclinicalresearch.com.

HOW WILL THE BANK SHARE SAMPLES AND INFORMATION WITH OTHER RESEARCHERS?

Your sample or information may be shared with University of Kentucky (UK) researchers and researchers outside of UK.

Researchers may contact the bank to request permission to use samples or information for their studies. An oversight committee will review the researcher's qualifications and proposed research. The committee will also determine if any additional review or approval is necessary.

The bank will remove all information that could identify you such as your name, address, medical record number, etc, before sharing with researchers. The bank will use a code to match your samples with your medical information without releasing your identity. The researchers will sign an agreement promising not to try to use any of the sample or information to identify you. The bank will not share information that could identify you without your permission.

WILL YOU BENEFIT FROM TAKING PART IN THE (BANK)?

There is no direct benefit to you. The knowledge gained from research on your sample may help others in the future.

ARE THERE RISKS FROM TAKING PART IN THE (BANK)?

Blood draw
Risks associated with blood sampling are generally slight, but may include soreness, bruising, pain, infection, possible fainting, bleeding. No additional blood will be drawn for the bank.

Privacy and Social/Psychological:
There is a risk that someone could get access to the information stored in the bank. In spite of the security measures and safeguards we will use, we cannot guarantee that your identity will never become known.

Even without your name or identifiers, genetic information is unique to you making it possible for someone to trace it back to you. The results of genetic research apply to both you and your family members. In some cases, it could be used to make it harder for you to get or keep a job or insurance.

Genetic information could be used in ways that could cause you or your family distress.

There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). Generally, GINA makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that GINA does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. It also does not prohibit discrimination on the basis of already known genetic disease.

Unknown:
There may be risks that at this time are unknown. As technology advances, there may be new ways of linking information back to you that we cannot foresee now.

HOW IS YOUR PRIVACY AND CONFIDENTIALITY PROTECTED?

The bank will take careful steps to keep your information confidential. Electronic records will only be accessible to authorized personnel and will require passwords for access.

We will remove information such as your name or other direct identifiers from your sample and medical information. We will label your samples and information with a code. The coded samples will be kept in locked facilities only accessible by authorized research staff. Data will be stored in a password protected database.

Only select bank staff will have access to the list that links the code to you. The bank staff members sign an agreement to keep your identity a secret to the extent allowed by law. In very unusual cases, staff at the bank may be required to release your identifiable medical and research information in response to an order from a court of law.

Officials of the Food and Drug Administration, the National Cancer Institute (NCI) and the University of Kentucky may look at or copy pertinent portions of records that identify you.

DOES TAKING PART IN THE BANK COST ANYTHING?

There will be no additional costs or charges to you for taking part in the bank.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THE BANK?

You will not be paid for donating your sample or information to the bank. The sample and information that you are donating will no longer belong to you. The research may lead to new medical knowledge, tests, treatments, or products. These products could have some financial value. There are no plans to provide financial payment to you or your relatives should this occur.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Do you give permission for Dr. John Villano to contact you with information about research results or incidental findings that are determined to be important to you/your family's health? (Incidental findings are unforeseen findings discovered during the course of the research that may affect you or your family's health).

? Yes ? No _____Initials

You may also withdraw your consent to be contacted with information about research results or incidental findings by sending a written request to Dr. John Villano_ c/o Markey Cancer Center Clinical Research Organization, cc140 Markey Cancer Center, 800 Rose Street, Lexington, KY. 40536-0093.

ARE THERE OTHER CHOICES IF YOU DO NOT WANT TO PARTICIPATE IN THE BANK?

If you do not want to take part in the repository, there are no other choices except not to take part. Your decision will not affect your current or future medical care.

WHAT IF YOU CHOOSE NOT TO PARTICIPATE OR CHANGE YOUR MIND AND WANT TO WITHDRAW FROM TAKING PART IN THE BANK?

Taking part in the bank is voluntary. Choosing not to take part will not affect your care or cause you to lose benefits to which you are entitled. You may withdraw your permission to continue taking part in the bank at any time. To do so, you must send a written withdraw request to the bank at Dr. John Villano c/o Markey Cancer Center Clinical Research Organization, cc140 Markey Cancer Center, 800 Rose Street, Lexington, KY. 40536-0093. The bank will destroy any remaining samples and information that has been stored. In addition, it may be possible for the bank to destroy the code that links you with your sample and medical information. However, the samples and information that has already been shared with other researchers or placed in shared databases cannot be withdrawn.

Please read each sentence below and think about your choice. After reading each sentence, mark "yes" or "no". If you have questions, please talk to the investigator or staff. Remember, no matter what you decide to do about the storage, or banking, and future use of your blood and tissue samples, you may still take part in the main study. If you answer yes to either choice below you also give your authorization for your accompanying health information to be used and disclosed along with the blood.

The sample(s) (blood) you are giving will no longer belong to you and might be used in studies that lead to new products for research, diagnosis or treatment. These products might have some commercial value. There are no plans to provide financial compensation to you should this occur.

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.
When recruiting Non-English-speaking subjects, provide a consent document in the subject's primary language. After saving this section, attach both the English and translated consent documents in the "Informed Consent" section.

Cultural and Language Consultants:

The PI is required to identify someone who is willing to serve as the cultural consultant to the IRB.

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.
- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

Local Requirements:

If you will conduct research at an international location, identify and describe:

- relevant local regulations
- data privacy regulations
- applicable laws
- ethics review requirements for human subject protection

Please provide links or sources where possible. If the project has been or will be reviewed by a local ethics review board, attach a copy in the "Additional Information/Materials" section. You may also consult the current edition of the International Compilation of Human Research Standards

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?

○ Yes ◉ No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the "Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing" [D65.0000] [PDF], and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?

○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the investigator assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials [PDF], IDE regulatory requirements for SR device trials [PDF], and abbreviated regulatory requirements for NSR device trials [PDF]. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe the experience/knowledge/training (if any) of the investigator serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if any sponsor obligations have been transferred to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

IRB policy requires mandatory training for investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?

○ Yes ○ No

If the sponsor-investigator has completed equivalent sponsor-investigator training, submit documentation of the content for the IRB's consideration.

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

I have attached a HIPAA Waiver of Authorization. ○ Yes ◉ No

Attachments

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve a drug including an FDA approved drug; unapproved use of an FDA approved drug; and/or an investigational drug?

○ Yes ◉ No

If yes, complete the questions below. Additional study drug guidance.

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Note: Inpatient studies are required by Hospital Policy to utilize Investigational Drug Service (IDS) pharmacies (Oncology or Non-Oncology). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Is the study being conducted under a valid Investigational New Drug (IND) application?

○ Yes ○ No

If Yes, list IND #(s) and complete the following:

IND Submitted/Held by:

Sponsor: ☐	Held By:	
Investigator: ☐	Held By:	
Other: ☐	Held By:	

☐ Checkmark if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) or if this is an Individual Patient Expanded Access IND (FDA Form 3926).

FDA's Expanded Access Program Information for Individual Patient Expanded Access INDs, and attach the following:

- FDA Form 3926;
- FDA expanded access approval or correspondence;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Expanded Access SOP.

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any

applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

- component, part, accessory;
- assay, reagent, or in-vitro diagnostic device;
- software, digital health, or mobile medical app;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

○ Yes ◉ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer "no" above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

Is the study being conducted under a valid Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE) or Compassionate Use?

○ Yes ○ No

If Yes, complete the following:
IDE or HDE #(s)

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment IDE or Compassionate Use under the Food and Drug Administration (FDA) Expanded Access program.

For Individual or Small Group Expanded Access, see FDA's Early Expanded Access Program Information, and attach the following:

- FDA expanded access approval or sponsor's authorization;
- An independent assessment from an uninvolved physician, if available;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Medical Device SOP.

Does the intended use of any research device being tested (not clinically observed) in this study meet the regulatory definition of Significant Risk (SR) device?

- Yes. Device(s) being tested in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- No. All devices being tested in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Complete and attach the required Study Device Form, picking the "Study Device Form" for the document type. Any applicable device documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.) should be attached using "Other Device Documentation" for the document type.

Attachments

RESEARCH SITES

0 unresolved comment(s)

To complete this section, ensure the responses are accurate then click "SAVE".

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☑ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☑ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's IRB Application Instructions - Off-site Research web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☐ Other Hospitals and Med. Centers

- ☐ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky (UK) or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see IRB Application Instructions - Off-Site Research web page), including:

- A letter of support and local context is required from non-UK sites. See *Letters of Support and Local Context* on the IRB Application Instructions - Off-Site Research web page for more information.
- Supportive documentation, including letters of support, can be attached below.
- NOTE: If the non-UK sites or non-UK personnel are engaged in the research, there are additional federal and university requirements which need to be completed for their participation. For instance, the other site(s) may need to complete their own IRB review, or a cooperative review arrangement may need to be established with non-UK sites.

- Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

List all other non-UK owned/operated locations where the research will be conducted:

Describe the role of any non-UK site(s) or non-UK personnel who will be participating in your research.

Please describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites:

Attachments

B) If your research involves collaboration with any sites and/or personnel outside the University of Kentucky, then it is considered multisite research and IRB reliance issues will need to be addressed. This may include national multi-center trials as well local studies involving sites/personnel external to UK. If you would like to request that the University of Kentucky IRB (UK IRB) serve as the lead IRB for your study, or if you would like the UK IRB to defer review to another IRB, please contact the IRBReliance@uky.edu.

RESEARCH ATTRIBUTES

0 unresolved comment(s)

Instructions: For various reasons, it is necessary to determine whether your research activities meet the definition of clinical research and/or a clinical trial. Your responses to the next series of questions will make that determination. For more details on the definitions, go to ORI's clinical research vs. clinical trial web page or visit NIH's decision tree for the NIH Clinical Trial definition.

My research activities include one or more of the following:

Patient-oriented research regarding mechanisms of human disease, therapeutic interventions, clinical studies, or development of new technologies
◉ Yes ○ No

Material of human origin (such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects
◉ Yes ○ No

Epidemiologic or Behavioral Studies
○ Yes ◉ No

Outcomes Research or Health Services Research
○ Yes ◉ No

Does your research involve one or more human subjects prospectively assigned into one or more health-related biomedical or behavioral interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes?
◉ Yes ○ No

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

☐ Academic Degree/Required Research
☐ Alcohol/Drug/Substance Abuse Research
☐ Biological Specimen Bank Creation (for sharing)
☑ Cancer Research
☐ CCTS-Center for Clinical & Translational Science
☐ Certificate of Confidentiality
☐ Collection of Biological Specimens for banking and use
☐ Community-Based Participatory Research
☐ Deception
☐ Educational/Student Records (e.g., GPA, test scores)
☐ Emergency Use (Single Patient)
☐ Gene Transfer
☐ Genetic Research
☐ NIH Genomic Data Sharing (GDS) (databases such as GWAS, dbGaP, GenBank)
☐ Treatment with Human Cells, Tissues, and Cellular and Tissue Based Products
☐ Individual Expanded Access or Compassionate Use
☐ International Research
☐ Planned Emergency Research Involving Exception from

For additional requirements and information:

- Cancer Research (MCC PRMC)
- Certificate of Confidentiality (look up "Confidentiality/Privacy...")
- CCTS (Center for Clinical and Translational Science)
- Clinical Research (look up "What is the definition of....)
- Clinical Trial
- Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection...")
- Collection of Biological Specimens (look up "Specimen/Tissue Collection...")
- Community-Based Participatory Research (look up "Community-Engaged...")
- Data & Safety Monitoring Board (DSMB)

  *For Medical IRB: Service Request Form for CCTS DSMB

- Data & Safety Monitoring Plan
- Deception*

  *For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF)
- Genetic Research (look up "Specimen/Tissue

Informed Consent

- ☐ Recombinant DNA
- ☐ Registry or data repository creation
- ☐ Stem Cell Research
- ☐ Suicide Ideation or Behavior Research
- ☐ Survey Research
- ☐ Transplants
- ☐ Use, storage and disposal of radioactive material and radiation producing devices
- ☐ Vaccine Trials

Collection...")

- Gene Transfer
- HIV/AIDS Research (look up "Reportable Diseases/Conditions")
- Screening for Reportable Diseases [E2.0000] (PDF)
- International Research (look up "International & Non-English Speaking")
- NIH Genomic Data Sharing (GDS) Policy (PDF)
- Planned Emergency Research Involving Waiver of Informed Consent*

*For Planned Emergency Research Involving Waiver of Informed Consent, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Use, storage and disposal of radioactive material and radiation producing devices

FUNDING/SUPPORT

0 unresolved comment(s)

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

- ☐ Grant application pending
- ☐ (HHS) Dept. of Health & Human Services
  - ☐ (NIH) National Institutes of Health
  - ☐ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☐ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☑ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Click applicable listing(s) for additional requirements and information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy Summary and Department of Energy Identifiable Information Compliance Checklist
- (EPA) Environmental Protection Agency

Other:

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

Markey Cancer Center

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application using the "Add Related Grants" button.
If required by your funding agency, upload your grant using the "Grant/Contract Attachments" button.

Add Related Grants

Grant/Contract Attachments

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP and DoD Summary for details)

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in the DoD SOP.

DOD SOP Attachments

Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

◉ Yes ○ No

☐ Institutional Biosafety Committee
☐ Radiation Safety Committee
☐ Radioactive Drug Research Committee
☑ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
☐ Graduate Medical Education Committee (GME)
☐ Office of Medical Education (OME)

Additional Information

- Institutional Biosafety Committee (IBC) - Attach required IBC materials
- Radiation Safety Committee (RSC) - For applicability, see instructions and attach form
- Radioactive Drug Research Committee (RDRC)
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)** - Attach MCC PRMC materials, if any, per instructions.
- Office of Medical Education (OME)
- Graduate Medical Education Committee (GME)

Attachments

Attach Type	File Name
OtherReviewCommittees	2017-033+MCC-17-MULTI-20-PMC_PRMC+Memo+AM+10_vd071020+Review.pdf
OtherReviewCommittees	2017-033+MULTI-20_PRMC%2BMemo%2BAmend%2Bv9%2Bvd021720%2BReview.pdf
OtherReviewCommittees	PRMC Initial Approval Memo.pdf

**** If your study involves cancer research, be sure to select "Cancer Research" in the "Research Attributes" section.** ORI will send your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRMC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

ADDITIONAL INFORMATION/MATERIALS

1 unresolved comment(s)

Do you want specific information inserted into your approval letter? ◉ Yes ○ No

Approval Letter Details:

If you wish to have specific language included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type that language in the box below exactly as it should appear in the letter. The text you enter will automatically appear at the top of all approval letters, identical to how you typed it, until you update it. Don't include instructions or questions to ORI staff as those will appear in your approval letter. **If these details need to be changed for any reason, you are responsible for updating the content of this field.**

CR 2025 KP updated removed Kolesar , Groleau, moved to expedited per ORI request

Additional Materials:

If you have other materials you would like to include for the IRB's consideration, check all that apply and attach the corresponding documents using the Attachments button below.

- ☑ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☑ Other Documents

Protocol/Other Attachments

Attach Type	File Name
Protocol	MULTI-20. Amdmnt 12_29July2022_Clean.pdf
Protocol	MULTI-20. Amdmnt 12_29July2022_trk.pdf

NOTE: Instructions for Dept. of Health & Human Services (DHHS)-approved protocol]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

To view the materials currently attached to your application, click “All Attachments” on the left menu bar.

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

Introduction

All IRB applications require additional assurances by a Department Chairperson or equivalent (DA), and when applicable, a Faculty Advisor or equivalent (FA). This signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. The person assigned as DA *should not* also be listed in the Study Personnel section, and the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, refer to "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

For a detailed illustration of how to complete this section, please review the short online video tutorial "Signatures (Assurance) Section - How to Complete." Otherwise, follow the steps below.

Required Signatures:

Individuals chosen as signees may remove the application from their Inbox without signing the Assurance Statement by clicking "Return to PI" with a comment about why it is being returned (e.g., specific edits are deemed necessary).

The PI, and personnel chosen as a contact, will receive an email notification that edits are needed, and can find the draft application in both the "Draft" folder and the "Signatures Status" folder located in the menu in the left margin of the default Inbox page. The researcher does not have a 'reply' option to the signee's comments and must make the requested edits directly in the application, or communicate outside the E-IRB system as to why not. Once the response is finalized, the researcher must re-visit the "Assurances Required" section to click the "Return to Signee" button for their re-consideration; the signee will receive an email notification at that time.

Hover your mouse cursor here for additional instructions.

First Name	Last Name	Role	Department	Signee Return Comment	Date Signed	
Bernard	Evers	Other Signee	Surgery/General		06/28/2018 09:07 AM	View/Sign
Lowell	Anthony	Department Authorization	Internal Medicine		06/28/2018 11:27 AM	View/Sign
John	Villano	Principal Investigator	Internal Medicine		07/25/2018 08:55 PM	View/Sign

Other Signee's Assurance Statement

☑ This is to certify, that at the request of the Principal Investigator (PI), I have reviewed this research protocol and agree it is appropriate per departmental/college policy and/or procedures and I will support the PI as needed.

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator has been notified of the additional regulatory requirements of the sponsor and by signing the principal investigator Assurance Statement, confirms he/she can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

**IF APPLICABLE FOR RELIANCE: I attest that the principal investigator has been notified of the regulatory requirements of both the Reviewing and Relying IRBs, according to the information provided in the E-IRB application. The attached Reliance Assurance Statement, signed by the principal investigator, confirms that he/she can comply with both sets of IRB requirements.

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that:

- I have appropriate facilities and resources for conducting the study;
- I am aware of and take full responsibility for the accuracy of all materials submitted to the IRB for review;
- If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.
- If applying for an Abbreviated Application (AA) to rely on an external IRB, I understand that certain items above (1, 3, 4, 7-8) may not apply, or may be altered due to external institutional/IRB policies. I document my agreement with the Principal Investigator Reliance Assurance Statement by digitally signing this application.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Once all Assurance Statement signatures have been acquired, return to this section to submit your application to ORI.

SUBMISSION INFORMATION

0 unresolved comment(s)

***** If this Continuation Review entails a change in the scope of your activities to include COVID-19 related research, please insert "COVID19" at the start of your Project and Short Titles.*****

Each Section/Subsection in the menu on the left must have a checkmark beside it (except this Submission section) indicating the Section/Subsection has been completed. Otherwise your submission for IRB review and approval cannot be sent to the Office of Research Integrity/IRB.

If applicable, remember to update the Approval Letter Details text box under the Additional Information section

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and you will receive a message to notify you of the date.

If you are making a change to an attachment, you need to delete the attachment, upload a highlighted version that contains the changes (use Document Type of "Highlighted Changes"), and a version that contains the changes without any highlights (use the appropriate Document Type for the item(s)). Do **not** delete approved attachments that are still in use.

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects, and I attest to:

1. Having reviewed all the investigational data from this study, including a compilation of all internal and external unanticipated problems.
2. Having reviewed, if applicable, information from the sponsor including updated investigator brochures and data and safety monitoring board reports.

I also attest that I have reviewed pertinent materials concerning the research and concluded either:

A. The human subject risk/benefit relationship is NOT altered, and that it is not necessary to modify the protocol or the informed consent process,
OR,
B. The human subject risk/benefit relationship has been altered, and have previously submitted or am including with this continuation review submission, a modification of the research protocol and informed consent process.

☑ By checking this box, I am providing assurances for the applicable items listed above.

Your protocol has been submitted.

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	Document Type	File Loaded	Document Description	File Size	Modified By	Mod Date
	ApprovalLetter	ApprovalLetter.pdf		0.084	jchine2	2/6/2025 11:58:15 AM
	CR_DataSafetyMonitoring	s5_MCC-17-MULTI-20-PMC_DSMC Findings Memo_13Dec2024 deferred (BS).pdf	DSMC Findings memo Dec 2024	0.241	smurp3	1/22/2025 4:27:13 PM
	CR_DataSafetyMonitoring	20_MCC-17-MULTI-20-PMC_DSMC Memo_13Dec2024 (BS).pdf	DSMC Dec 2024	0.272	smurp3	1/22/2025 4:26:41 PM
	CR_DataSafetyMonitoring	s2_MCC-17-MULTI-20-PMC_DSMC Findings Memo_18Oct2024 (TB).pdf	DSMC Findings memo Oct 2024	0.257	smurp3	1/22/2025 4:26:13 PM
	CR_DataSafetyMonitoring	21_MCC-17-MULTI-20-PMC_DSMC Memo_18Oct2024 (TB).pdf	DSMC October 2024	0.286	smurp3	1/22/2025 4:25:40 PM
	CR_DataSafetyMonitoring	min11_MCC-17-MULTI-20-PMC_DSMC Findings Memo_20Sep2024 (TB).pdf	DSMC Findings memo September 2024	0.259	smurp3	1/22/2025 4:25:05 PM
	CR_DataSafetyMonitoring	MCC-17-MULTI-20-PMC_DSMC Audit Findings Memo_10Sep2024 - MCC (TB).pdf	DSMC September 2024	0.180	smurp3	1/22/2025 4:24:39 PM
	CR_DataSafetyMonitoring	20_MCC-17-MULTI-20-PMC_DSMC Memo_16Aug2024.pdf	DSMC August 2024	0.275	smurp3	1/22/2025 4:24:09 PM
	CR_DataSafetyMonitoring	17_MCC-17-MULTI-20-PMC_DSMC Memo_26Jul2024.pdf	DSMC July 2024	0.195	smurp3	1/22/2025 4:23:43 PM
	CR_DataSafetyMonitoring	ers3_MCC-17-MULTI-20-PMC_DSMC Findings Memo_21Jun2024 - TB.pdf	DSMC Findings June 2024	0.136	smurp3	1/22/2025 4:23:10 PM
	CR_DataSafetyMonitoring	20_MCC-17-MULTI-20-PMC_DSMC Memo_21Jun2024 - TB.pdf	DSMC Memo June 2024	0.138	smurp3	1/22/2025 4:22:35 PM
	CR_DataSafetyMonitoring	s4_MCC-17-MULTI-20-PMC_DSMC Findings Memo_10May2024 - TB.pdf	DSMC Findings memo May 2024	0.184	smurp3	1/22/2025 4:22:05 PM
	CR_DataSafetyMonitoring	22_MCC-17-MULTI-20-PMC_DSMC Memo_10May2024 - TB (1).pdf	DSMC May 2024	0.199	smurp3	1/22/2025 4:21:42 PM
	CR_DataSafetyMonitoring	s1-3_MCC-17-MULTI-20-PMC_DSMC Findings Memo_19Apr2024.pdf	DSMC Findings Memo April 2024	0.186	smurp3	1/22/2025 4:21:16 PM
	CR_DataSafetyMonitoring	20_MCC-17-MULTI-20-PMC_DSMC Memo_19Apr2024.pdf	DSMC April 2024	0.197	smurp3	1/22/2025 4:20:51 PM
	CR_DataSafetyMonitoring	s1_MCC-17-MULTI-20-PMC_DSMC Findings Memo_17Jan2025 (TB).pdf	DSMC finding memo	0.266	smurp3	1/22/2025 4:20:03 PM
	CR_DataSafetyMonitoring	16_MCC-17-MULTI-20-PMC_DSMC Memo_17Jan2025 (TB).pdf	DSMC Jan 2025	0.287	smurp3	1/22/2025 4:19:45 PM
	AddInfoProtocol	MULTI-20. Amdmnt 12_29July2022_trk.pdf	MULTI-20. Amdmnt 12_29July2022_trk	0.480	spengl2	9/28/2022 1:46:40 PM
	AddInfoProtocol	MULTI-20. Amdmnt 12_29July2022_Clean.pdf	MULTI-20. Amdmnt 12_29July2022_Clean	0.562	spengl2	9/28/2022 1:46:21 PM
	Advertising	Amend 12 dtd 29July2022-Appendix eligibility criteria.pdf	Amend 12 dtd 29July2022-Appendix eligibility criteria	0.204	spengl2	9/28/2022 1:44:51 PM
	AdditionInfoConsiderations	SAE report MULTI 20 28APR2022.pdf	SAE report MULTI 20 28APR2022	0.238	spengl2	4/28/2022 2:20:01 PM
	OtherReviewCommittees	2017-033+MCC-17-MULTI-20-PMC_PRMC+Memo+AM+10_vd071020+Review.pdf	PRMC Amendment Review Memo	0.153	llgill3	7/27/2020 4:13:37 PM
	ResearchProcedures	Calendar Protocol vd 17Feb2020.pdf	Research Procedures	0.033	llgill3	3/6/2020 4:13:25 PM

StudyPopulation	Full eligibility from current protocol.pdf	Study Population	0.074	llgill3	3/6/2020 4:10:25 PM
StudyDesign	Schema and study design_PA 17Feb2020.pdf	Study Design	0.106	llgill3	3/6/2020 4:06:32 PM
StudyDesign	objectives and background_PA 17Feb2020.pdf	objectives and background	0.076	llgill3	3/6/2020 4:03:24 PM
OtherReviewCommittees	2017-033+MULTI-20_PRMC%2BMemo%2BAmend%2Bv9%2Bvd021720%2BReview.pdf	PRMC Amendment Review Approval	0.380	llgill3	3/3/2020 3:42:05 PM
AdditionInfoConsiderations	Research Description reivsed - HL.pdf	Research description showing revisions since initial approval	0.161	sktemp2	7/5/2018 8:39:01 AM
OtherReviewCommittees	PRMC Initial Approval Memo.pdf	Initial approval by Markey PRMC	0.365	sktemp2	6/27/2018 3:46:51 PM

Protocol Changes

Click link to sort Changed Date
Additional Information/Materials AdditionalInformation changed by smurp3 on 2/6/2025 10:47:35 AM
CR 2025 KP updated removed Kolesar , Groleau, moved to expedited per IRBORI request
Additional Information/Materials AdditionalInformation changed by smurp3 on 2/6/2025 8:43:42 AM
CR 2025 KP updated removed Kolesar , Groleau, moved to expedited per IRB
Additional Information/Materials AdditionalInformation changed by smurp3 on 1/22/2025 4:02:35 PM
~~Adding Murphy and Young~~CR 2025 KP updated removed Kolesar , Groleau
Continuation/Final Review RiskLevelChanged changed by smurp3 on 2/6/2025 8:41:11 AM
~~N~~Y
Continuation/Final Review RiskLevelChangedDesc changed by smurp3 on 2/6/2025 10:46:55 AM
Study enrollment is permanently closed; subjects have completed all research-related interventions; and the study remains active only for long-term follow-up of subjects- study had been previously reviewed by full committee
Continuation/Final Review RiskLevelChangedDesc changed by smurp3 on 2/6/2025 10:44:28 AM
~~notified for expedited~~Study enrollment is permanently closed; subjects have completed all research-related interventions; and the study remains active only for long-term follow-up of subjects- study
Continuation/Final Review RiskLevelChangedDesc changed by smurp3 on 2/6/2025 8:41:11 AM
qualified for expedited
Expedited Categories XPCategory0 changed by smurp3 on 2/6/2025 8:40:09 AM
Y
Expedited Categories XPCategory1 changed by smurp3 on 2/6/2025 8:40:09 AM
N
Expedited Categories XPCategory2 changed by smurp3 on 2/6/2025 8:40:09 AM
N
Expedited Categories XPCategory3 changed by smurp3 on 2/6/2025 8:40:09 AM
N
Expedited Categories XPCategory4 changed by smurp3 on 2/6/2025 8:40:09 AM
N
Expedited Categories XPCategory5 changed by smurp3 on 2/6/2025 8:40:09 AM
N
Expedited Categories XPCategory6 changed by smurp3 on 2/6/2025 8:40:09 AM
N
Expedited Categories XPCategory7 changed by smurp3 on 2/6/2025 8:40:09 AM
N
HIPAA HIPAADeIdentificationCertForm changed by smurp3 on 1/22/2025 4:03:03 PM
~~N~~
Informed Consent ElectronicConsent changed by smurp3 on 1/22/2025 3:58:38 PM
N
Informed Consent InformedConsentHIPAACombinedForm changed by smurp3 on 1/27/2025 3:45:21 PM
~~Y~~N
Informed Consent StampedConsent changed by smurp3 on 1/22/2025 3:58:38 PM
~~N~~Y
Project Information IsSubEnrollDataSpecimen changed by smurp3 on 2/6/2025 8:41:52 AM
~~Y~~N
Project Information SubjectCount changed by smurp3 on 2/6/2025 10:42:21 AM
~~100~~97
Research Attributes ClinicalResearch changed by smurp3 on 1/22/2025 4:03:37 PM
~~Y~~
Research Attributes EpidemiologicBehavioralStudies changed by smurp3 on 1/22/2025 4:03:37 PM
N
Research Attributes MaterialOfHumanOrigin changed by smurp3 on 1/22/2025 4:03:37 PM
Y
Research Attributes OutcomesHealthServicesResearch changed by smurp3 on 1/22/2025 4:03:37 PM
N
Research Attributes PatientOrientedResearch changed by smurp3 on 1/22/2025 4:03:37 PM
Y
Research Sites MultisiteLeadInvestigator changed by smurp3 on 1/22/2025 4:03:23 PM
~~N~~
Risk Level RiskCategory changed by smurp3 on 2/6/2025 8:41:17 AM
~~2~~1

Study Personnel Changes:

Status	PPIdentity	ProtocolID	PersonID	RoleInProtocol	IsContact	LastName	FirstName	Email	DeptCode	RoomBuilding	SpeedSort	PhoneNum	DeptDesc	AuthorizedConsent	ResponsibilityInProject	Degree	Rank	StatusFlag	IsRemoved	ModBy	ModDate	SFI	IsPIRN	MiddleName
Deleted	987068	102321	12230714	SP	N	Kolesar	Jill	Jill.Kolesar@uky.edu						Y	Sub-Investigator	PharmD			Y	smurp3	1/22/2025 3:59:51 PM	N		M.
Deleted	987075	102321	12605827	SP	N	Groleau	Jonathan	Jonathan.Groleau@uky.edu						N	Project Assistance/Support				Y	smurp3	1/22/2025 3:59:37 PM	N		

Protocol Type Comment by Joanne Hines - ORI to PI on 2/6/2025 10:35:01 AM
Returned to PI/study team - see comments dated today from ORI Expedited/XP staff.

Project Information Comment by Joanne Hines - ORI to PI on 2/6/2025 10:30:34 AM
Returned to PI/study team - please update the total enrolled here - according to the Continuation section - 97 have been enrolled since initial review.

Additional Information/Materials Comment by Joanne Hines - ORI to IRB/PI on 2/6/2025 10:26:10 AM
The "move to expedited" was "per ORI", not "per IRB" - the IRB must review before making determination.

Continuation/Final Review Comment by Joanne Hines - ORI to PI on 2/6/2025 10:33:05 AM
Question #8 - please update the box to describe why the risk level and why the study "qualified for expedited" review (see question #1 for response).

After completion of the study, a final historical control will be calculated using the actual distribution of patients by disease type (1st and 2nd line NSCLC and 2nd line HNSCC) and the historical 6-mo PFS rates from the original sample size justification. The 6-month PFS rate from the Kaplan-Meier analyses will be compared to this final weighted historical control using a 95% confidence interval about the observed 6-mo PFS rate.

All patients who received study drug will be included in the safety analysis. Incidence tables will be generated to summarize incidence of patients reporting at least one episode of each specific AE, incidence of AE causing withdrawal and incidence of SAE. The total number of episodes for each event reported (Frequency Table), the severity and attribution to study therapy of each episode reported (Severity Table and Attribution Table) will also be displayed.

Listings of AEs by patients will include the time to onset, the duration of each event, the severity of each event, the relationship of the event to study therapy, whether it was a serious event, and whether it caused withdrawal. Toxicities will be graded according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0. All correlative measures will be summarized and presented with confidence intervals in aggregate and by disease type.