



AIDS MALIGNANCY CONSORTIUM

AMC PROTOCOL #115:

Use of a Screening Tool to Describe HIV-Related Cancer Burden and Patient Characteristics in the AIDS Malignancy Consortium

A Trial of the AIDS Malignancy Consortium (AMC)

Sponsored by: National Cancer Institute
Office of HIV and AIDS Malignancy (OHAM)

NCT Registration Number: TBD

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Version 4.0, August 11, 2022
NCI Version Date August 11, 2022

AMC PROTOCOL SIGNATURE PAGE

I, _____, Principal Investigator at site _____, agree to conduct and follow this protocol: **AMC Protocol #115 – Use of a Screening Tool to Describe HIV-Related Cancer Burden and Patient Characteristics in the AIDS Malignancy Consortium (Version 4.0, 11AUG2022)**, as written according to AMC and NCI, and standards of Good Clinical Practice (GCP, ICH E6 R2). I understand that no deviations from the protocol eligibility criteria or waivers for protocol deviations will be permitted.

Signature

Date (DDMMYYYY)

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PROTOCOL ROSTER

AMC Protocol #115

Use of a Screening Tool to Describe HIV-Related Cancer Burden and Patient Characteristics in the AIDS Malignancy Consortium

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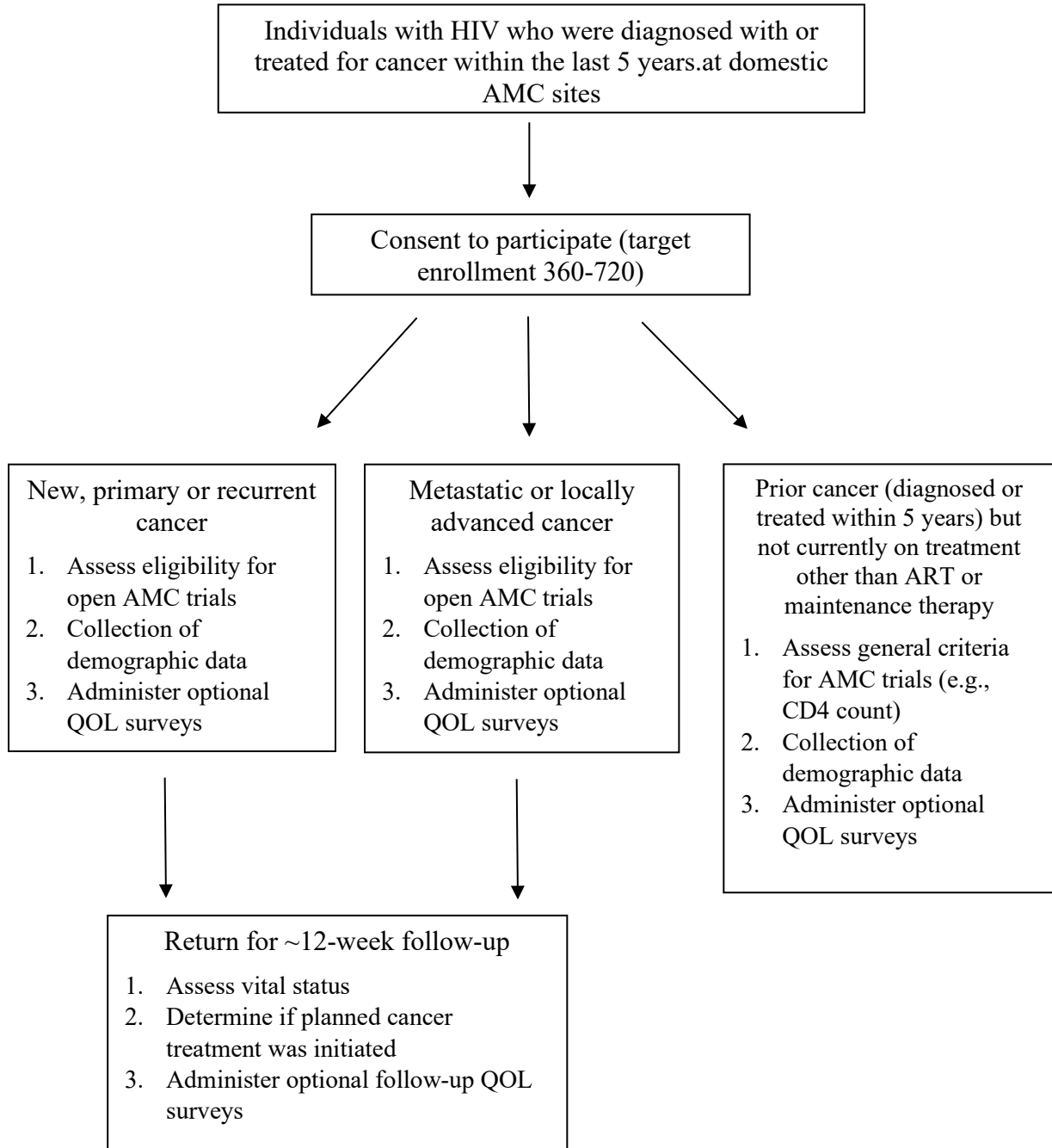
CONTACT INFORMATION

For regulatory requirements:	For patient enrollments:	For data submission:
<p>Regulatory documentation must be submitted to the CTSU via the Regulatory Submission Portal.</p> <p>(Sign in at www.ctsuh.org and select the Regulatory > Regulatory Submission.)</p> <p>Institutions with participants waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 1-866-651-2878 to receive further instruction and support.</p> <p>Contact the CTSU Regulatory Help Desk at 1-866-651-2878 for regulatory assistance.</p>	<p>Refer to the patient enrollment section of the protocol for instructions on using the Oncology Patient Enrollment Network (OPEN). OPEN is accessed at https://www.ctsuh.org/OPEN_SYS_TEM/ or https://OPEN.ctsuh.org.</p> <p>Contact the CTSU Help Desk with any OPEN-related questions by phone or email 1-888-823-5923, or ctsuhcontact@westat.com.</p>	<p>Data collection for this study will be done exclusively through Medidata Rave. Refer to the data submission section of the protocol for further instructions.</p>
<p>The most current version of the study protocol and all supporting documents must be downloaded from the protocol-specific page located on the CTSU members' website (https://www.ctsuh.org). Access to the CTSU members' website is managed through the Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM) registration system and requires log in with a CTEP-IAM username and password.</p> <p>Permission to view and download this protocol and its supporting documents is restricted and is based on person and site roster assignment housed in the CTSU Regulatory Support System (RSS).</p>		
<p><u>For clinical questions (i.e., patient eligibility)</u></p> <p>Contact the protocol team via email at amc-115protocolteam@emmes.com.</p> <p><u>For clinical data submission questions:</u></p> <p>AMC Operations and Data Management Center The Emmes Company, LLC Phone: (301) 251-1161 Email: amc-115@emmes.com</p>		
<p><u>For non-clinical questions (i.e., unrelated to patient eligibility, treatment, or clinical data submission)</u> Contact the CTSU Help Desk by phone or email:</p> <p>CTSU General Information Line – 1-888-823-5923, or ctsuhcontact@westat.com. All calls and correspondence will be triaged to the appropriate CTSU representative.</p>		

PROTOCOL SYNOPSIS

Title:	Use of a Screening Tool to Describe HIV-Related Cancer Burden and Patient Characteristics in the AIDS Malignancy Consortium
Accrual Target:	A minimum of 360 and maximum of 720 participants
Regulatory Status:	Non-Interventional
Population:	Participants with a dual diagnosis of both cancer (current or diagnosed within 5 years) and underlying HIV infection, who present for care at AMC domestic sites.
Regimen:	Participants will be identified via screening of electronic medical records or institutional databases. All eligible participants will have one visit for the collection of broad demographic and clinical data. Participants initiating or receiving ongoing treatment for their cancer will attend a single follow-up visit. Data collection at study visits will occur via survey procedures and/or medical record review.
Anticipated Trial Duration:	Approximately 3 years for accrual and follow-up
Primary Objective:	To estimate the number of cancers in people with HIV (PWH) who present for care at domestic AMC sites
Secondary Objectives:	To characterize participants that are eligible but not enrolled onto AMC clinical trials to understand site-specific and trial-specific accrual barriers
Exploratory Objectives:	<ol style="list-style-type: none">1. To standardize and expand the quantity and quality of sociodemographic and cancer diagnostic and treatment characteristics collected for PWH receiving care at domestic AMC sites.2. To describe cancer patient health-related QOL for PWH at domestic AMC sites using validated tools: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ-C30] and Supportive Care Needs Survey Short Form 34 [SCNS-SF34].

PROTOCOL SCHEMA



LIST OF ABBREVIATIONS

AE	Adverse event
AIDS	Acquired immunodeficiency syndrome
AMC	AIDS Malignancy Consortium
ART	Antiretroviral therapy
CBC	Complete blood count
CDC	Centers for Disease Control and Prevention
CDUS	Clinical Data Update System
CRF	Case report form
CTEP	Cancer Therapy Evaluation Program
CTEP-AERS	Cancer Therapy Evaluation Program Adverse Event Reporting System
DSMB	Data and Safety Monitoring Board
ECOG	Eastern Cooperative Oncology Group
EORTC-QLQ	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FDA	Food and Drug Administration
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
IRB	Institutional review board
IND	Investigational new drug
NCI	National Cancer Institute
ODMC	Operations and data management center
PWH	People with HIV
POSEC	Patient Outcomes, Survivorship, and Engagement Committee
PrEP	Pre-exposure Prophylaxis
PROs	Patient-Reported Outcomes
QOL	Quality of Life
RNA	Ribonucleic acid
SAE	Serious adverse event
SCNS-SF34	Supportive Care Needs Survey Short Form 34
SES	Socioeconomic Status

1.0 OBJECTIVES

1.1 Primary Objective

To estimate the number of cancers in PWH who present for care at domestic AMC sites

1.2 Secondary Objectives

1.2.1 To characterize participants that are eligible but not enrolled onto AMC trials to understand site-specific and trial-specific accrual barriers, particularly for minority and underserved populations.

1.3 Exploratory Objectives

1.3.1 To standardize and expand the quantity and quality of sociodemographic (e.g., racial/ethnic distribution, SES), HIV-related [e.g., Antiretroviral Therapy (ART) medications, co-morbidities], and cancer diagnostic and treatment characteristics collected for PWH receiving care at domestic AMC sites.

1.3.2 To describe cancer patient health-related Quality of Life (QOL) for PWH at domestic AMC sites using validated tools: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ-C30] and Supportive Care Needs Survey Short Form 34 [SCNS-SF34].

2.0 BACKGROUND

2.1 Introduction

Accrual of adults onto cancer clinical trials is challenging, and the cancer burden in the U.S. HIV population is growing to include a broader spectrum of both AIDS-defining and age-related, non-AIDS-defining cancers [1]. The objective of this protocol is to collect high-quality data that will address both trends.

Fewer than 5% of U.S. adult cancer patients, and even fewer affected by both cancer and HIV/AIDS, enroll onto clinical trials. Research groups and government-sponsored organizations increasingly have focused on engaging communities to participate in cancer clinical trials. To broaden the understanding of characteristics of adults screened for, and those opting out of, NCI-sponsored cancer clinical trials, NCI Community Oncology Research Program (NCORP) developed a clinical trials screening tool (NCORP DCP-001). AIDS Malignancy Consortium (AMC) clinical trials share similar challenges to the NCI trials described in NCORP DCP-001 [2], so screening tools to identify consistent barriers to participation for people living with HIV (PWH), who have historically been under-represented in clinical trials, are urgently needed across the AMC. The AMC preliminarily examined patient-level characteristics and perceptions that influenced decision-making about trial participation for 67 patients diagnosed with anal cancer or high-grade anal intraepithelial neoplasia [3]. Of those 67 participants, most were male (92.5%) non-Hispanic white (89.5%) adults (48.3 years old on average); most learned about AMC clinical trials from a medical provider (98.5%); and most (73.1%) expressed little general knowledge about clinical trials. Participants recommended system-level changes to accelerate patient access to clinical trials. Participants further underscored the need to address knowledge barriers to clinical trial participation. This protocol will follow-up on these recommendations by proposing an AMC effort across all domestic sites to identify patient demographic (e.g., race/ethnicity), socioeconomic (e.g., homelessness/insurance status), and cancer-related (e.g., extent of disease) features associated with AMC clinical trial participation. This approach represents a large expansion beyond those preliminary data published from AMC-S006 by allowing enrollment across all domestic AMC sites, including all cancer types and AMC scientific working groups in data collection, and obtaining valuable information from not only participants who choose to enroll but, perhaps more importantly, from participants who present to AMC sites and are eligible for an open trial but who opt out of participation.

In 2019, the AMC implemented a screening and prospective observational cohort protocol in Latin America (AMC-S008), with the goal of estimating the number of HIV-associated cancers of various types presenting at participating AMC clinical sites in the region. That protocol captures broad demographic and clinical data to generate further clinical treatment outcome hypotheses and research questions within the AMC international portfolio. The effort proposed here would represent the first such protocol focused on uniform prospective cancer patient data collection across AMC domestic sites.

In summary, this protocol will implement a screening tool at domestic AMC sites that will capture cancer patterns in PWH, as well as broad demographic, cancer/clinical, and quality

of life (QOL) data from participants to generate future research questions and design efforts to improve AMC clinical trial participation.

2.2 Study Design and Rationale

Rationale: Collection of expanded patient demographics and clinical information to include socioeconomic status (SES), method of diagnoses, and engagement in recommended oncology care is one way to enhance our ability to evaluate both the full patient population served at AMC domestic sites and to identify factors influencing participation in AMC clinical trials. This includes features of both participants who are potentially eligible but elect not to screen for trials and participants who are screened but deemed ineligible. Understanding characteristics of those presenting for care at AMC sites is critical to inform the design of future AMC cancer prevention and treatment efforts and assessment of feasibility of proposed trials to make informed decisions for resource allocation. In addition, this information will be invaluable in informing survivorship programs for PWH and cancer.

Capturing patient health-related quality of life (QOL) experiences via patient-reported outcomes (PROs), is essential; thus, in 2020 the AMC formed the Patient Outcomes, Survivorship, and Engagement Committee (POSEC) to ensure that this data is documented in AMC trials using validated, culturally appropriate PRO tools that are of minimal burden to trial participants. Accordingly, this protocol will include an optional, brief PRO/QOL needs assessment that will allow for a better understanding of whether participant PRO/QOL features are potential barriers to clinical trial enrollment. This will serve as the first widespread use of QOL data across the AMC, both fulfilling the mission of POSEC and building a foundation for future, longitudinal survivorship efforts led by POSEC in the AMC.

In summary, anticipated outcomes of this observational protocol are as follows:

- Identify patient and clinical features associated with AMC clinical trial participation
- Capture a complete picture of cancer burden in PWH at domestic AMC sites to guide future clinical trial priorities
- Establish a robust population science framework for high-quality data collection across AMC sites
- Serve as the first protocol to build a foundation for future QOL-based and survivorship efforts across the domestic AMC

Study Design: All PWH who present for care at participating AMC clinical trial sites with a diagnosis of cancer will be tracked on a screening list. Institutional review board (IRB) approvals will be obtained to allow screening of the electronic medical record or institutional databases to identify these participants, as well as approach them after identification for further data collection. After identification, eligible patients will be approached to provide consent and participate in the collection of broad demographic and clinical data. To facilitate patient recruitment, and due to the on-going COVID-19 pandemic, remote consenting prior to further data collection will be allowed, within the guidelines provided by the NCI Central Institutional Review Board (NCI CIRB) policies (see <https://www.ncicirb.org/announcements/remote-consent-procedures-revised-faqs->

due-covid-19). Such communications will be done via HIPAA-compliant methods such as telephone, personal delivery of documents, US postal service, REDCap, or other compliant electronic platform. The remote consent process will parallel the consent processed used for in-person consenting. The only difference will be the method(s) of communication and optional use of eSignatures, only if implemented according to NCI CIRB SOP section 2.3.1.6. The study team will ensure that, as with in-person consenting, the participant is given sufficient opportunity to ask questions, is able to understand the nature of this study and what participation entails, and is provided a copy of the final, completed consent signed by all parties involved.

This trial is a one visit study for those with history of malignancy diagnosed in the past 5 years, including those with cancer currently in remission. There will be one follow-up visit for those initiating or receiving on-going treatment for their cancer. In all participants who consent to participate, data captured will include the following:

Table 2-A: Model data collection

Participant Characteristics	Date of birth, biological sex, gender identity, race, ethnicity, height and weight
Sociodemographic	Socioeconomic status (e.g., ZIP code, housing status [homeless y/n]), health insurance (insured/uninsured, type if insured)
Health Behaviors	Tobacco use (type, exposure [pack/day, years use]), illicit drug use (ever, type, years exposure), alcohol use (ever, exposure [drinks/week], years exposure)
Comorbid Conditions	Hepatitis B and C co-infection, cardiovascular disease (y/n, type), psychiatric conditions (y/n, type), non-cancer pulmonary conditions (y/n, type), hepatic dysfunction, hematologic abnormalities, renal dysfunction, neurologic disorders, endocrine disorders (including thyroid disorders, and diabetes)
HIV Care	Current ART regimen, years of ART use, year of HIV diagnosis, history of opportunistic infections, recent HIV viral load and CD4+ T-cell count
Status of Cancer Diagnosis	New, primary or recurrent disease; current metastatic or locally advanced, inoperable cancer; history of malignancy diagnosed within 5 years / cancer currently in remission
Cancer Details	Cancer type, date cancer diagnosed, diagnosis methods (clinical, cytology, histology), pathology performed, date of pathology, staging, staging methods (clinical, radiographic, surgical), current ECOG Performance Status (PS), current laboratory (CBC) values, cancer treatment history (for metastatic tumors or disease in remission)
Cancer Treatment Plan	Planned treatment (e.g., chemotherapy versus radiation versus surgery versus antiretroviral therapy [ART] only versus best supportive care/watchful waiting), location of planned treatment, timeline of planned treatment (start date), if past diagnosis and treatment- end date, enrollment in clinical trial, and clinical trial details

Quality of Life/Survivorship	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30: Global health status, physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial toxicity) and Supportive Care Needs Survey Short Form 34 (SCNS-SF34: psychological needs, health system and information needs, physical and daily living needs, patient care and support needs, sexuality needs)
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For participants initiating therapy or currently under treatment, a short interval follow-up (12 weeks \pm 2 weeks), will be used to ascertain vital status, state of planned cancer therapy (initiated as planned versus delayed initiation, no initiation, or initiation of alternate therapy instead of planned therapy) and any reasons for therapy not being initiated as planned (e.g., comorbidity, cancer progression, patient preference, insurance denial), and optional quality of life changes between initial registration and this short interval follow-up. An approximate 12-week follow-up assessment is expected to coincide with planned treatments/clinical follow-up and therefore minimize unnecessary clinic visits that could increase patient burden. The data collected at this later time point will be limited, as the intent capture is to ascertain the relationship between planned therapy and therapy received, as well as any QOL changes that coincide with start of therapy and/or clinical trial enrollment.

3.0 PARTICIPANT SELECTION

A rostered AMC investigator (CTEP-registered physician investigator or non-physician investigator) must document that each protocol participant meets all stated eligibility criteria. Participating sites must have documentation that each eligibility requirement is satisfied prior to participant enrollment. In compliance with CTEP policy, no exceptions to eligibility criteria will be granted under any circumstance.

NOTE: Institutions may use this section of the protocol as an eligibility checklist for source documentation if it has been reviewed, signed, and dated before registration/randomization by the study investigator. If used as source documentation, this checklist must be printed, the investigator must check each item to document their assessment that the participant meets each eligibility criterion, and the completed checklist must be maintained in the participant's chart.

Participant ID Number: AMC-115 - _____ - _____

Participant Initials (L, F, M [optional]): _____

NOTE: All questions regarding eligibility should be directed to the study chair.

3.1 Eligibility Criteria

_____ 3.1.1 Participant can understand and is willing to sign a written informed consent document.

_____ 3.1.2 HIV positive. Documentation of HIV-1 infection by means of any one of the following:

- Documentation of an HIV diagnosis in the medical record by a licensed health care provider;
- Documentation of receipt of antiretroviral therapy (ART) (i.e., at least two different medications that do not constitute a prescription for pre-exposure prophylaxis [PrEP]) by a licensed health care provider. Documentation may be a record of an ART prescription in the medical record, a written prescription in the name of the participant for ART, or pill bottles for ART with a label showing the participant's name;
- HIV-1 RNA detection by a licensed HIV-1 RNA assay demonstrating >1000 RNA copies/mL;
- Any licensed HIV screening antibody and/or HIV antibody/antigen combination assay confirmed by a second licensed HIV assay such as a HIV-1 Western blot confirmation or HIV rapid multispot antibody differentiation assay.

Note: The term "licensed" refers to a kit that has been certified or licensed by an oversight body within the participating country and validated internally (e.g., U.S. FDA).

WHO (World Health Organization) and CDC (Centers for Disease Control and Prevention) guidelines mandate that confirmation of the initial test result must use a test that is different from the one used for the initial assessment. A reactive initial

rapid test should be confirmed by either another type of rapid assay, or an E/CIA that is based on a different antigen preparation and/or different test principle (e.g., indirect versus competitive), a Western blot, or a plasma HIV-1 RNA viral load.

- _____ 3.1.3 Patient was diagnosed with or treated for cancer within the last 5 years. Participants will qualify under one of three categories:
- New, primary or recurrent diagnosis –Considering or currently receiving cancer treatment
 - Metastatic or locally advanced cancer – This includes cases for which there are no current definitive therapy options for cure (i.e., inoperable) but may be considered for non-standard / non-curative therapies.
 - Prior diagnosis (within 5 years), in remission – Not currently on cancer treatment other than ART or maintenance therapy.
- _____ 3.1.4 Age \geq 18 years.
- _____ 3.1.5 Participant presents to an AMC domestic clinical trial site for either clinical care or research.

3.2 Exclusion Criteria

Participants who do not fulfill the criteria as listed in [Section 3.1](#) above are ineligible.

3.3 Number of Participants to be Enrolled

NIH policy requires that women and members of minority groups and their subpopulations be included in all NIH-supported biomedical and behavioral research projects involving NIH-defined clinical research unless a clear and compelling rationale and justification establishes to the satisfaction of the funding Institute & Center (IC) Director that inclusion is inappropriate with respect to the health of the participants or the purpose of the research.

3.3.1 Proposed sample size

This study will enroll a minimum of 360 participants and a maximum of 720 participants.

3.3.2 Accrual rate

Approximately 10-20 participants per month across domestic AMC sites.

4.0 REGISTRATION PROCEDURES

4.1 Investigator and Research Associate Registration with CTEP

This study is non-interventional and is therefore exempt from IND requirements. However, **the following registration policy must be followed in accordance with Cancer Therapy and Evaluation Program (CTEP) policy.**

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

RCR utilizes five registration types.

- IVR: MD, DO, or international equivalent,
- NPIVR: advanced practice providers (*e.g.*, NP or PA) or graduate level researchers (*e.g.*, PhD),
- AP: clinical site staff (*e.g.*, RN or CRA) with data entry access to CTSU applications (*e.g.*, Roster Update Management System [RUMS], OPEN, Rave),
- Associate (A): other clinical site staff involved in the conduct of NCI-sponsored trials, and
- Associate Basic (AB): individuals (*e.g.*, pharmaceutical company employees) with limited access to NCI-supported systems.

RCR requires the following registration documents:

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

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

- Addition to a site roster,
- Assign the credit or consenting (IVR only) tasks in OPEN,

- Act as the site-protocol Principal Investigator (PI) on the IRB approval, and
- Assign the Clinical Investigator (CI) role on the AMC Delegation of Tasks Log (DTL).

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

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

4.2 Site Registration

All U.S. based sites must be members of the NCI Central Institutional Review Board (NCI CIRB). Sites participating with the NCI Central Institutional Review Board (NCI CIRB) must submit the Study Specific Worksheet for Local Context (SSW) to the CIRB using IRBManager to indicate their intent to open the study locally. The NCI CIRB's approval of the SSW is automatically communicated to the CTSU Regulatory Office, but sites are required to contact the CTSU Regulatory Office at CTSURegPref@ctsu.cocccg.org or amcpm@emmes.com to establish site preferences for applying NCI CIRB approvals across their Signatory Network. Site preferences can be set at the network or protocol level. Questions about establishing site preferences can be addressed to the CTSU Regulatory Office by emailing the email address above or calling 1-888-651-CTSU (2878), or by contacting the AMC ODMC (see protocol roster).

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

- Holds an active CTEP registration status,
- and on the AMC site roster,
- If using NCI CIRB, rostered on the NCI CIRB Signatory record,
- Includes the IRB number of the IRB providing approval in the Form FDA 1572 in the RCR profile, and
- Holds the appropriate CTEP registration type for the protocol.

Additional Requirements

Additional requirements to obtain an approved site registration status include:

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

4.1.1 Downloading regulatory documents

Download the site registration forms from the protocol-specific page located on the CTSU members' website. Permission to view and download this protocol and its supporting documents is restricted based on person and site roster assignment. To

participate, the institution and its associated investigators and staff must be associated with the LPO or a Participating Organization on the protocol.

- Log on to the CTSU members' website (<https://www.ctsuo.org>) using your CTEP-IAM username and password,
- Click on *Protocols* in the upper left of your screen
 - Enter the protocol number in the search field at the top of the protocol tree, or
 - Click on the By Lead Organization folder to expand, then select *AMC*, and protocol number *AMC-115*,
- Click on *Documents*, select *Site Registration*, and download and complete the forms provided. (Note: For sites under the CIRB initiative, IRB data will load automatically to the CTSU as described above.)

4.1.2 Protocol-specific requirements for site registration

Upon site registration approval in RSS, the enrolling site may access OPEN to complete enrollments. The enrolling site will select their credentialed provider enrolling the subject in the OPEN credentialing screen and will answer enrollment questions based on the eligibility checklist.

4.1.3 Submitting regulatory documents

Submit required forms and documents to the CTSU Regulatory Office via the Regulatory Submission Portal on the CTSU website.

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

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

Delegation of tasks log (DTL)

Each site must complete a protocol-specific registration packet, including an AMC DTL using the provided AMC template or local equivalent. The Clinical Investigator (CI) is required to review and sign the DTL prior to the site receiving an approved site registration status and enrolling participants to the study. The AMC DTL template is provided in the protocol registration packet for this protocol, located on the AMC Operations web site at www.AIDSCancer.org. Any individual at the enrolling site on a participating roster may initiate the site DTL. Instructions on completing the DTL are embedded in the AMC DTL template.

4.1.4 The AMC DTL must be updated contemporaneously as personnel are added or removed and/or study roles and delegated tasks change. Changes must be approved by the CI, and documented by his/her initials and date, before they are implemented.

4.1.5 Checking site registration status

You can verify your site's registration status on the members' side of the CTSU website.

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

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

4.3 Participant Registration

Sites must have this protocol approved by the NCI Central Institutional Review Board (CIRB) and be registered for study participation with the AMC Operations and Data Management Center (ODMC) before they may enroll participants.

After an informed consent form has been signed by the participant and it has been determined that the participant is eligible, the participant must be registered on-line via the Oncology Patient Enrollment Network (OPEN).

4.3.1 OPEN

The Oncology Patient Enrollment Network (OPEN) is a web-based registration system available on a 24/7 basis. OPEN is integrated with CTSU regulatory and roster data and with the Lead Protocol Organization (LPOs) registration/randomization systems for retrieval of participant registration assignments. OPEN will populate the patient enrollment data in NCI's clinical data management system, Medidata Rave.

Requirements for OPEN access:

- A valid CTEP-IAM account.
- To perform enrollments or request slot reservations: Be on the AMC roster, or Participating Organization roster with the role of Registrar. Registrars must hold a minimum of an AP registration type.
- If a DTL is required for the study, the registrar(s) must hold the OPEN Registrar task on the DTL for the site.
- Have an approved site registration for a protocol prior to patient enrollment.

To assign an Investigator (IVR) or Non-Physician Investigator (NPiVR) as the crediting, consenting, or receiving investigator for a patient transfer in OPEN, the IVR or NPiVR must list the IRB number used on the site's IRB approval on their Form FDA 1572 in RCR. If a DTL is required for the study, the IVR or NPiVR must be assigned the appropriate OPEN-related tasks on the DTL.

Prior to accessing OPEN, site staff should verify the following:

- Patient has met all eligibility criteria within the protocol stated timeframes, and
- All participants have signed an appropriate consent form and HIPAA authorization form (if applicable).

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

Access OPEN at **<https://open.ctsuo.org>** or from the OPEN link on the CTSU website **<https://www.ctsuo.org>**. Further instructional information is in the OPEN section of the AMC members' website at **www.AIDSCancer.org**. For any additional questions, contact the AMC ODMC (contact information in protocol roster).

4.3.3 OPEN questions

Further instructional information on OPEN is provided on the OPEN link of the CTSU website at <https://www.ctsuo.org> or at <https://open.ctsuo.org>. For any additional questions contact the CTSU Help Desk at 1-888-823-5923 or ctsuocontact@westat.com.

5.0 TREATMENT PLAN

This is a non-interventional study. Please refer to the Study Design ([Section 2.3](#)), Clinical and laboratory evaluations ([Section 8](#)), and Measurement of Effect ([Section 9](#)) for a description of the trial procedures.

5.1 Duration of Follow-Up

For participants not currently receiving cancer therapy, participation only involves the initial encounter for study data collection. For participants initiating therapy or currently under treatment, a short-interval follow-up will occur at 12 Weeks (\pm 2 Weeks). This is expected to coincide with planned treatments/clinical follow-up and therefore minimize unnecessary clinic visits that could increase participant burden (see [Section 8.3](#) for requirements).

6.0 ADVERSE EVENTS: LIST AND REPORTING REQUIREMENTS

As this study is non-interventional that focuses on data collection with limited follow-up, no adverse event data will be collected.

7.0 PHARMACEUTICAL INFORMATION

Not applicable (non-interventional study).

8.0 CLINICAL AND LABORATORY EVALUATIONS AND DATA COLLECTION

Evaluations required for this protocol are enumerated below and summarized in the Schedule of Events in [Appendix I](#).

8.1 Screening

All PWH who present for care at participating AMC clinical trial sites with a histologically confirmed diagnosis of cancer (within the past 5 years) will be tracked on a screening list. Eligibility will be assessed for each patient on the list, and if they are determined eligible, they will be approached to participate in AMC-115.

To determine the types of cancer cases that present to the clinical sites, all participants presenting at these sites have a minimum set of de-identified data collected. This minimal risk data collection will only include the participant's age, sex at birth, race/ethnicity, and type of cancer and will be performed prior to formal consent. Data collected during screening will be maintained separately from data on enrolled cases. This data will be compared to the total number of enrolled participants at each site to estimate the proportion of participants who consent to participate in this trial.

The protocol chair has established a set of IT logic codes that can be applied to electronic health record (EHR) systems to automate screening for "HIV status" among cancer patients. This is critical as it (1) makes the ascertainment of PWH and cancer uniform across participating domestic AMC sites and (2) reduces physician and study coordinator burden by leveraging the electronic medical record and automating the search. To ensure that this IT-based approach can be implemented across domestic AMC sites, the feasibility survey included a question specifically about the ability of sites to search their electronic medical record systems for HIV-specific disease codes.

8.2 Enrollment Data Collection

Following informed consent, additional, identifiable data will be collected, including:

- 8.2.1 Patient characteristics: Date of birth, biological sex, gender identity, race, ethnicity, height and weight
- 8.2.2 Sociodemographic: Socioeconomic status (e.g., ZIP code, housing status [homeless y/n, categories for frequency of housing insecurity]), health insurance (insured/uninsured, type if insured)
- 8.2.3 Health behaviors: Tobacco use (type, exposure [pack/day, years use]), illicit drug use (ever, type, years exposure), alcohol use (ever, exposure [drinks/week], years exposure)
- 8.2.4 Comorbid conditions: Hepatitis B and C co-infection, cardiovascular disease (y/n, type), psychiatric conditions (y/n, type), non-cancer pulmonary conditions (y/n, type), hepatic dysfunction, hematologic abnormalities, renal dysfunction, neurologic disorders, endocrine disorders (including thyroid disorders, and diabetes)
- 8.2.5 HIV care: Current ART regimen, years of ART use, year of HIV diagnosis, history of opportunistic infections, most recent HIV viral load and CD4+T-cell count relative to participant visit).

8.2.6 Status of cancer diagnosis (one of the following):

- New diagnosis, pre-treatment phase
- New diagnosis, treatment phase
- Prior diagnosis, in remission (within 5 years of initial diagnosis or treatment)
- Prior diagnosis, recurrent, pre-treatment phase
- Prior diagnosis, recurrent, treatment phase
- Prior diagnosis, recurrent, no treatment planned

8.2.7 For participants with a new diagnosis (pre-treatment or treatment), the following will be collected:

- Cancer type, date of cancer diagnosis, method of diagnosis (clinical, cytology, histology), type of pathology performed (Hematoxylin and Eosin, immunohistochemistry, other), date of pathology, staging, staging methods (clinical, radiographic, surgical), date(s) of staging, current ECOG Performance Status (PS), current laboratory values (this would include complete blood count, renal and liver function, electrolytes)
- Cancer treatment plan: Detailed planned or current treatment. This should encompass surgical interventions, radiotherapy, and chemotherapy (agent names), including dates of planned or current therapy, and whether cancer care is being received or will occur at the enrolling institution.

8.2.8 For participants with a prior diagnosis in remission, the following will be collected:

- Cancer history: Cancer type, date of diagnosis, prior method of diagnosis (cytology, histology), pathology performed, date of pathology, staging, staging methods (clinical, radiographic, surgical), current ECOG PS. Records from a prior diagnosis/treatment should be requested, but if they are unavailable, participant report will be sufficient.
- Current method of post-treatment surveillance (clinical, laboratory, radiographic), and current schedule of follow-up with this center.
- Prior cancer treatment. This should encompass surgical interventions, radiotherapy, and chemotherapy. Records from a prior diagnosis/treatment should be requested, but if they are unavailable, participant report will be sufficient.

8.2.9 For participants with a prior diagnosis, recurrent (pre-treatment, treatment, or no planned treatment) the following will be collected:

- Initial cancer type, date of diagnosis
- Cancer history: prior method of diagnosis (cytology, histology), pathology performed, date of pathology, staging, staging methods (clinical, radiographic, surgical), date(s) of staging. Records from a prior diagnosis/treatment should be requested, but if they are unavailable, participant report will be sufficient.

- Prior cancer treatment. This should encompass surgical interventions, radiotherapy, and chemotherapy. Records from a prior diagnosis/treatment should be requested, but if they are unavailable, participant report will be sufficient.
- Current date of cancer diagnosis, method of diagnosis (clinical, cytology, histology), pathology performed, date of pathology, staging, staging methods (clinical, radiographic, surgical), date(s) of staging, current ECOG Performance Status (PS), current laboratory values (this would include complete blood count, renal and liver function, electrolytes).
- IF THERAPY IS PLANNED OR UNDERWAY: Detailed planned or current treatment. This should encompass surgical interventions, radiotherapy, and chemotherapy, dates of planned or current therapy, and whether cancer care is being received or will occur at the enrolling institution.
- IF NO THERAPY IS PLANNED: Reason for no further therapy, e.g., if the decision for no therapy is based on lack of options for treatment, lack of benefit of further treatment, or participant choice not to pursue further treatment.

8.2.10 Optional QoL questionnaires will be administered in the following languages understandable to the participant: English, Spanish, Italian, Chinese, Dutch, Amharic and Turkish. The QOL questionnaires have been validated for use in these languages and participants who do not speak English, Spanish, Italian, Chinese, Dutch, Amharic and Turkish will not be asked to complete these optional questionnaires. These questionnaires are optional for study participation:

- EORTC QLQ-C30: Global health status, physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial toxicity
- SCNS-SF34: psychological needs, health system and information needs, physical and daily living needs, patient care and support needs, sexuality needs

8.2.11 Biospecimens:

- As collection of HIV viral load or CD4 are standard of care for patients with HIV and cancer, HIV viral load and/or CD4 will be taken from the medical record from the date closest to the participant's visit. Biospecimens will not be collected as part of this study.

8.3 Follow-up Evaluations

For participants initiating therapy or currently under treatment, a short interval follow-up will occur at 12 Weeks (\pm 2 Weeks). This is expected to coincide with planned treatments/clinical follow-up and therefore minimize unnecessary clinic visits that could increase participant burden.

8.3.1 Vital status

8.3.2 State of planned cancer therapy (initiated as planned versus delayed initiation, no initiation, or initiation of alternate therapy in place of planned therapy)

8.3.3 Optional QoL questionnaires as described in [Section 8.2.10](#):

- EORTC QLQ-C30
- SCNS-SF34

8.4 Final Evaluations, Off Study

Participants who are not currently receiving any treatment will not complete a follow-up evaluation. Therefore, the Off Study Summary Form should be completed in iMedidata Rave after completing the Enrollment Data Collection in [Section 8.2](#).

For participants who are planning to initiate therapy or are currently under treatment, at the completion of all follow-up evaluations described in [Section 8.3](#), the Off Study Summary Form should be completed in iMedidata Rave.

9.0 MEASUREMENT OF EFFECT

This is a non-interventional protocol.

The following definitions will be employed for case classification and data reporting for the primary protocol objective, to estimate the number of cancers in PWH who present for care at domestic AMC sites:

Table 9-A: Definitions for case classification and data reporting

Site-specific frequency of primary cancer cases	Total number of participants that present to the site with a first diagnosis of cancer. This encompasses cases that are in the period from histologically proven cancer to initiation of planned first-line therapy, as well as cases already receiving the planned first-line therapy for primary disease.
Site-specific frequency of recurrent cancer cases	Total number of participants that present to the site with a diagnosis of cancer within the last 5 years. This includes participants on surveillance, or best supportive care.
Site-specific frequency of prior cancer cases	Total number of participants that present to the site with a recurrent (i.e., non-primary) cancer diagnosis. This encompasses cases that are pre-treatment for recurrent disease, undergoing planned non-first-line therapy, or cases for whom no anti-cancer therapy is planned, including due to metastatic or locally advanced, inoperable disease.
Pre-treatment phase	The period in which a participant has a histologically diagnosed cancer, with cancer-specific treatment planned but not yet initiated.
Treatment phase	The period in which the participant has started therapy for cancer. This can include surgery, radiation, and/or chemotherapy. This period completes when all planned therapy has been completed within a therapeutic encounter.
First-line therapy	All therapy performed as part of a treatment plan with a new/primary diagnosis of cancer, including surgery, radiotherapy, and chemotherapy, alone or in combination.
No treatment planned	The point at which no further active cancer treatments are planned. Initiation of best supportive care or palliative care.

10.0 STATISTICAL CONSIDERATIONS

10.1 Study Design/Endpoints

This is a non-interventional protocol. This study will utilize a prospective design to identify the frequency of new and existing cancer cases among PWH receiving care at AMC clinical trial sites.

10.1.1 Primary endpoint

The primary endpoint is to estimate the number of cancers in PWH who present for care at domestic AMC sites. These estimates will help to inform the target populations for subsequent AMC clinical trials.

10.1.2 Primary endpoint analysis

For each cancer group listed below, the number of new and existing cases per month will be estimated using a 95% Poisson confidence interval. Additionally, the distribution of cancer types will be computed as percentages and compared to the cancer type distribution in the HIV/AIDS Cancer Match (HACM) Study, a nationally representative HIV and cancer linkage database [4]. For reference, the HIV/AIDS Cancer Match (HACM) Study estimated that the proportion of participants with the following cancer types as:

1. Solid organ tumors associated with human papillomavirus (HPV) infection = 12.5%
2. Solid organ tumors unrelated to HPV = 49.3%
3. Kaposi sarcoma = 10.9%
4. Hematologic malignancies = 27.3%

10.2 Sample Size/Accrual Rate

10.2.1 Target accrual is 20 participants per month, with a target of 720 participants enrolled over 36 months. Because the primary objective's focus is estimation, we note below in [Table 10-A](#) both the width of the 95% confidence intervals (CIs) for prevalence, and the accompanying estimated case counts, for the minimum and maximum target sample sizes of 360 and 720. For each cancer group, anticipated prevalence estimates are based on those observed in other national datasets (see [Section 10.1.2](#) above). 95% CIs are computed using PASS 2021 software, utilizing a simple asymptotic estimation approach (i.e., a normal approximation to the binomial approach with a continuity correction.)

Table 10-A: Estimated case counts

Cancer Types	Sample Size of 360		Sample Size of 720	
	Prevalence	Case Count	Prevalence	Case Count
Solid Organ Tumors Associated with HPV	12.5% (95% CI: 8.9-16.1%)	45 cases (95% CI: 32-58 cases)	12.5% (95% CI: 10.0-15.0%)	90 cases (95% CI: 72-108 cases)
Solid Organ Tumors Unrelated to HPV	49.3% (95% CI: 44.0-54.6%)	177 cases (95% CI: 158-197 cases)	49.3% (95% CI: 45.6-53.0%)	355 cases (95% CI: 328-382 cases)
Kaposi Sarcoma	10.9% (95% CI: 7.5-14.3%)	39 cases (95% CI: 27-52 cases)	10.9% (95% CI: 8.6-13.2%)	78 cases (95% CI: 62-95 cases)
Hematologic Malignancies	27.3% (95% CI: 22.6-32.0%)	98 cases (95% CI: 81-115 cases)	27.3% (95% CI: 24.0-30.6%)	197 cases (95% CI: 173-220 cases)

One example of how this will translate into monthly enrollment targets is provided here: If 355 participants with solid organ tumors unrelated to HPV are to be enrolled across 36 months, or 9.9 such participants per month, the 95% CI would be 9.1-10.6 cases (i.e., 9-11 participants) per month.

- 10.2.2. The goal is to open this protocol at $\geq 75\%$ of domestic AMC sites. Based on updated responses from 19 domestic AMC sites on the protocol-associated feasibility survey, 16 AMC domestic sites indicated that this study would be feasible to open. The table below ([Table 10-B](#)) includes results for those 16 domestic sites. Based on their estimates for annual number of cancers seen at their AMC site, we anticipate that this protocol will meet accrual targets.

Table 10-B: AMC domestic site annual numbers of cancers in PWH

AMC Site	Kaposi Sarcoma	Heme Malignancies	HPV+ Solid Tumors	Non-HPV Solid Tumors	Total Cancers
LSUHSC	10	30	10	50	100
Anal Dysplasia Clinic MidWest	0	0	1	0	1
Penn	25	10	10	10	55
Wash U	30	10	15	30	85
Laser Surgery	2	3	10	0	15
MSK	5	8	5	5	23
Montefiore	2	15	15	15	47
Moffitt	3	20	15	20	58
Boston Medical Center	8	8	15	15	46
Virginia Mason	7	3	4	4	18
Miami Cancer Institute	5	30	25	25	85
George Washington	2	5	10	10	27
Puerto Rico	2	4	4	2	12
UCSF	2	1	5	3	11
UCSD	32	59	23	52	166
UNC	4	4	2	4	14
Total	139	210	169	245	763

The above estimates indicate that sites, including those with a history of consistent enrollment onto AMC trials and new sites added in current AMC grant years, see 763 cancer cases with underlying HIV infection each year. Even with a conservative patient participation rate for this minimal burden study, the protocol chairs deem the target accrual range (360-720) to be feasible.

10.3 Analysis of Secondary Endpoint and Analysis

The secondary endpoint is the proportion of participants eligible for AMC trials who are successfully enrolled.

For this calculation, the denominator will be computed based on PWH deemed eligible at each site, based only on AMC trials open at that respective site.

For participants with active disease, each participant's data will be evaluated to determine whether they meet minimal eligibility criteria for an AMC clinical trial open at

their respective domestic site, defined as meeting the following minimum eligibility criteria per the protocol:

- a. Cancer diagnosis including stage and histology
- b. Age range specified in the protocol for which the patient is being screened
- c. Indication for the study intervention (e.g., symptom, toxicity)

These data will be compared to the actual number of participants enrolled onto AMC trials open at each site to estimate the proportion of trial-eligible participants who enroll. For participants with a history of malignancy diagnosed within the past 5 years / cancer currently in remission, each patient's performance status and HIV metrics (CD4+ T-cell count and HIV viral load) will be evaluated to determine whether they meet general levels that are consistent with eligibility criteria for prior AMC clinical trials. To characterize participants who are eligible but not enrolled onto AMC trials, participant characteristics for eligible participants will be compared according to successful enrollment versus not using two-sample tests for continuous and categorical data (e.g., t-test, Wilcoxon rank sum test, chi-square test). Characteristics will include demographic features, clinical/cancer features, and optional QOL responses.

EORTC QLQ-C30 subscale and overall scores will be used to describe participant symptom and health-related quality of life burden. SNSCS-SF34 scores will be used to categorize participants based on the degree to which their needs are met. Baseline EORTC QLQ-C30 and SCNS-SF34 scores will also be compared according to successful enrollment versus not using t-test or Wilcoxon rank sum tests depending on distribution of scores. These data may describe enrollment barriers previously unknown. For example, comorbidity burden, prior cancer treatment history, or self-reported quality of life at initial cancer presentation may be risk factors for elective participation. These analyses will provide preliminary data to inform evidence-based interventions aimed at increasing clinical trials participation among PWH at domestic AMC sites. To address minority and underserved populations, additional analyses will examine the interaction with race, ethnicity, socioeconomic status, and health insurance status to compare participant characteristics according to groups defined by enrollment status and these variables. Similarly, interactions with age, cancer type, treatment, and time since diagnosis will be investigated. Finally, these analyses will inform a multivariable logistic model that predicts successful trial outcome that includes dependent variables for participant characteristics; interactions with indicators of minority, socioeconomic status, and health insurance will be investigated in this model as well as with age, cancer type, treatment and time since diagnosis.

10.4 Exploratory Endpoints

Exploratory endpoints for this study include:

- To standardize and expand the quantity and quality of sociodemographic (e.g., racial/ethnic distribution, SES), HIV-related health [e.g., Antiretroviral Therapy (ART) medications, co-morbidities], and cancer diagnostic and treatment characteristics collected for PWH receiving care at domestic AMC sites.

- To describe cancer patient health-related QOL for PWH at domestic AMC sites using EORTC QLQ-C30 and SCNS-SF34.

Exploratory endpoints will be analyzed as described below:

1. The distribution of participant characteristics from [Table 2-A](#) will be summarized.
2. The frequency of planned cancer treatment regimens successfully initiated will be summarized.
3. PRO assessment scores from the EORTC QLQ-C30 and SCNS-SF34 will be summarized, both overall and at the ~12-week follow-up, according to participant characteristics and cancer groups. Overall change in PRO measures will be compared with paired tests and change according to groups will be compared using t-tests, ANOVA, or nonparametric tests. In an exploratory manner, PRO scores for PWH who are in remission will be analyzed separately to understand longer-term QOL issues that may inform future POSEC-led survivorship efforts.

10.5 Data and Safety Monitoring Board Review

Per the AMC's Data and Safety Monitoring Plan (DSMP; see [Appendix III](#)), DSMB reviews are only required for phase III randomized trials by NCI policy. This study will be monitored for safety and trial progress according to the procedures outlined in the DSMP only.

11.0 ROLE OF DATA MANAGEMENT AND DATA REPORTING

11.1 Study Oversight

This protocol is monitored at several levels, as described in this section. The Protocol Principal Investigator is responsible for monitoring the conduct and progress of the clinical trial, including the on-going review of accrual and patient-specific clinical and laboratory data. The Protocol Principal Investigator and statistician have access to the data at all times through the CTMS web-based reporting portal.

All Study Investigators at participating sites who register/enroll participants on a given protocol are responsible for timely submission of data via Medidata Rave. This includes timely review of data collected on the electronic CRFs submitted via Medidata Rave.

Permission to view and download this protocol and its supporting documents is restricted and is based on person and site roster assignment housed in the CTSU Regulatory Support System (RSS).

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

All studies are also reviewed in accordance with the enrolling institution's data safety monitoring plan.

11.2 CRF Instructions

Access to the internet data entry system for this study, iMedidata Rave, and instructions for recording of study data on eCRFs will be provided by the AMC ODMC at www.AIDSCancer.org. Participating institutions are responsible for submitting data and/or data forms via iMedidata Rave in accordance with the AMC Data Entry Guide and specific form instructions, within the timelines specified by the AMC's Standards of Procedure for Site Performance Measures.

11.3 Data Quality

It is the responsibility of the AMC ODMC to assure the quality of data for the study (See [Appendix III](#), AMC Data and Safety Monitoring Plan). This role extends from protocol development to generation of the final study database.

11.4 Data Reporting

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

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

- To hold Rave Investigator role, the individual must be registered as an NPIVR or IVR, and
- To hold Rave Read Only role, site staff must hold an Associates (A) registration type.

If the study has a DTL, individuals requiring write access to Rave must also be assigned the appropriate Rave tasks on the AMC DTL.

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

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

11.5 Data Monitoring

Required submission of patient demographic data for this study will be submitted automatically via OPEN.

12.0 ETHICAL AND REGULATORY CONSIDERATIONS

12.1 IRB Approval and Informed Consent

Records of all study review and approval documents must be kept on file by the Investigator and are subject to inspection during or after completion of the study. The IRB should receive notification of completion of the study and final report within 3 months of study completion and termination. The Investigator will maintain an accurate and complete record of all submissions made to the IRB, including a list of all reports and documents submitted.

To determine the types of cancer cases that present to the clinical sites, it is requested that all cancer patients presenting at these sites have a minimum set of de-identified data collected. This will be performed prior to formal consent and meets criteria for minimal risk data collection. Data collected on cancer patients presenting to the clinical site will include age, sex at birth, race/ethnicity, and type of cancer. Data collected during screening will be maintained separately from data on enrolled cases. No other data will be collected on patients who do not consent to participate in AMC-115.

Written informed consent will be obtained from the participant to collect identifiable data. The nature, significance and risks associated with the study must be explained to the participant. The informed consent will describe the purpose of the study, the procedures to be followed, the risks and benefits of participation, all risks of the investigational agent(s) and/or study participation as listed in the model informed consent form, and all other elements of informed consent as required by regulation. A copy of the consent form will be given to the participant to keep.

In addition, any institution(s) conducting research according to the guidelines of this protocol is required to adhere to local and national laws and regulations governing the confidentiality and disclosure of health information.

12.2 Changes to the Protocol

Any change or addition to this protocol requires a written protocol amendment that must be approved by CTEP and the Investigator before implementation. All amendments require approval by the CIRB.

12.3 Women and Minorities

This study is being conducted by the NCI-sponsored AMC. As part of their contractual obligations, each participating site within the AMC and the AMC as a whole is required to assure that the participation of women and minority participants reflects the percentage representation of these populations in their geographic region and, for the AMC, PWH in the United States as a whole. As such, it is expected that the representation of participants on this trial will reflect the constitution of the respective populations see [Table 12-A](#) for accrual targets.

Table 12-A: Accrual targets

DOMESTIC PLANNED SCREENING ENROLLMENT REPORT					
Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	1	3	10	23	37
Asian	3	10	0	0	13
Native Hawaiian or Other Pacific Islander	1	2	0	0	3
Black or African American	98	230	10	23	361
White	38	88	30	70	226
More Than One Race	10	20	15	35	80
Total	151	353	65	151	720

13.0 REFERENCES

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APPENDIX I: SCHEDULE OF EVALUATIONS

The screening and enrollment evaluations below applies to all participants on study, while the follow-up evaluations at Week 12 only apply to participants who are planning to initiate therapy or currently under treatment.

	Screening	Enrollment ¹	Week 12 Follow-up (± 2 weeks) ^{2*}
Informed consent	X		
De-identified Demographics	X		
Participant Characteristics		X	
Sociodemographic		X	
Health Behaviors		X	
Comorbid Conditions		X	
HIV Care		X	
Status of Cancer Diagnosis		X	
Cancer history		X	
Cancer Treatment Plan (Prior and/or current)		X	X
EORTC QLQ-C30 ³		X	X
SCNS-SF34 ³		X	X
Performance status		X	X
<p>* Participants in whom no further treatment is planned after enrollment do not require the Week 12 follow-up</p> <p>¹Please see Section 8.2 for specific records to be collected.</p> <p>²Please see Section 8.3 for specific records to be collected.</p> <p>³Optional</p>			

APPENDIX II: PERFORMANCE STATUS SCALES

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

APPENDIX III: AMC DATA AND SAFETY MONITORING PLAN

(Version 9.0 • October 6, 2020)

Introduction

The AIDS Malignancy Consortium (AMC) Data and Safety Monitoring Plan (DSMP) outlines the measures employed by the group to monitor the safety of participants and ensure the data validity and integrity for all clinical trials it conducts. This includes methods to: 1) monitor the progress of trials and the safety of participants; 2) comply with regulatory requirements for adverse event (AE) reporting; 3) processes for trial termination or temporary suspension and major modifications; and 4) plans for ensuring data accuracy and protocol compliance. As the AMC conducts protocols of varying research phase, region of conduct (which may include trials conducted in the U.S., international sites, or both), IND sponsor (AMC investigator, CTEP, or industry-sponsored) and clinical data entry system use, this plan addresses broad processes applying to the range of trial designs and requirements. Refer to the individual AMC protocol to identify the applicable study characteristics for the relevant requirements described in this plan.

Monitoring the Progress of Trials and the Safety of Participants

Routine and expedited AE reporting

All AMC protocols that collect safety data adhere to the *National Cancer Institute (NCI), Cancer Therapy Evaluation Program (CTEP) Guidelines: Adverse Event Reporting Requirements* (https://ctep.cancer.gov/protocolDevelopment/adverse_effects.htm), as applicable to the clinical protocol. AEs are to be recorded in the source documents, assessed by a clinical investigator for the AE reporting criteria, and promptly reported in the clinical data entry system as required by each protocol. For AMC trials conducted under a CTEP IND and AMC trials conducted within the U.S., all AEs that meet the NCI's expedited reporting requirements are reported to the NCI via the CTEP Adverse Event Reporting System (CTEP-AERS) web application, either directly or through integration with Medidata Rave where this system is employed for AMC protocols. Use of this system ensures notification to the protocol chair and Investigational Drug Branch (IDB) at CTEP, as required for trials conducted under a CTEP IND, and a uniform expedited reporting and safety review process for AMC domestic trials. The system may also be programmed to include sponsor notification as required for trials with industry support. Alternate process for expedited AE reporting to the AMC protocol chairs and AMC Operations and Data Management Center (ODMC) within the clinical data entry system (AdvantageEDC or Advantage eClinical only) may be defined in the protocol for select trials (international studies and The ANCHOR Study).

All serious adverse events (SAEs) received by the AMC ODMC will be reviewed by the AMC medical monitor at the AMC ODMC for consideration of individual participant safety, safe trial conduct, data reporting quality for AE term selection, and appropriate application of the regulatory criteria for seriousness, expectedness, and relatedness to the investigational therapy. If alternate procedures are followed for SAE review, the process for adequate medical monitoring will be defined in the AMC protocol and the Transfer of Regulatory Obligations (TORO) with the sponsor. AMC medical monitor review includes review of the CTEP-AERS report before CTEP submission for IDB review (if applicable), or review of the SAE report in the data entry system for trials not using CTEP-AERS for expedited reporting. The IND sponsor or its designee will

issue the determination as to whether the AE requires IND safety reporting to FDA as a serious and unexpected suspected adverse drug reaction (SUSAR). For protocols not conducted under an IND, in the event of disagreement between the reporting physician and the AMC medical monitor regarding the relationship of the AE to the investigational agent(s) (i.e., determination of whether the attribution is unrelated or unlikely, or possible, probable, or definite), the AMC medical monitor will provide the final determination of the relationship. IND safety reporting to FDA is performed by CTEP for trials conducted under a CTEP IND; IND safety reporting is performed by the sponsor or sponsor's designee (AMC ODMC or other party defined in the study agreement or TORO) for IND studies sponsored by AMC investigators or industry sponsors.

Expedited reporting to the Institutional Review Board (IRB)

The requirements for IRB review will be identified in the protocol section on ethical and regulatory obligations. All AMC trials initiated before September 1, 2020 and all international sites for all AMC studies are subject to local IRB review; only U.S. sites are subject to the NCI requirement to use a single IRB for protocols initiated on or after September 1, 2020. For trials subject to local IRB review, the site principal investigator is responsible for ensuring that expedited AE reports for its trial participants and any unanticipated problems that affect the local institution only are submitted to the local IRB of the reporting institution, per the local IRB's requirements for such reporting. For studies reviewed by the single IRB, the protocol chair will render a determination as to whether a SAE or other problem constitutes a trial-wide unanticipated problem that requires reporting to that RB, in accordance with its standards of procedure.

To comply with investigator notification requirements for IND studies under 21 CFR 312.32 and 312.55, IND safety reports from all trials the AMC conducts and reports from external sponsors investigating the same agents are made available to all investigators upon receipt from the sponsor or its designee, either via the password-protected section of the AMC Operations web site (AMC trials subject to local IRB review only) or the CTSU website (U.S. trials subject to single IRB review/CTEP IND agents). The site clinical investigator responsible for the applicable AMC protocol(s) is responsible for reviewing any IND safety reports received and documenting submission to the IRB of record (if required by local policy) within the timeline defined by the Clinical Trials Monitoring Branch (CTMB) audit guidelines.

Procedures for monitoring trial progress and pharmacovigilance

For trials using AdvantageEDC or Advantage eClinical for clinical data entry, the AMC ODMC provides on demand tabular listings of all reported AEs and SAEs on a participant level to the protocol chair and co-chair(s) for review via the password-protected section of the AMC Operations web site, www.AIDScancer.org. For trials using OPEN and Medidata Rave for clinical data collection, data listing will be made available using that system. Summary reports of AEs by frequency and relationship to the investigational agent(s) are provided to all AMC investigators and their staff. It is the responsibility of each site to provide trial-specific AE listings to their respective IRB, if required by its policies. For blinded studies, the AE and SAE listings are reviewed and tabulated without treatment assignment.

Accrual summaries for each AMC trial are updated nightly on the password-protected section of the AMC web site. The progress of each AMC trial is reviewed regularly by the protocol chair and also by the appropriate Scientific Working Group (SWG) during scheduled conference calls (monthly SWG calls and as required, protocol-specific monitoring conference

calls). Summary accrual, summary AE, and individual SAE reports are provided to SWG leadership and protocol chairs to monitor participant safety during these monthly calls.

The AMC medical monitor reviews listings of all reported AEs on a quarterly basis for assuring compliance with the protocol requirements for AE reporting and the identification of any safety concerns (individual AE or increased frequency/severity of expected AEs) for the agents under investigation. Findings from these reviews are communicated to the protocol chairs and all AMC investigators, and posted to the AMC Operations web site.

Data and Safety Monitoring Board Review (DSMB) review

The AMC has formed an independent Data and Safety Monitoring Board (DSMB) for AMC trials and for the ANCHOR Study. As required by NCI policy, the AMC requires DSMB review for all phase III randomized trials. All other clinical trials that the AMC initiates will be reviewed by the AMC ODMC and AMC Statistical Center during protocol development to issue a recommendation as to whether the study requires DSMB oversight, which will require the approval of the AMC Executive Committee. This determination will be based on the phase of the study, experimental design, risk posed by the investigational approach, extent of data available on the safety of an investigational agent, risk posed by the natural course of the health condition under research, and the categories of vulnerable populations involved. The involvement of a DSMB in reviewing an AMC protocol will be identified in each clinical protocol as approved by CTEP and, as applicable, required by the IRB of record.

Regarding the composition of the AMC DSMB, voting members usually include physicians, statisticians, an ethicist, and a patient advocate. All voting members have no other affiliation to the AMC and are appointed by the AMC Executive Committee with the approval of the OHAM Director. Nonvoting members are the AMC group statistician, the protocol statistician, an AMC ODMC staff member, two representatives (normally a clinician or statistician) from CTEP, and the grant program directors from the NCI Office of HIV and AIDS Malignancy (OHAM).

The DSMB reviews all applicable AMC studies in accordance with the National Cancer Institute's Policy for Data and Safety Monitoring. Confidential reports of all trials under review are prepared by the AMC group statistician with support from the AMC ODMC. A written report containing the current status of each trial monitored, and when appropriate, any toxicity and outcome data, are sent to DSMB members by the AMC ODMC within the timelines specified by the DSMB charter. This report addresses specific toxicity issues and any other concerns about the conduct of the trial, as defined by the protocol plan for DSMB review. The report may contain information for the DSMB to render determinations for participant safety, early trial termination, results reporting, or continuing accrual or follow-up.

The results of each DSMB meeting are summarized in a formal report sent by the DSMB chair to the AMC group chair and AMC ODMC. The DSMB report contains recommendations on whether to close each study reviewed, whether to report the results, and whether to continue accrual or follow-up. A primary recommendation (e.g., continue with no change; recommended or required modification; stop) must be included in the document. The group chair or designee is then responsible for notifying the protocol chair and relevant SWG chair before the recommendations of the DSMB are carried out. In the unlikely event that the protocol chair does not concur with the DSMB, then the OHAM program directors and the NCI division director or designee must be informed of the reason for the disagreement. The protocol chair, relevant SWG chair, group chair, DSMB chair, and NCI division director or designee will be responsible for reaching a mutually

acceptable decision about the study. CTEP approval of a protocol amendment will be required prior to any implementation of a change to the study.

Following a DSMB meeting, the DSMB's recommendations are provided to all AMC investigators and staff. It is each site principal investigator's responsibility for conveying this information to its local IRB as relevant for its protocol participation. For trials reviewed by a single IRB, the AMC ODMC will support notification to the IRB as required per its procedures.

Cohort trial reviews not subject to DSMB review

For phase I dose escalation trials, dose escalation (or dose de-escalation) is based on the rules in the protocol and the protocol chair, AMC medical monitor, and protocol statistician determine whether these criteria have been met based on a review of all safety data for the protocol-defined evaluation period. If applicable for phase II trials, stopping the trial for toxicity or efficacy, or suspending enrollment pending observation of responses in a multi-stage phase II trial, is based on meeting criteria stated in the protocol, and the protocol chair, AMC medical monitor, and protocol statistician determine whether these criteria have been met.

Plans for Assuring Compliance with Requirements Regarding AE Reporting

The protocol chair, AMC group chair, and the AMC ODMC share responsibility in assuring that participating investigators comply with applicable regulatory and protocol requirements for AE reporting. The AMC site principal investigator certifies compliance with NCI and FDA requirements for trial conduct by signing the site subaward agreement for the grant and the AMC Adherence Statement for site membership; clinical investigators also certify compliance in completing the protocol signature page for each protocol active at the site, and Form FDA-1572 for CTEP investigator registration, and also for AMC IND studies sponsored by AMC investigators or industry sponsors. Protocol compliance with AE identification, assessment and reporting requirements is assessed by the AMC ODMC using several methods: 1) programmed system checks and messages to instruct the site to complete routine and/or expedited reporting when certain criteria are reported in the clinical data entry system; 2) programmed data reports provided to the protocol chairs that identify reports requiring expedited AE reporting; 3) remote review of data entry or data reports to ensure compliance with protocol and NCI AE reporting requirements; 4) AMC medical monitor review described in the section above; and, 5) routine site audits by reviewing the site's source documentation.

The clinical data entry systems used for AMC studies include the Oncology Patient Enrollment Network, OPEN for enrollment, and Medidata Rave for clinical data entry for enrolled participants; trials activated before September 1, 2020 or that involve only AMC international sites may be reported in AdvantageEDC/Advantage eClinical, a web-based data entry and enrollment system. These data entry systems are programmed to notify the site investigator, protocol chair, AMC medical monitor, and AMC ODMC via email in the event that a site reports an AE that meets expedited reporting criteria to NCI and/or FDA. Additional reporting conditions may be programmed depending on the sponsor reporting requirements of a given protocol (e.g., adverse events of special interest [AESI]). If the site does not follow with an expedited report, the AMC ODMC contacts sites to request compliance with reporting requirements. Additionally, the protocol chair, AMC ODMC, and the AMC medical monitor review reported AEs on a routine basis to identify AEs reported by sites that require expedited reporting. The protocol chair, AMC SWG chairs, AMC group chair, and IND sponsors have general oversight for assuring that routine and expedited adverse reporting requirements are met by the responsible parties.

For studies monitored by CTEP using the Data Mapping Utility (DMU), cumulative protocol- and patient-specific data will be submitted weekly to CTEP electronically via the DMU. For trials monitored by the NCI's Clinical Data Update System (CDUS), AE information is transmitted electronically to NCI on a quarterly basis. For trials monitored by NCI's Clinical Trials Monitoring Service (CTMS), AE information is transmitted electronically to NCI every two weeks.

Plans for Assuring that any Action Resulting in a Temporary or Permanent Suspension of an NCI-Funded Clinical Trial is Reported to the NCI Grant Program Director Responsible for the Grant

In the event that temporary or permanent suspension of a trial, or major modification to the protocol is under consideration, the protocol chair will convene the AMC ODMC, AMC Statistical Center, and SWG chair by conference call to discuss the options. Suspension actions will also be reviewed by the AMC Executive Committee for program oversight and direct communication of the action with the OHAM program directors. For phase III trials, closure decisions are typically rendered by the AMC DSMB; if the trial in question is under AMC DSMB oversight but rendered by the AMC investigators, the AMC DSMB will be notified of the suspension and the reason. For phase I and II trials, the protocol chair also has the option of asking the DSMB to review the study. The AMC ODMC will inform the CTEP Protocol Information Office (PIO), with copy to OHAM Directors, when studies are temporarily or permanently closed. In the event of major trial modification, CTEP must approve all protocol amendments prior to distributing to the AMC sites.

Plans for Assuring Data Accuracy and Protocol Compliance

All study data for AMC clinical trials are entered directly by AMC clinical site staff into the applicable clinical data entry system for the trial. During data entry, the system performs validation checks on many fields and performs consistency checks between select fields. Range checks are placed on each field to eliminate entry of out-of-range values. Edit check programs are run on the database on a set schedule to identify and resolve inconsistencies between forms or data collected at different points in time. Submitted data entry forms are reviewed for compliance with the protocol and data entry instructions according to the AMC ODMC's standards for data quality processes. AMC ODMC staff routinely interacts with site staff to resolve any data submission problems.

In accordance with NCI guidelines, the AMC ODMC conducts audits at the AMC sites to evaluate compliance with regulatory issues, and to review data for specific cases by checking source documents. These reports are sent to the site principal investigator and to the NCI. In the event that major violations are identified, sites are asked to provide a written corrective and preventative action plan to correct deficiencies. If needed, a repeat site audit is conducted. In the event that a site does not correct deficiencies in a pre-determined time frame, the AMC Executive Committee has the option to implement remedial action(s) for the site. Possible actions include, but are not limited to, suspending enrollment of new participants to AMC trials until deficiencies are corrected; recommending a decrease in funding to the site; and requiring specific training for site investigators or staff members.