

# RFA Reissuance Request

## **AIDS Malignancy Consortium**

*Office of HIV and AIDS Malignancy (OHAM)*

Cooperative Agreement

5 Years Funding

\$18,100,000 year 1

\$96,956,954 over 5 years

# Background - HIV Epidemic

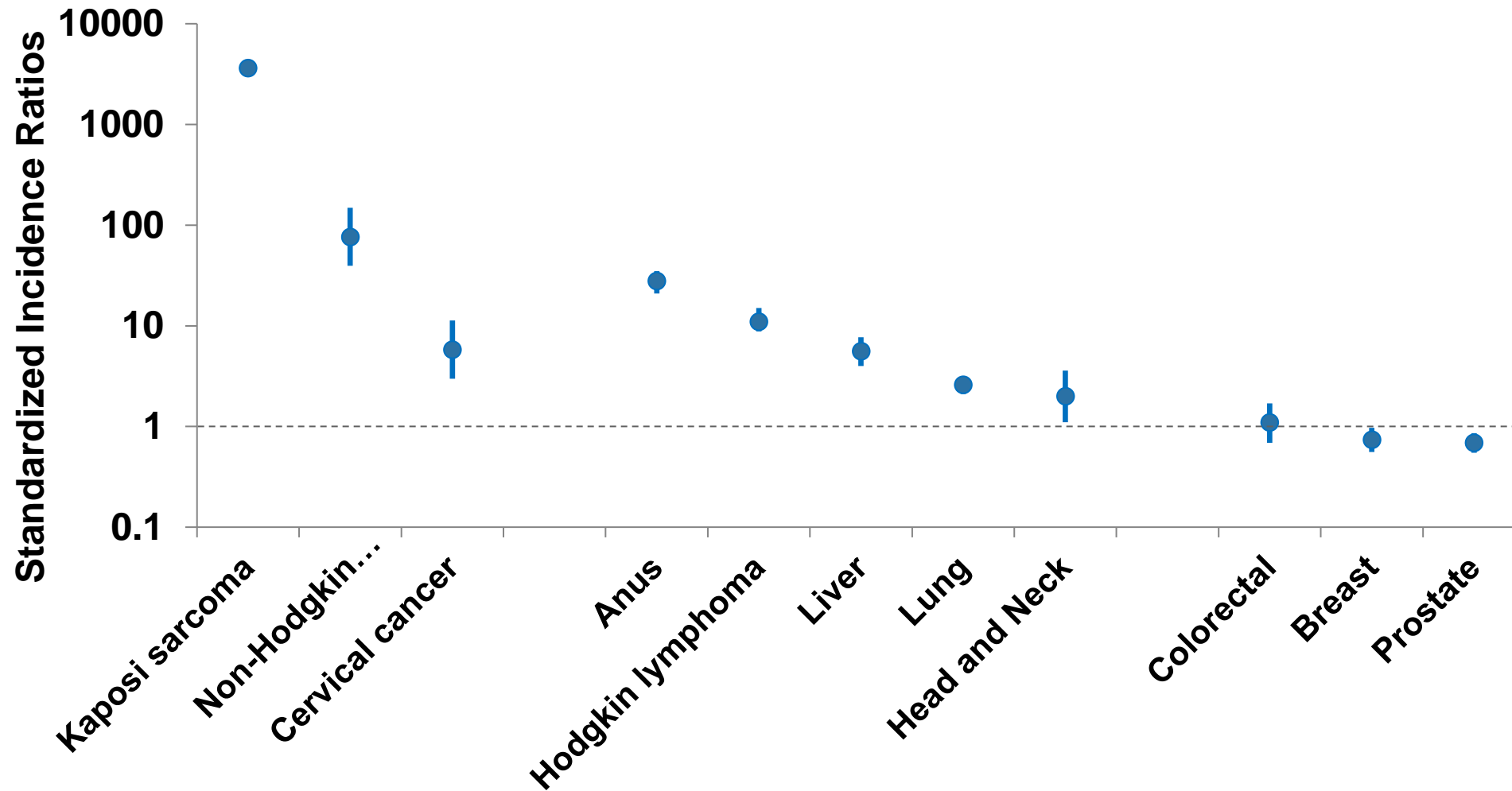
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Approximately **39 million** people live with HIV worldwide, and there are **~1.3 million** new infections per year:

- United States
  - **~1.2 million** people live with HIV
  - ~32,000 new infections per year
- Sub Saharan Africa (SSA)
  - **~25.6 million** people live with HIV
  - ~660,000 new infections per year
- Latin America
  - **~2.2 million** people live with HIV
  - ~110,000 new infections per year

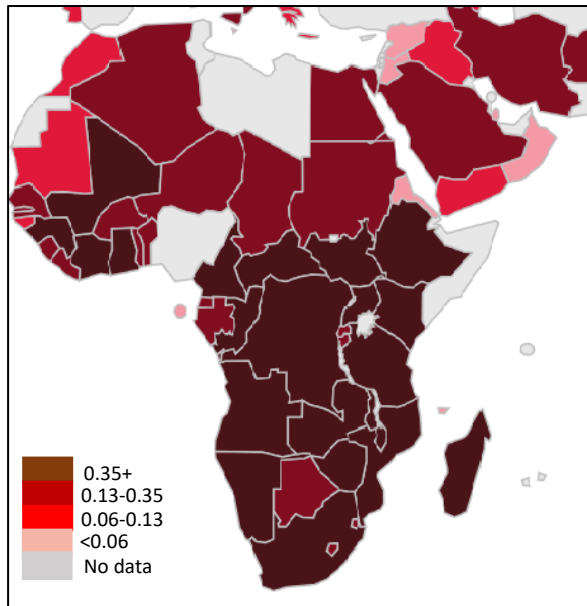
*Cancer has been a prominent manifestation of HIV/AIDS since the beginning of the epidemic and is a leading cause of morbidity and mortality among people with HIV (PWH)*

# HIV and Elevated Risk of Cancer



# Burden of HIV/AIDS, Cervical Cancer and Kaposi Sarcoma in Sub Saharan Africa (SSA)

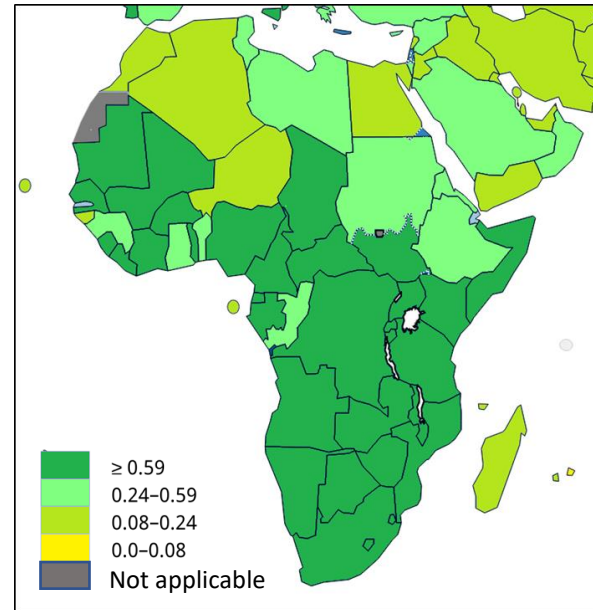
HIV Incidence per 1000



UNAIDS 2022

- ~90% in low- and middle-income countries (LMICs)

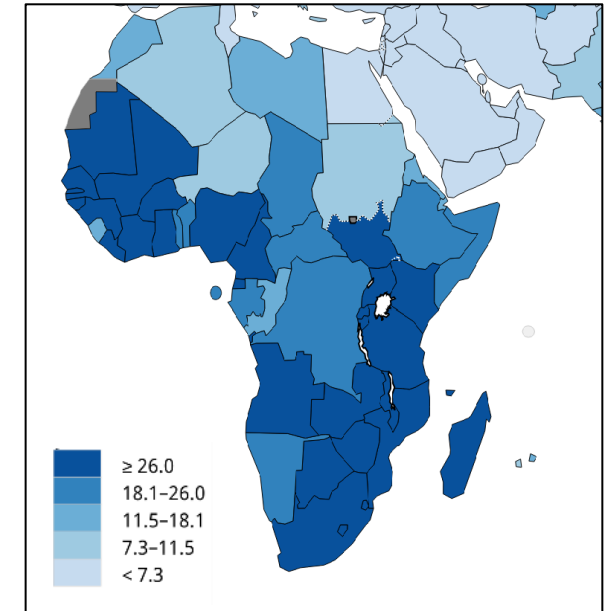
Kaposi Sarcoma Incidence per 100,000



Globocan 2020

- 34,270 new cases/year worldwide
- 15,086 deaths/year
- > 90 % of cases in LMICs
- Most common cancer in men <65 years of age **overall** in some countries in SSA

Cervical Cancer Incidence per 100,000



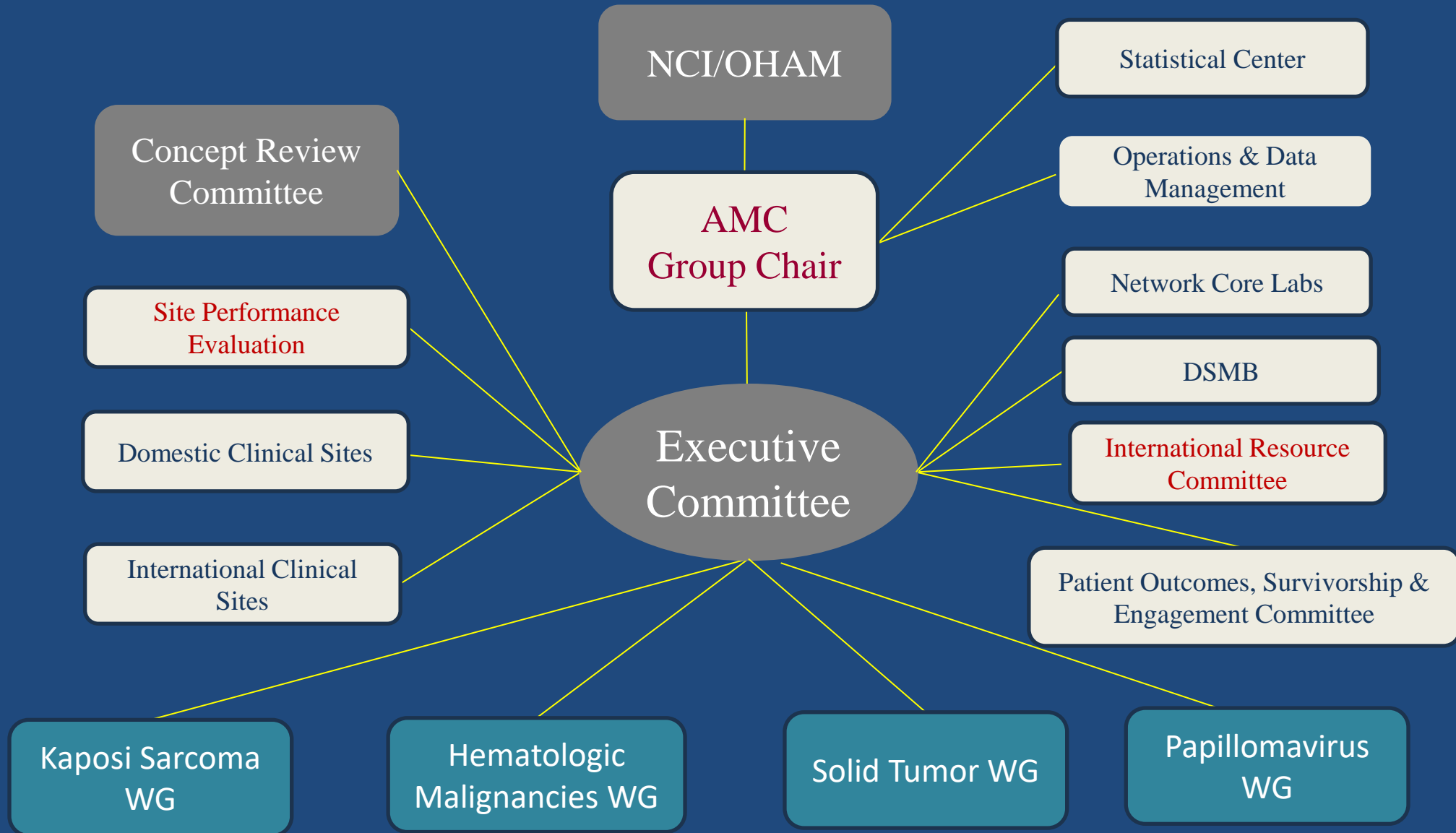
Globocan 2020

- 1<sup>st</sup>/2<sup>nd</sup> most common cancers in women in many LMICs
- 117,316 new cases/year

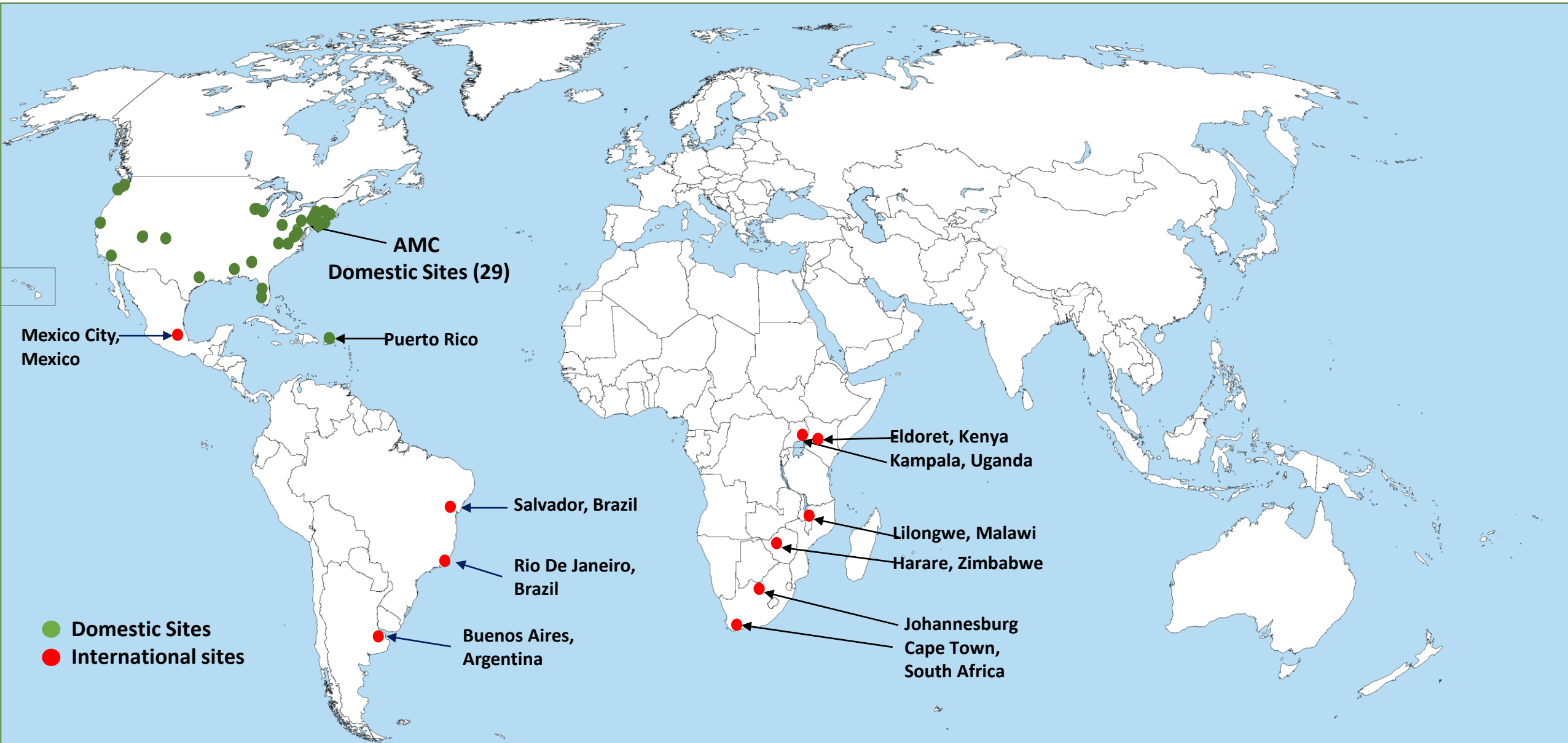
# AMC Mission

- Develop and evaluate clinical interventions for the treatment and prevention of malignancies in people with HIV
- Conduct Phase I, II and III clinical trials of HIV-related malignancies
- Investigate the biology of these malignancies in the context of clinical trials
- Contribute specimens and clinical data to the AIDS and Cancer Specimen Resource (ACSR)

# AIDS Malignancy Consortium



# AMC Sites



# Strengths of the AMC

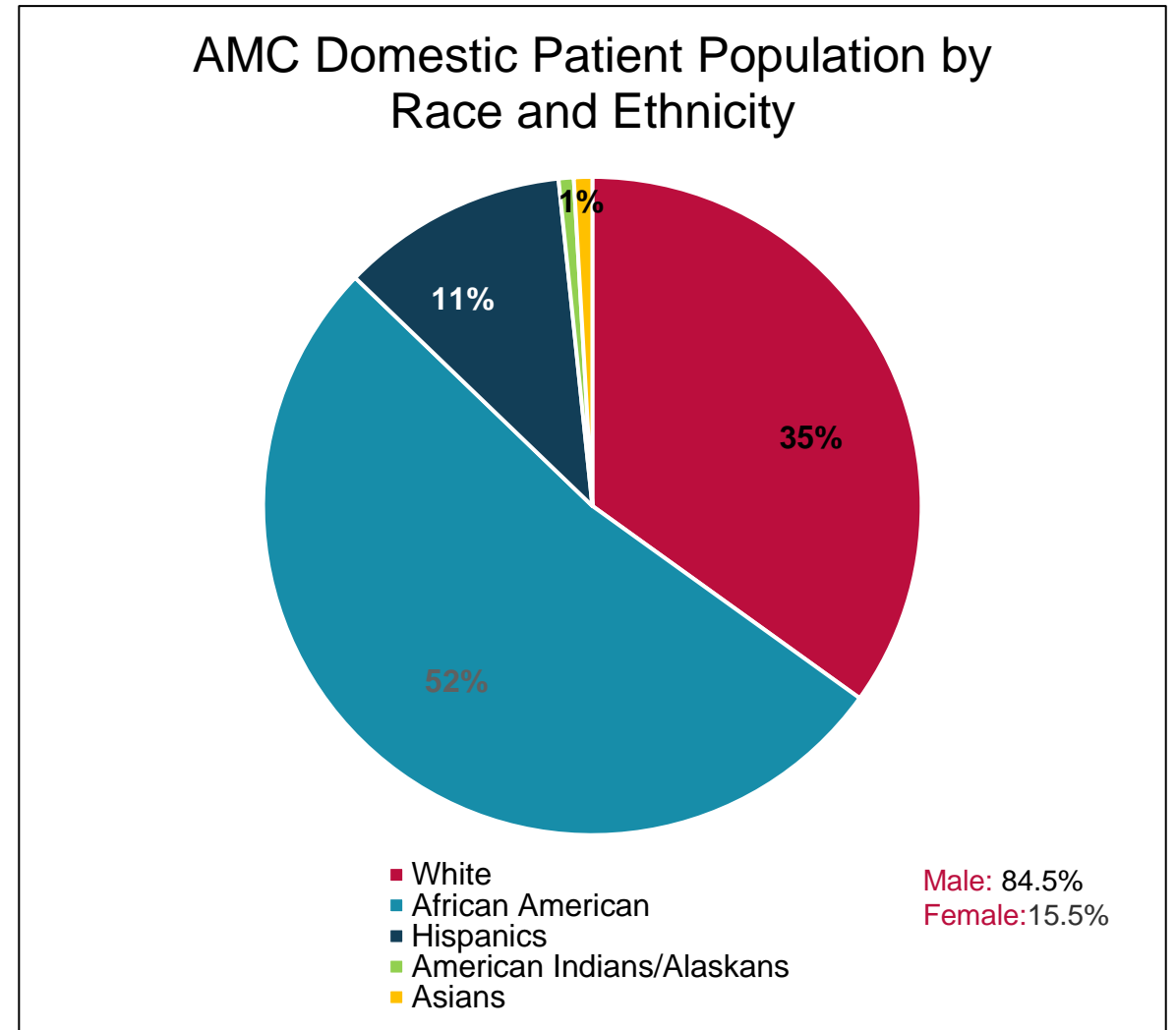
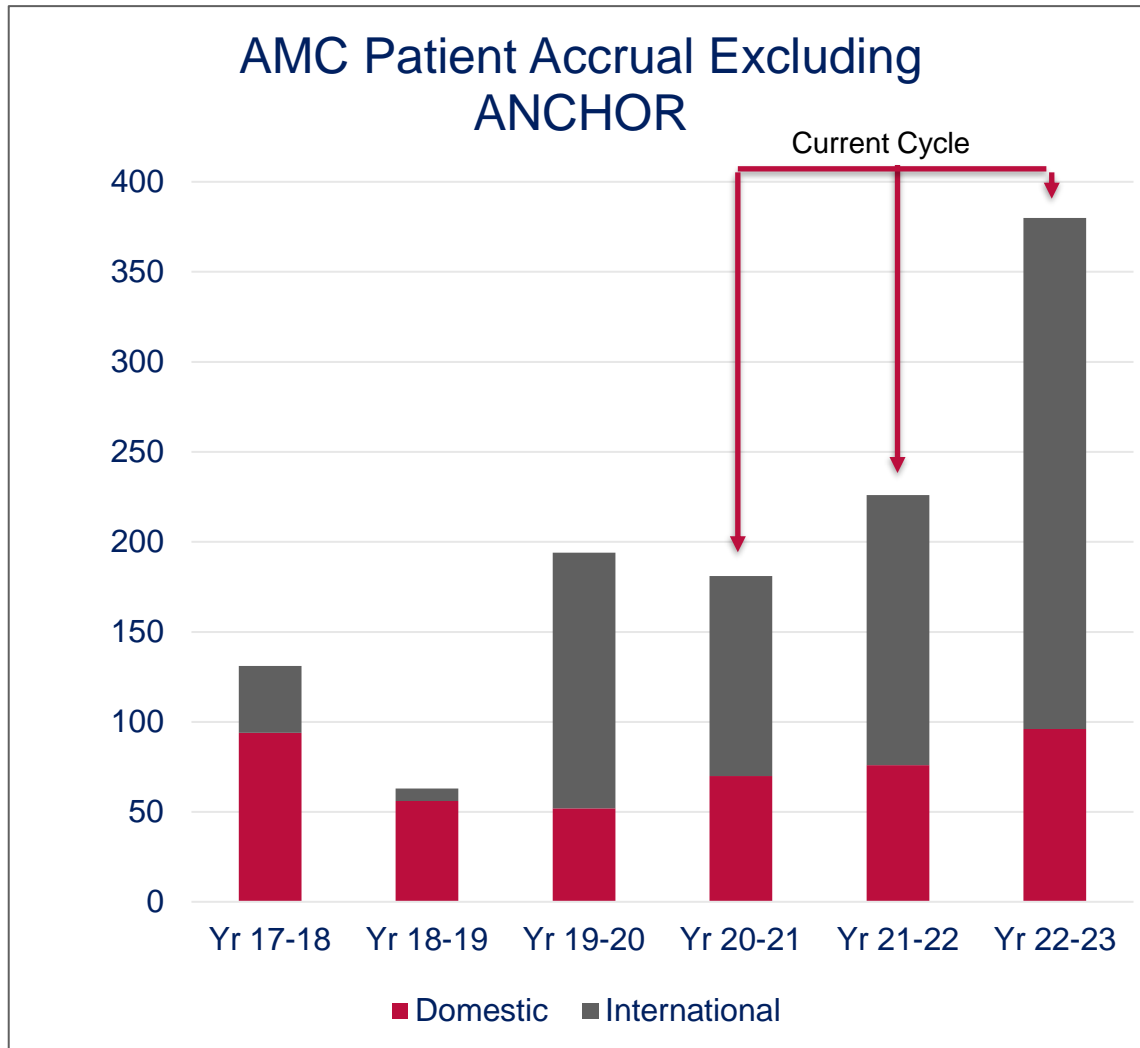
- Specialized clinical expertise of investigators in studying and treating tumors in PWH.
- Success in recruiting a diverse population of patients, including underserved populations.
- Provides PWH needed access to clinical trials for cancer therapy. These patients often are marginalized, stigmatized and otherwise lack access to care.



# Some Performance Parameters

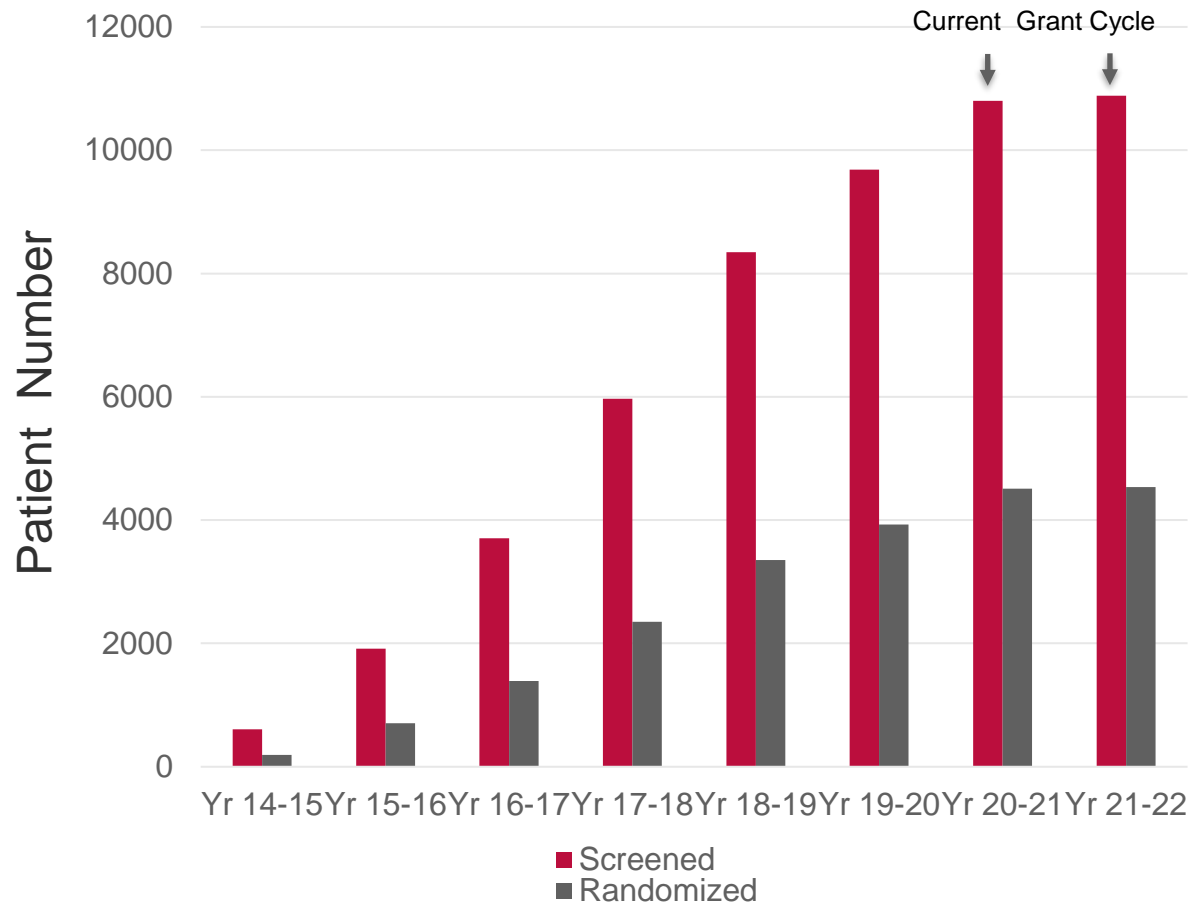
- Developed **12** protocols to date in this grant cycle (the past 36 months).
- **10** protocols completed enrollment.
- **1422** patients accrued (609 ANCHOR + 813 non-ANCHOR); excludes survey, laboratory and quality of life studies.
- **17** protocols actively accruing patients.
- Approximately **63%** of accrued US participants are of African-American or Hispanic origin.
- In the last 3 years, published approximately **45** papers in peer-reviewed journals.

# AMC Accrual and Demographics



# Anal Cancer HSIL Outcomes Research (ANCHOR) Study

## Cumulative Accrual



- A randomized controlled trial to establish whether treatment of anal high grade squamous intraepithelial lesions (HSIL) is an effective strategy to prevent anal cancer.
- **10,885** participants screened and **4535** randomized to a **treatment** or **active monitoring** arm
- The results showed that the treatment of anal HSIL is effective in **preventing anal cancer**, which has led to **change** of practice guidelines.

## AMC Accomplishments this Grant Cycle

- Evaluated **immunotherapy approaches** to solid tumors: e.g., use of ipilimumab and nivolumab in advanced solid tumors, and brentuximab vedotin, or nivolumab for Hodgkin lymphoma.
- Development and assessment of new approaches for the front-line treatment of AIDS lymphoma: e.g., **ibrutinib and R-DA-EPOCH**; and **piloting the use of CAR-T cell therapeutic approach** for refractory HIV-associated lymphoma.
- Investigated treatments with novel mechanisms of action for KS (e.g., **sEphB4-HAS, nelfinavir, pomalidomide, ixazomib**).
- Evaluation of the feasibility of treating **ocular surface squamous neoplasia (OSSN)** by surgical excision in SSA.

# AMC Accomplishments this Grant Cycle (Cont.)

- Assessment of a **therapeutic vaccine** directed to E6 and E7 HPV 16/18 genes using electroporation.
- Evaluated **HPV vaccinations** to reduce the recurrence of cervical HSIL after LEEP for cervical HSIL in SSA in WLWH.
- Trained a network of clinicians in **high resolution anoscopy** for screening and treating anal HSIL in LATAM AMC sites.
- **Assessing smoking cessation** interventions in patients undergoing low dose computerized tomography of the chest for lung cancer screening.

# AMC Mid-Cycle Evaluation

- Uniquely positioned to carry forward the NCI clinical agenda in HIV-associated malignancies.
- The evaluation noted that AMC contributions had significantly impacted the field in the United States and globally, including seminal practice-changing contributions.
- The evaluators highlighted the value of the infrastructure developed by the ANCHOR trial which will further continue to grow the field.
- Outstanding productivity of the disease Working Groups and the renewed focus on cutting-edge immunotherapy-based clinical trials.
- Commended the significant and laudable efforts of the Career Enhancement Program; and the development and capacity building of international clinical sites.

# Evaluation Recommendations

- Formation of an External Advisory Board for periodic review of AMC's prioritization and evaluation processes.
- The AMC should increase the proportion of AMC studies being conducted in LMICs due to the burden of HIV-infection in LMICs.
- AMC should continue to facilitate greater involvement of international junior investigators and trainees, especially those from Africa in AMC studies.
- The AMC should develop and convey plans to overcome obstacles to expanding novel therapies to international sites.

# Total Proposed AMC Budget

	Year 1	Year 2	Year 3	Year 4	Year 5
AMC	18,100,000	18,849,000	19,414,240	19,996,904	20,596,810
Total	96,956,954				

*Source of Funds: NCI AIDS funds*, apportioned by the NIH Office of AIDS Research (OAR) and targeted for AIDS research ("AIDS funds").



# Difference in AMC Year One Proposed Budget from Current Budget

Estimated AMC year 5 total budget: ~ \$ 21,331,737

Proposed Year 1 Budget (AMC): \$18,100,000

Estimated AMC year 5 non-ANCHOR funds: ~ \$14,000,000

**Difference from year 5 non-ANCHOR funds : \$ 4,100,000**

This cost increase includes:

- **ANCHOR correlative science** \$1,000,000;
- Support for **Data Commons platform** to meet NIH mandated data-sharing responsibilities) \$1,000,000;
- Support for **statistics and data analysis** staff \$ 200,000
- **International** site support for drug sourcing, storage, distribution; imaging and radiation monitoring...etc. \$300,000;
- Adding two new International clinical sites \$300,000
- Support for the **operation center** to meet the growing administrative, clinical, regulatory and logistic needs of the AMC, \$800,000;
- Support for 2 more **international fellows**, \$80,000; and
- **Inflation increase**, \$420,000.

# AMC Patient Costs

Core structure + patient care \$7,750,000

Cost per patient ~ \$25,800

Minimum 300 patients

30 domestic sites + 12 in SSA & Latin America

# Areas Where the AMC Makes Unique Contributions

- Only group with expertise and focus on HIV/AIDS-associated cancers.
- Poised to further evaluate **immunotherapy** approaches for malignancies in PWH.
- Conducts preventive and therapeutic trials for **Kaposi sarcoma and HPV-related precancers and cancers** in PWH.
- Only NCI-supported clinical trial network to conduct interventional trials for HIV malignancies in LMIC.
- Investigation of pharmacokinetic interactions between novel anticancer drugs and antiretroviral drugs - will facilitate the inclusion of PWH on larger **CTEP studies**.
- Has established a network of clinicians trained in high resolution anoscopy and treating anal HSIL. This resource can be used for other key studies in this area.

# Questions