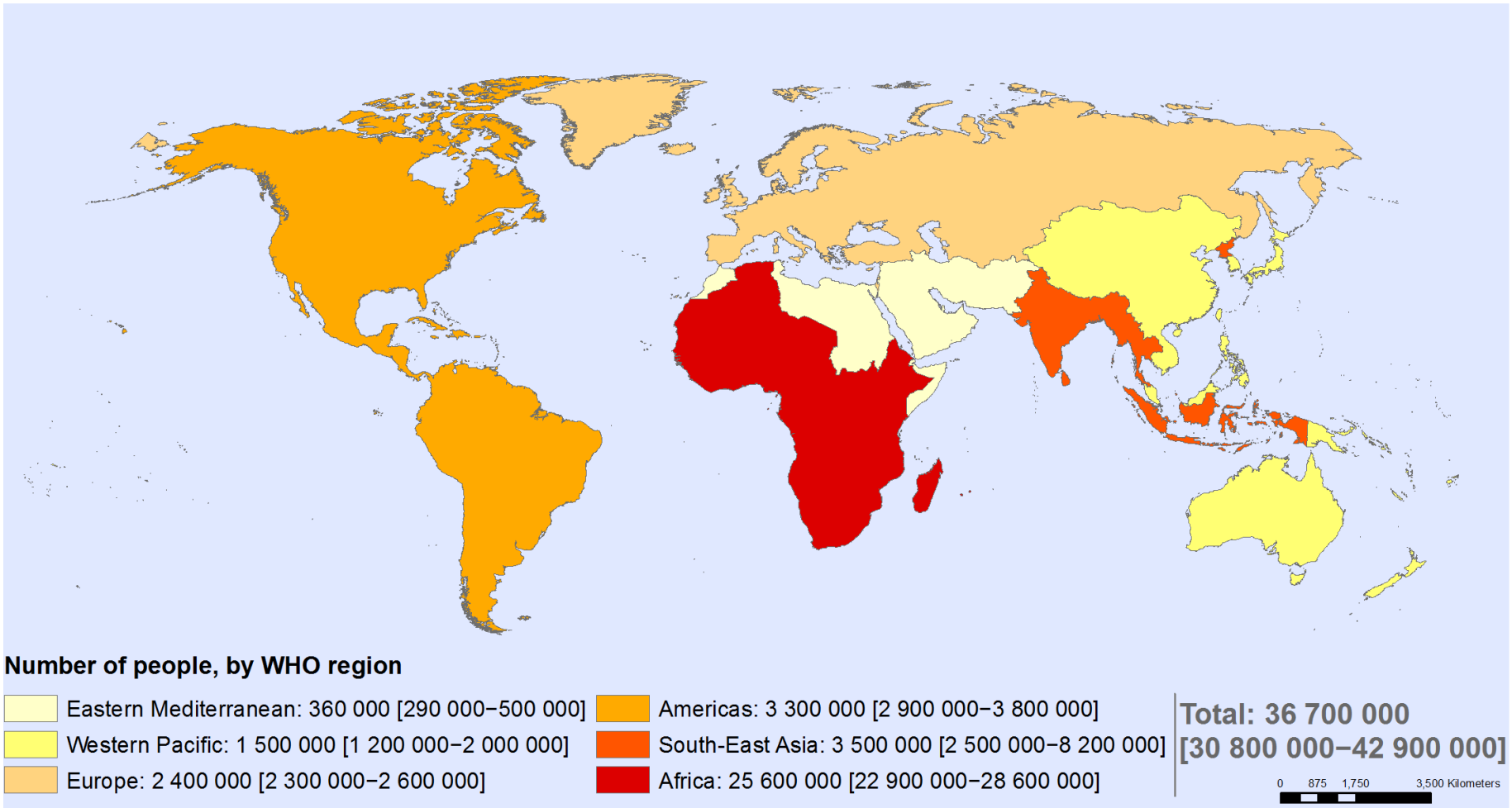


U.S. and Low- and Middle-Income Country (LMIC) HIV Malignancy Research Networks

Geraldina Dominguez, PhD



Estimated number of people living with HIV, 2016 By WHO region



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

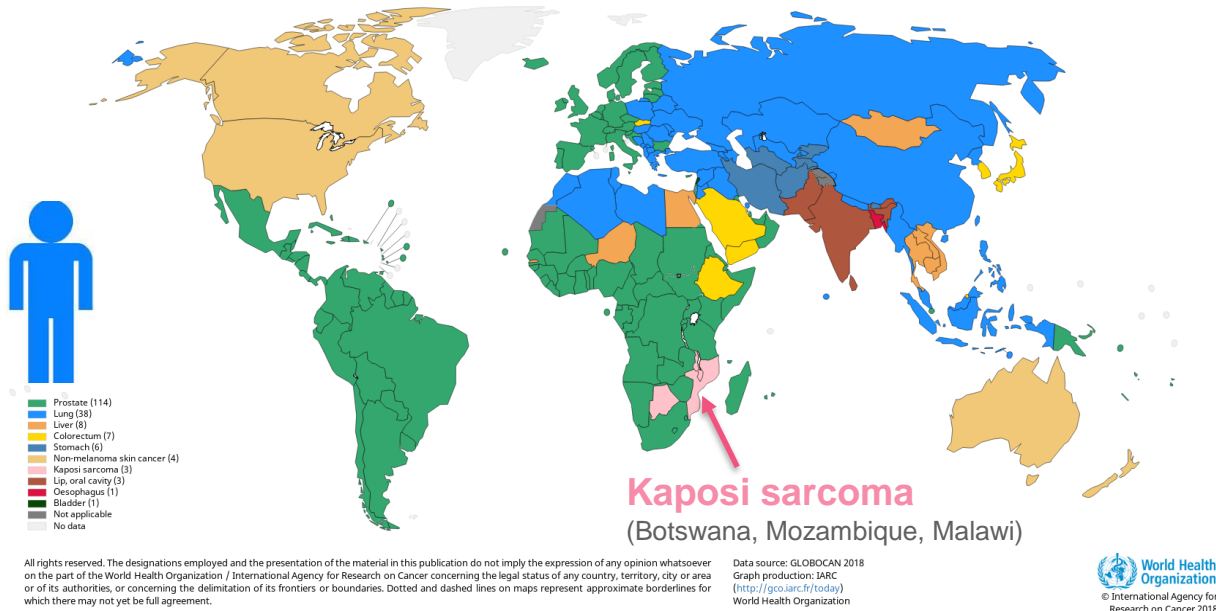
Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization



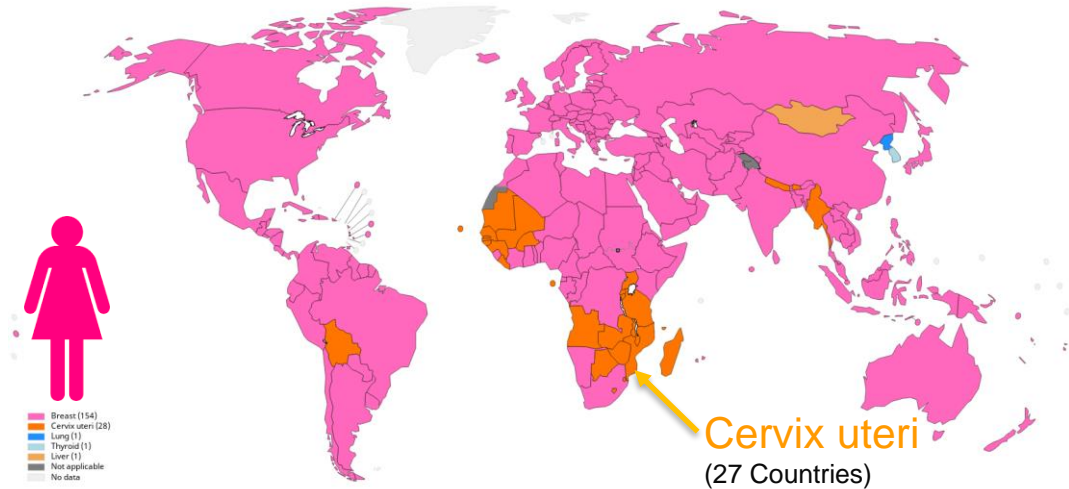
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Top Cancer Per Country-2018

Top cancer per country, estimated age-standardized incidence rates (World) in 2018, males, all ages



Top cancer per country, estimated number of new cases in 2018, females, all ages



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Data source: GLOBOCAN 2018
Graph production: IARC (<http://gco.iarc.fr/today>)
World Health Organization

<http://gco.iarc.fr/today/online-analysis-map>

Phase 1 and 2: Collaborative Consortia in HIV-Associated Cancers

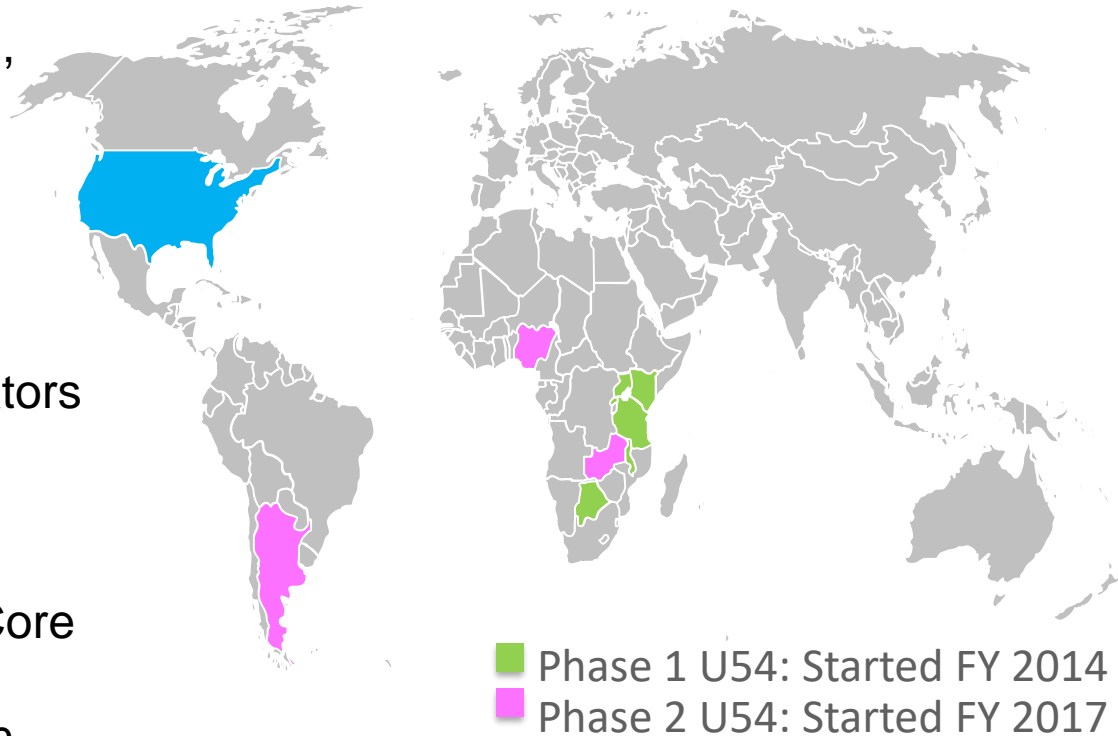


Collaborative Consortia in HIV-Associated Cancers

- Phase 1 U54 (Limited to Africa)
 - RFA-CA-13-010: Sub-Saharan African Collaborative HIV and Cancer Consortia (U54)
- Phase 2 U54 (Expanded to include other LMICs)
 - RFA-CA-16-018: Collaborative Consortia for the Study of HIV-Associated Cancers: U.S. and Low-and Middle-Income Country Partnerships (U54)
- Conduct research projects that address high-priority research questions in HIV-associated cancers in the partnering country
- Accelerate basic, translational, population, and implementation research in HIV-associated malignancies in the partnering country
- Enhance the ability of LMIC institutions to serve as a national/regional resource for training and career development of scientific leaders in cancer research
- Improve research infrastructure in the partnering country towards becoming independent research centers

Collaborative Consortia in HIV-Associated Cancers

- 11 consortia that are partnerships between a U.S. institution and a LMIC institution
 - 10 in sub-Saharan Africa
 - Tanzania, Kenya, Uganda (3), Rwanda, Botswana, Malawi, Zambia, Nigeria
 - 1 in South America
 - Argentina
- Shared leadership between U.S. investigators and LMIC investigators
- Structure
 - Research Projects
 - Shared Resource Cores
 - Mentoring/Career Enhancing Core
 - Administrative Core
- FY 2018 funding was \$8.3 million



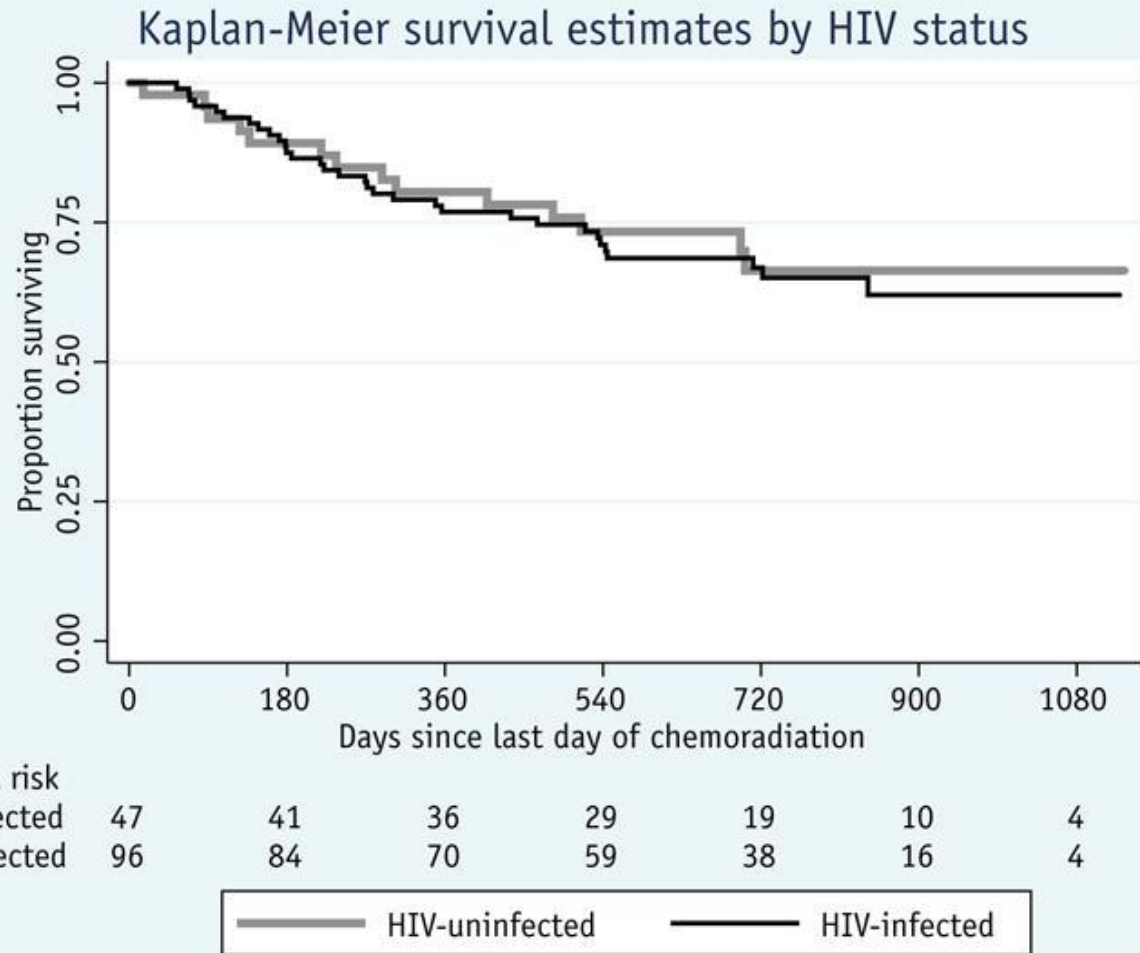
Examples of Research Project Topics

- HPV/cervix/anal
 - HPV typing for rural vs urban women
 - HPV natural history and modifiable risk factors
 - Cervix treatment outcomes
- KS/Kaposi sarcoma-associated herpesvirus (KSHV)
 - Predictors of KS recurrence or progression
 - KSHV genomic variability
 - KSHV Ab response in KS patients
- Lymphoma
 - Biomarkers and tumor characteristics that lead to better lymphoma treatment outcomes
 - Sequencing the T cell receptor repertoire in patients with lymphoma
- Liver cancer
 - HIV's role in HCC and early detection
- Other
 - Cancer burden using HIV-cancer record linkage

Some Accomplishments of the Collaborative Consortia in HIV-Associated Cancers

- Developed regional hubs for translational research in HIV-associated cancers
 - Publications (49)
 - New grant submissions from young LMIC investigators (2 K43)
 - Submission of R01 and K08 grants using data and/or samples
- Mentoring
 - Developed a novel model for career development centered around peer mentoring (Journal of Global Oncology 2018 41-11)
- Training
 - Inter-consortia training
 - Community sensitization in early detection of KS
 - Cryotherapy and Loop Electrosurgical Excision Procedure (LEEP)
 - Laboratory assays (e.g. immunohistochemistry, HPV typing, KSHV PCR)
 - Anal pap and High Resolution Anoscopy (HRA)
 - Transient elastography using Fibroscan®

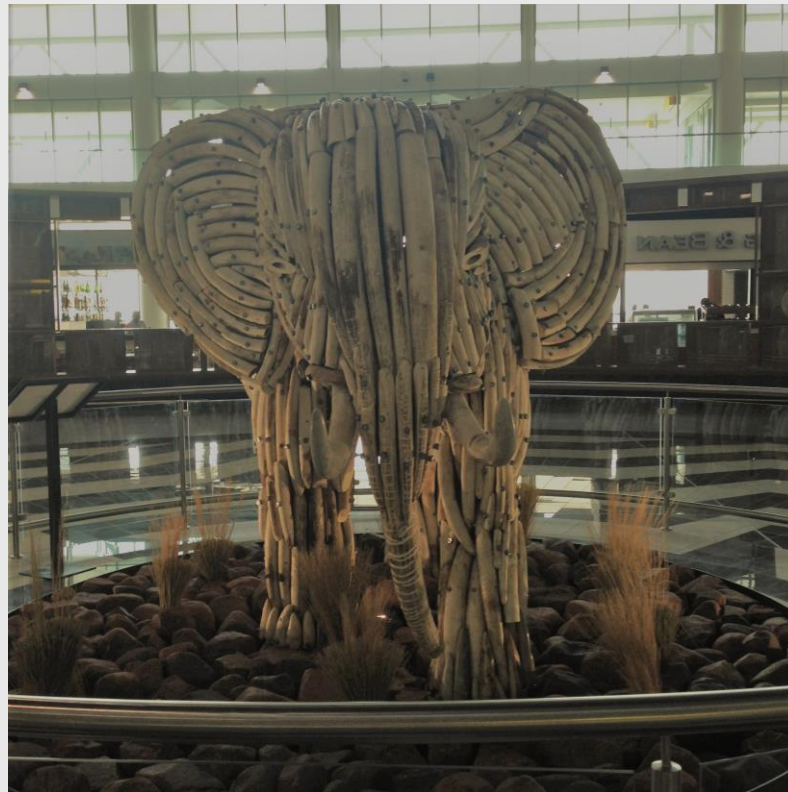
Impact of Human Immunodeficiency Virus Infection on Survival and Acute Toxicities from Chemoradiation Therapy for Cervical Cancer Patients in a Limited- Resource Setting



Overall survival by HIV status for cervical cancer patients treated with curative-intent chemoradiation in Botswana

- HIV status had no effect on 2-year OS or on acute toxicities in women with well-managed HIV infection

Phase 3: U.S. and Low- and Middle-Income Country (LMIC) HIV Malignancy Research Networks



Goals of the New RFA

- Accelerate scientific knowledge in HIV-associated cancers
- Continue to develop research capacity in LMICs with a significant burden of HIV-associated cancers
- Support collaborations between U.S. investigators and LMIC investigators
- Foster the development of early career investigators from the U.S. and LMICs interested in conducting research in HIV-associated cancers

Main Features of the Proposed Phase 3 RFA

- Partnerships between U.S. and LMIC investigators
 - Open to all investigators (Phase 2 investigators are eligible as long as they propose new projects)
- U54 mechanism
 - Supports a full range of research (basic, translational and clinical) plus research capacity building
 - Allows multiple projects in a single application
 - Allows for scientific and programmatic input
- Research projects that address questions in one related topic area
 - Up to 3 projects
- Cores
 - Shared resource cores (e.g. laboratory, data management, biospecimen)
 - Administrative (mandatory)
 - Coordination and support for trans-network activities
 - Developmental Core (mandatory)
 - Mentoring for LMIC and U.S. young investigators
 - Pilot projects

Examples of Possible Research Topics

- Research that addresses gaps in knowledge in the pathogenesis of cancers that are relatively rare in the U.S. but frequent in people living with HIV in an LMIC (e.g., Kaposi sarcoma, cervical cancer, ocular surface squamous neoplasia)
- Research to better understand the pathogenesis of cancers that affect people living with HIV and differences between analogous cancers in people without HIV
- Research that provides new insights into the role of social determinants in cancer risk, cancer care, and adherence to care and how it impacts survivorship in the era of combination antiretroviral therapy in LMICs
- Research that seeks to identify novel interactions of HIV with other co-factors (biological, environmental or exogenous) that modulate risk to cancer
- Research focused on development of novel, low cost and technologically feasible approaches for the prevention, diagnosis, and treatment of HIV-associated cancers particularly those that can be implemented in LMICs
- Research that evaluates optimal approaches that will guide strategies to improve the integration of cancer care with HIV care in the public health settings of LMICs

What is New in the Proposed Phase 3 RFA?

- Larger networks composed of institutions in one or more LMICs and one or more institutions in the U.S.
- Multiple PI applications
 - At least one PI from U.S. institution and one from the LMIC institution
 - PIs must demonstrate previous research collaborations
 - However, the teams assembled can include new collaborations
- Mechanistic clinical studies that NIH considers a clinical trial are allowed
 - Studies that are trying to understand a biological or behavioral process, the pathophysiology of disease, or the mechanism of action of an intervention
- Support the development of U.S. **AND/OR** LMIC junior investigators
 - Individual research projects can be led by a U.S. early stage investigator or a junior LMIC investigator

Proposed Budget

- Can request up to \$800,000 **direct costs** per year for 5 years
 - F&A costs to LMIC institutions limited to 8% of modified total direct costs
 - Requested set-aside: **\$6 million** per year for 5 years (30 million)
 - Expect to support 5-6 networks
- Funds will come from NCI's HIV/AIDS allocation that must be used to support HIV/AIDS research
 - \$5.7 million will come from ending Phase 1 projects
 - Will require \$300,000 new HIV/AIDS dollars
 - Fogarty International Center may be interested in co-funding
- The concept is tentatively approved by the NIH Office of AIDS Research as a FY2020 NCI initiative
- Identified as a priority by the NCI BSA Ad Hoc Subcommittee on HIV/AIDS Malignancy

Evaluation Criteria for the Proposed Phase 3 RFA

- Number of applications received
- Impact Scores
 - Weaknesses and strengths particularly those that reference scientific and technical merits
- Evidence that the proposed networks will advance or accelerate HIV-associated malignancy research
- Diversity of topic areas (epidemiology, pathology, basic, clinical studies, behavioral sciences, and implementation science)
- Synergy of the proposed research projects
- Number of LMIC and U.S. early career investigators supported
- Diversity of geographic areas
- How the application leverages other infrastructure and capacity of previously funded initiatives
- Evidence of LMIC institutional commitments (e.g. resources and support for a research environment)



Tanzania, 2019



Kenya, 2017

Thank You!



**NATIONAL
CANCER
INSTITUTE**



Uganda, 2016



Malawi, 2018

www.cancer.gov

www.cancer.gov/espanol