

# **Global Oncology** FY20 Annual Report





### VISION

Eliminate cancer as a cause of human suffering and death worldwide by ensuring that effective prevention and curative treatments are available to all patients.

## MISSION

Generate cancer research that has global impact and support the development of research capacity and clinical care to reduce the burden of cancer in low- and middle-income countries. Specimen is being examined at histopathology lab at UCI-Fred Hutch Cancer Centre by Diana Basemera. Photo by Jiro Ose

# **FY20 ANNUAL REPORT**

The Fred Hutch Global Oncology program's annual report includes information on FY20 achievements, grants and awards, financial overview, and publications. It also addresses the impact of the COVID-19 pandemic on our scientific and administrative operations and our immediate and future mitigation efforts.

Over the next decade, the global cancer burden is projected to grow by 75 percent to more than 22 million cases, with more than two-thirds of cancer deaths predicted to occur in low- and middle-income countries. The urgency to address the increasing cancer burden drives Fred Hutch Global Oncology to continue to advance its mission.

Despite the challenges presented by the pandemic, Global Oncology leadership, faculty, fellows, collaborators, physicians and nurses, and staff from Seattle and Kampala, Uganda came together to commit to a flexible and responsive approach that prioritizes science and the health and safety of research participants, patients, and staff. The teams continue to move Global Oncology's mission forward in the service of the most vulnerable populations.



### GLOBAL ONCOLOGY LEADERSHIP AND FACULTY



DR. EDUS H. WARREN M.D., Ph.D Program Head



DR. THOMAS ULDRICK M.D., M.S. Deputy Head



RAQUEL SANCHEZ M.B.A Managing Director



DR. WARREN PHIPPS M.D., M.P.H Medical Director of the UCI-Fred Hutch Collaboration



DR. MANOJ MENON M.D.

Assistant Professor, Vaccine and Infectious Disease and Clinical Research Divisions



Hutchinson Centre Research Institute of Uganda staff at a retreat in Kampala, Uganda. Photo by Raquel Sanchez

# FY20 OVERVIEW

Global Oncology faculty, together with the Uganda Cancer Institute, led by Executive Director, Dr. Jackson Orem, continued and launched clinical trials in Uganda — one study focused on an all-oral chemotherapy regimen for breast cancer patients and another on a novel, targeted treatment for lymphoma patients. In addition, our research team recently met accrual targets for a study comparing Ugandan women with HIV who are found to have precancerous lesions that spontaneously resolve compared to those who develop cancer.

The results of the study could lead to improved prevention and treatment of HPV-associated cancers. Further, the first cohort of the Adult Hematology-Oncology Fellowship completed their first of two years, the UCI-Fred Hutch Cancer Centre developed new testing capabilities, and Global Oncology launched new initiatives with its partners to strengthen the global cancer community in Seattle.

# THE COVID-19 PANDEMIC

During approximately the first half of the fiscal year 2020, Global Oncology committed its energy to implementing innovative oncology and infectious disease research and training initiatives, primarily in Kampala, Uganda, in collaboration with the UCI. However, in early 2020, the global spread of a novel coronavirus, SARS-CoV-2, required Global Oncology to be nimble in approaches to move its mission forward. By March 11, 2020, the World Health Organization characterized the COVID-19 outbreak, a pandemic. At the time of this report, July 1, 2020, there were an estimated 10.5 million confirmed cases of COVID-19 worldwide, with more than 500,000 deaths according to the WHO.

With early research suggesting that cancer patients with COVID-19 and additional comorbidities are at an increased risk for serious disease. This underscores the importance of cancer research and care amid this pandemic, especially in resource-limited settings where there is often limited access to diagnostics, treatment or supportive care.

### UGANDA CANCER INSTITUTE LEADERSHIP



DR. JACKSON OREM MBChB., MMed, Ph.D., UCI Executive director

# FY20 GRANTS & AWARDS

### • 1 NIH Award

NIH/NCI, RO1 Characterizing the Determinants of Primary KSHV Infection Among Children and Adolescents in Uganda \$2,868,449 (PIs, Phipps, Orem (UCI), Schiffer (FH) (Q1)

#### 2 Fred Hutch Internal Awards

Public Health Sciences Pilot, \$78,397 [1 year] 7/1/2019-6/30/2020 [PI, Adams] [Q1]

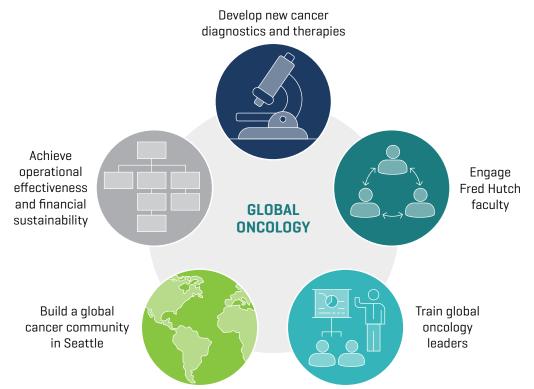
Pathogen-Associated Malignancies Integrated Research Center Innovation Grant \$100,000 (PIs, Phipps, Koelle (UW), Warren) (Q2)

### • 2 Industry Awards

Celgene, Optimizing Nephroblastoma Treatment Outcomes in Uganda Children \$100,000 (PI, Uldrick) (Q1)

Celgene Cancer Care Links. East African Adult Hematology-Oncology Fellowship International Exchange Program (PI, Uldrick) (Q2)





# UNANTICIPATED IMPACTS TO GLOBAL ONCOLOGY

# **Administration and Operations**

In March 2020, a cross-functional incident command team was quickly formed, led by leadership teams in Uganda and Seattle. Effective March 23, 2020, the incident command team reduced research, nonessential study visits, and operational activity at the UCI-Fred Hutch Cancer Research Centre in Kampala. Measures included a mandatory telecommuting/remote working policy for most of our staff, suspension of recruitment activity across all studies, a limit on follow-up activities to participants receiving an interventional treatment, and suspension of conferences that are not determined to be clinically relevant. Clinical activity continued with increased safety measures; including, mandated screening upon entry, handwashing, masking, and physical distancing measures.

Additionally, a collaborative working group made up of UCI and Fred Hutch members was formed and continues to meet weekly to quickly implement needed changes on campus.

# **Global Oncology Research Impacts**

Due the COVID-19 pandemic, five studies were fully suspended in March 2020. Two studies implemented in Kampala are clinical trials, and therefore, participants in follow-up visits continue to be seen to prevent the disruption of the intervention or treatment benefits. In addition to the aforementioned clinical trials, the studies that were suspended due to the pandemic include:

### Human Herpesvirus-8 (HHV-8) Replication and Kaposi Sarcoma Response to Treatment Suspended (Uganda)

The study aims to characterize HHV-8 replication in oral, plasma, and lesion sites and define its relationship to the clinical manifestations of KS. Further, the study aims to determine if HHV-8 replication in oral, plasma, and/or lesion sties predicts KS response to treatment and determine if HHV-8 replication in all sites predicts KS relapse following treatment. Lastly, the study aims to define the characteristics of effective immune responses to KS.



### **FINANCIAL OVERVIEW**

# ANNUAL GRANT FUNDING

FY20 \$8.2 million FY19

\$5.6 million

TOTAL OPERATING EXPENSES
FY20
\$2.6 million

FY19 \$2.3 million

### ANNUAL GRANT FUNDING

By Funding Type, FY20 Q4

NIH - 11 awards (includes subawards) \$6.2 million

Industry - 3 awards \$1.5 million

Private - 5 awards
\$0.5 million

Lazarus Okoche dyes tissue samples at the UCI - Fred Hutch Cancer Centre. Photo by Jiro Ose

### • Tumor Tissue Collection for Molecular Characterization and Viral Discovery Suspended (Uganda)

The study aims to obtain specimens for molecular characterization of malignancies and viral discovery.

### • Bacteremia in Hematologic Cancer Patients with Febrile Neutropenia in Uganda (Uganda)

The study objectives are to determine the microbiological characteristics of bacteria isolated from blood of febrile neutropenic patients and identify risk factors for bacteremia among episodes of febrile neutropenia with hematologic malignancies at the Uganda Cancer Institute. Lastly, the study aims to determine 30-day mortality among febrile neutropenic patients and to compare 30-day mortality by bacteremia versus no bacteremia at first febrile neutropenic episode in patients with hematological malignancies.

### Assessing the Clinical Utility of an Automated Molecular Diagnostic Test (GeneXpert Breast Cancer STAT4 Assay) in the Diagnosis and Management of Women with Breast Cancer in Uganda (Uganda)

The study objective is to evaluate the sensitivity and specificity of the STRAT4 assay to detect the presence of the ER, PR, and HER2 in core needle biopsy specimens of patients with breast cancer at the Uganda Cancer Institute [UCI].

On June 11, 2020, the Uganda National Council for Science and Technology (UNCST) shared quidance on the resumption of research activities during the COVID-19 pandemic. The UNCST outlines six guidelines that must be adhered to while conducting research. They have asked all study investigators develop Risk Management Plans to ensure research teams' and participants' safety during the study implementation before resuming participant recruitment and enrollment. At the time of this report, the research team developed and submitted comprehensive guidelines which are under review by local regulatory authorities. Our goal is for research activities to resume in the near future.





Specimen is being prepared at UCI-Fred Hutch Cancer Centre by Lazarus Okoche. Photo by Jiro Ose

# TRAINING THE NEXT GENERATION OF GLOBAL CANCER LEADERS

## East African Adult Hematology Oncology Fellowship

Fred Hutch Global Oncology, the UCI and other partners implement the East African Adult Hematology Oncology (AHO) Fellowship, launched in 2018, with support from the African Development Bank and Government of Uganda. The goals are to train Ugandan physicians so that they can, in turn, train their East African colleagues in high-quality clinical care and research — and guide and mentor new oncologists. The AHO Fellowship achieved several milestones during FY20, including:

- Several U.S. faculty professors visited Kampala to offer specialized lectures for the AHO fellows.
- Dr. Abrahams Omoding, co-director of AHO Fellowship, spend one week in Seattle for a benchmarking visit and gave a lecture about the fellowship at a Global Oncology Lecture Series.

# AHO FELLOWSHIP LEADERSHIP



DR. ABRAHAMS OMODING UCI, AHO Fellowship co-Director



**DR. JOHN HARLAN** UW, AHO Fellowship co-Director

- The four first-year fellows were reviewed by the Clinical Competency Committee (CCC) in October. The CCC recommended to the Training Advisory Committee (TAC) that all qualified to enter the second year of training (September 1, 2019-August 31, 2020).
- In December, Dr. Uldrick received notice of funding for the application to Celgene Cancer Care Links for an East African Adult Hematology-Oncology Fellowship Program International Exchange Program. This grant will support travel of the AHO fellows to Seattle for 4-6 weeks for additional training and attendance at a national meeting.

However, the AHO Fellowship activities have been impacted by the COVID-19 pandemic, and the directors are taking steps to adapt program implementation. Additional lectures by Fred Hutch and UW faculty, as well as training visits in Seattle, were canceled due to travel restrictions.

# Ongoing Training Activities at the UCI-Fred Hutch Cancer Center

Global Oncology continues to support key training activities through the Peer Mentoring Career Development Program, which includes weekly Research-in-Progress meeting, monthly journal club, and expert consultant sessions. The program has also advertised a call for applications for two Ph.D. candidates to start in September 2020 who will be supported by the new NIH Fogarty D43 training grant.

Maggie Lubwama, MBChB, MMed, Ph.D., researcher and lecturer at Makerere University and with the UCI-Fred Hutch Collaboration was awarded the 2020 Center for AIDS Research Mentored International Investigator Award. Lubwama plans to expand her research on causes of fever among patients at the UCI by using next-generation sequencing to more fully characterize mechanisms of antimicrobial resistance in bacterial isolates and to identify nonbacterial causes of fever in our cancer patients.



Dr. Geriga Fadhil, of the Uganda Cancer Institute, reviews x-rays at the Pediatric Service in the UCI-Fred Hutch Cancer Centre in Kampala, Uganda.





Pediatric outpatient department check-in at the UCI-Fred Hutch Cancer Centre.

# GLOBAL ONCOLOGY'S RESPONSE TO THE COVID-19 PANDEMIC — CURRENT AND FUTURE

## **Supporting the National Response**

As threat of the SARS-CoV-2 virus increased to cause a global pandemic, the UCI-Fred Hutch Collaboration worked closely with the UCI and the Ugandan Ministry of Health to develop response preparedness plans. Following the identification of the first case of SARS-CoV-2 infection in Uganda on March 21, the team moved rapidly to implement many of these plans, and support the UCI's capacity to screen patients and staff.

Further, the UCI-Fred Hutch Collaboration began discussions early in the pandemic with the Ugandan Ministry of Health about offering assistance with the national coronavirus response, including conducting SARS-CoV-2 testing for our cancer patients, staff, and the general population of Uganda at the UCI-Fred Hutch Cancer Centre. Global Oncology recognizes the support and expertise of colleagues both at Fred Hutch and the University of Washington to help guide our response in Uganda.



### 2019 GLOBAL ONCOLOGY PILOT GRANT RECIPIENTS

Molecular landscape of acute leukemias in Uganda



DR. SOHEIL MESHINCHI Fred Hutch, PI



DR. JOYCE BALAGADDE-KAMBUGU UCI, co-PI

Utility of a Liquid Biopsy in Patients with Lung Cancer at the Uganda Cancer Institute



DR. ALICE BERGER Fred Hutch, PI



DR. NIXON NIYONZIMA UCI, co-PI

# Scale Up Testing and Medical Supplies

During the week of June 8, 2020, the Ministry of Health completed an inspection of the labs at the UCI-Fred Hutch Cancer Centre in preparation for SARS-CoV-2 testing which received the highest of marks. Under the leadership of Andrea Towlerton, acting laboratory director, the laboratory is underway with preparations that include but are not limited to personal protective equipment (PPE) training, standardized operating procedures training and validation runs of the assays in conjunction with the Ugandan Ministry of Health. Towlerton also coordinated much needed donations and shipments of PPE to the UCI-Fred Hutch Cancer Centre. The items include: N95 respirator masks, surgical masks, gowns, arm sleeves, scrubs/ rubber shoes, safety glasses and face shields, hair nets, shoe covers, and gloves. In partnership with Fred Hutch's Business Development & Strategy and Philanthropy teams, the program secured a generous donation from BGI Americas and Lynden International. The global logistics company donated RT-PCR test kits to the UCI-Fred Hutch Cancer Centre towards the goal of conducting testing to better understand and respond to the COVID-19 pandemic in sub-Saharan Africa. The 2,000 tests donated (\$40,000 estimated value) will allow the laboratory team the capability to run up to 50 tests daily. This important effort was led by Andrea Towlerton, Dr. Warren Phipps, and Dr. Hootie Warren.

# FY20 Key Achievements

- Built critical research and laboratory capacity to conduct clinical trials at the UCI-Fred Hutch Cancer Centre, including the installation of MiSeq DNA sequencer. Conducting clinical trials, including:
  - The first trial aims to determine the feasibility an all-oral cancer regimen for breast cancer patients and is one aim of the ongoing study funded by GSK's Africa NCD Open Lab to define the molecular profile of breast cancer in Uganda and explore clinical implications, co-led by Dr. Manoj Menon (FH) and Dr. Jackson Orem (UCI). Preliminary data suggest that most women present in advanced stages of breast cancer and have hormone receptor-positive disease.

- The second clinical trial, in partnership with Roche and the UCI, is evaluating a novel-targeted treatment, Rituximab, that can be administered under the skin of both adult and pediatric patients with lymphoma. This trial is led by Dr. Thomas Uldrick, GO Deputy Head, and Drs. Henry Ddungu, Joyce Balagadde-Kambugu, and Jackson Orem of the UCI.
- Awarded two \$75,000 GO Pilot Grants that will use next generation sequencing applications for prevalent tumors in LMICs, using the MiSeq system.
- Global Oncology hosted eight Global Oncology Lectures in FY20 with dynamic and engaging global cancer experts, in which the most recent two lectures were held virtually in response to the global pandemic.
- In collaboration with the University of Washington and other Seattle-based institutions and partners, the team has launched a new Global Cancer Community in Seattle to bring together global health and global cancer experts to generate shared knowledge, learning, and new partnership as well as Internal Advisory Committee and External Advisory Board.
- Global Oncology bolstered its reach and social media presence by joining Twitter in December 2019 to share research and related news.
   Visit Global Oncology at fredhutch.org/go or follow us on Twitter @FredHutchGO.

# **GLOBAL ONCOLOGY FY20 MILESTONES**

Al

JULY 2019	Public Health Sciences Pilot Award (PI: Scott Adams, Staff Scientist, VIDD & GO)
JGUST/SEPTEMBER	Marc Stewart, Medical director, SCCA, visit to and lectures in Kampala for AHO fellowship focused on "Building a Great Cancer Center"
SEPTEMBER	<ul> <li>NIH/NCI, RO1 ("Characterizing the Determinants of Primary KSHV Infection Among Children and Adolescents in Uganda", PIs: Phipps, Orem, Schiffer)</li> </ul>
	<ul> <li>Celgene Award, "Optimizing Nephroblastoma Treatment Outcomes in Uganda Children" (PI: Uldrick)</li> </ul>
	1st UCI-Fred Hutch Collaboration Faculty Retreat (Kampala)
OCTOBER	Roche / Subcutaneous Rituximab Trial Launched
	Dr. William Harris and Dr. Tom Uldrick give lectures in Uganda for Adult Hematology-Oncology Fellowship
DECEMBER	2019 Global Oncology Pilot Recipients Awarded
	Ist Internal Advisory Committee Meeting Held
	<ul> <li>GO enhances social media presence by launching a Twitter handle, @FredHutchGO</li> </ul>
	Inaugural Global Cancer Community in Seattle event held
JANUARY 2020	<ul> <li>Pathogen-Associated Malignancies Integrated Research</li> <li>Center Innovation Grant (Pls, Phipps, Koelle (UW), Warren)</li> </ul>
	HCRI-Ug All-Staff Retreat (Kampala)
FEBRUARY	50 new Global Oncology Affiliate Faculty and Researchers joined
	<ul> <li>Ground-level construction of the UCI-Fred Hutch Centre begins with estimated completion of Nov. 2020 (went on hold during initial pandemic; resumed in May 2020)</li> </ul>
MARCH	Celgene International Exchange Program (PI: Uldrick)
	New UCI-Fred Hutch COVID-19 Incident Command Team Created and Discussions with Uganda Ministry of Health on SARS-CoV-2 Testing
JUNE	<ul> <li>Ministry of Health Site Inspection – UCI-Fred Hutch Cancer Centre Received Highest Rating out of 12 Labs in the Country</li> </ul>

FRED HUTCH



Ronald Lumala hugs his son Mike Kiragga who is healthy again after having been successfully treated for Burkitt lymphoma at the Uqanda Cancer Institute. Photo by Robert Hood

# **RESEARCH TO PUBLICATIONS**

During fiscal year 2020, Global Oncology faculty and colleagues published 14 publications. It is important to highlight that five of the articles were independent research from a former or current fellow of the UCI-Fred Hutch Collaboration in Uganda (indicated by an asterisk\*).

Menon M, Orem J, Adams S, Bakenga A, Basemera D, Kasozi D, Quentin Konnick E, Mubiru K, Mulumba Y, Muwonge C, Okoche L, Pierce R, Gralow J, Niyonzima N. ER, PR, and HER2 expression in Ugandan breast cancer patients: An evaluation of in-country RT-PCR compared to IHC. Journal of Clinical Oncology, 2020 May 25; 38 Suppl 15. DOI: 10.1200/ JC0.2020.38.15\_suppl.e19009

ABSTRACT: Background: Breast cancer, the most common cancer in sub-Saharan Africa (SSA), is characterized by poor survival. An accurate assessment of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor 2 receptor (HER2) status, typically via immunohistochemistry (IHC), is considered essential to provide prognostic data and quide therapeutic decision-making. However, due to inaccessible IHC services, these data are often unavailable in many parts of SSA; alternate methods need to be explored. Given the lab infrastructure developed in response to the HIV pandemic, RT-PCR testing is more readily accessible and feasible in SSA. Here we assess the potential of RT-PCR in evaluating the receptor status of women with breast cancer in Uganda. Methods: We enrolled women with a new diagnosis of invasive breast cancer at the Uganda Cancer Institute. Demographic and clinical data were obtained. A formalin-fixed paraffin embedded (FFPE) specimen was utilized for quantitative RT-PCR, using a validated assay for the detection of the ER, PR and HER2. Receptor expression levels were expressed

as relative quantity (RQ) compared to housekeeping genes (CALM2). HER2 IHC results were categorized as negative [score 0 or 1+] or positive [3+]; 2+ results (n=6) were excluded as FISH testing was not performed. Unstained slides were sent to the Fred Hutchinson Cancer Research Center for IHC. Receiver operating characteristic (ROC) analysis was applied to compare RT-PCR to IHC [qold standard]. Results: We analyzed interim data (anticipated N=100 of an ongoing study) from 32 women aged 35 to 56 years. The majority of women (25, 78%) presented with advanced stage disease. Of the 32 cancers, 18 were ER+ [56%], 10 were PR+ [31%], 9 were HER2+ [28%] and 8 were triple negative [25%] by IHC. From ROC analysis, the AUC were 0.94, 0.95, and 0.81 for ER, PR, and HER2 respectively with high sensitivity and specificity [Table]. Conclusions: Despite the tremendous need, the ability to detect the ER, PR, and HER2 via IHC in SSA is limited. Here we demonstrate the favorable test characteristics of RT-PCR when compared to IHC. Given the relatively wide accessibility of RT-PCR and endocrine therapy for breast cancer, as well as the recent inclusion of trastuzumab in the WHO's Essential Medicines List, the results of this study have both direct diagnostic and therapeutic implications.

Mutebi M, Anderson BO, Duggan C, Adebamowo C, Agarwal G, Ali Z, Bird P, Bourque JM, DeBoer R, Gebrim LH, Masetti R, Masood S, **Menon M**, Nakigudde G, Ng'ang'a A, Niyonzima N, Rositch AF, Unger-Saldaña K, Villarreal-Garza C, Dvaladze A, El Saghir NS, Gralow JR, Eniu A. Breast cancer treatment: A phased approach to implementation. Cancer, 2020 May 15;126 Suppl 10, 2365–2378. https://doi.org/10.1002/cncr.32910

ABSTRACT: Optimal treatment outcomes for breast cancer are dependent on a timely diagnosis followed by an organized, multidisciplinary approach to care. However, in many low- and middle-income countries, effective care management pathways can be difficult to follow because of financial constraints, a lack of resources, an insufficiently trained workforce, and/ or poor infrastructure. On the basis of prior work by the Breast Health Global



Dr. Hootie Warren talks about Dr. Nixon Niyonzima during a reception marking the 10-year anniversary of the Fred Hutch-UCI collaboration. Photo by Robert Hood

Initiative, this article proposes a phased implementation strategy for developing sustainable approaches to enhancing patient care in limited-resource settings by creating roadmaps that are individualized and adapted to the baseline environment. This strategy proposes that, after a situational analysis, implementation phases begin with bolstering palliative care capacity, especially in settings where a late-stage diagnosis is common. This is followed by strengthening the patient pathway, with consideration given to a dynamic balance between centralization of services into centers of excellence to achieve better quality and decentralization of services to increase patient access. The use of resource checklists ensures that comprehensive therapy or palliative care can be delivered safely and effectively. Episodic or continuous monitoring with established process and quality metrics facilitates ongoing assessment, which should drive continual process improvements. A series of case studies provides a snapshot of country experiences with enhancing patient care, including the implementation of national cancer control plans in Kenya, palliative care in Romania, the introduction of a 1-stop clinic for diagnosis in Brazil, the surgical management of breast cancer in India, and the establishment of a women's cancer center in Ghana.

Ddungu H, Krantz EM, Kajja I, Naluzze S, Nabbanja H, Nalubwama F, **Phipps W,** Orem J, Wald A, Kiwanuka N. Transfusion Challenges in Patients with Hematological Malignancies in Sub-Saharan Africa: A Prospective Observational Study from the Uganda Cancer Institute. Sci Rep. 2020 Feb 18;10[1]:2825. doi: 10.1038/s41598-020-59773-y.

ABSTRACT: Blood transfusion is fundamental in managing hematologic malignancies. We sought to evaluate the need and availability of blood products for patients with hematological malignancies at Uganda Cancer Institute. We prospectively studied the demand and supply of blood for patients with thrombocytopenia (platelet count ≤50 × 109/L], anemia (hemoglobin ≤10 g/dL), and bleeding (WHO grade  $\geq 2$ ). We used Poisson generalized estimating equation regression models for longitudinal binary outcomes. Among 91 patients, the median age was 26 years (IQR, 11-47). Thrombocytopenia occurred on ≥1 day in 58% of patients and on 49% of hospital days. Platelets were transfused to 39% of patients. The mean number of platelet units requested per day was 16.2 (range 0-30]; 5.1 (range 0-15) were received. Anemia occurred on ≥1 day in 90% of patients; on 78% of days; and 68% received at least one blood transfusion. The mean number of blood units requested was 36.3 (range 8-57) units per day; 14 (range 0-30) were received. Bleeding occurred on ≥1 day in 19% of patients on 8% of hospital days. Thrombocytopenia and anemia were common, but product availability was substantially below that requested. We recommend increased blood collection and adherence to strict transfusion triggers as strategies to improve blood availability.

Mayer BT, Krantz EM, Wald A, Corey L, Casper C, Gantt S, Schiffer JT. Estimating the Risk of Human Herpesvirus 6 and Cytomegalovirus Transmission to Ugandan Infants from Viral Shedding in Saliva by Household Contacts. Viruses. 2020 Feb 3;12[2]. pii: E171. doi: 10.3390/ v12020171.

ABSTRACT: Human herpesvirus 6 (HHV-6) and cytomegalovirus (CMV) infections are common in early childhood. In a prospective Ugandan birth cohort study, most infants acquired HHV-6 (24/31; 77%) and CMV (20/30; 67%) during followup. To assess the transmission risk, we modeled a dose-response relationship between infant HHV-6 and CMV infections and weekly oral viral shedding by mothers and all other ("secondary") children in the home. Oral viral loads that were shed by mothers and secondary children were significantly associated with HHV-6 but not CMV transmission. While secondary children had higher and more frequent HHV-6 shedding than their mothers, they had a lower per-exposure transmission risk, suggesting that transmission to maternal contacts may be more efficient. HHV-6 transmission was relatively inefficient, occurring after <25% of all weekly exposures. Although HHV-6 transmission often occurs following repeated, low dose exposures, we found a non-linear dose-response relationship in which infection risk markedly increases when exposures reached a threshold of > 5 log10 DNA copies/mL. The lack of association between oral CMV shedding and transmission is consistent with breastfeeding being the dominant route of infant infection for that virus. These affirm saliva as the route of HHV-6 transmission and provide benchmarks for developing strategies to reduce the risk of infection and its related morbidity.

Wu ES, Urban RR, Krantz EM, Mugisha NM, Nakisige C, Schwartz SM, Gray HJ, Casper C. The association between HIV infection and cervical cancer presentation and survival in Uganda. Gynecol Oncol Rep. 2019 Nov 19;31:100516. doi: 10.1016/j. gore.2019.100516. eCollection 2020 Feb. Review.

ABSTRACT: Our objective was to determine how HIV infection impacts cervical cancer stage at presentation and overall



survival (OS) among Ugandan women. This was a prospective study of 149 women diagnosed with cervical cancer from 2013 to 2015 at the Uganda Cancer Institute. Poisson regression models were fit to calculate prevalence ratios (PR) for the association between HIV infection and late stage at cancer diagnosis. The association between HIV infection and OS after cervical cancer diagnosis was evaluated using Cox proportional hazards models. The cohort included 53 HIVpositive and 96 HIV-negative participants. Median age at diagnosis was 44 years for HIV-positive and 54 years for HIV-negative participants. Seventy-seven percent of HIV-positive participants received antiretroviral therapy. Median baseline CD4 count was 373 cells/mm3 for HIV-positive participants versus 926 cells/mm3 for HIV-negative participants. Thirty-two percent of HIV-positive participants were diagnosed with late stage cervical cancer [III-IV] versus 39% of HIV-negative participants. No association was found between late stage at cancer diagnosis and HIV infection (PR adjusted for age, parity and transport cost 1.0, 95%Cl 0.6-1.8]. Most women presenting for care received cancer treatment, though almost half who received radiotherapy did not complete treatment. The median OS was 13.7 months for HIV-positive participants and 24.3 months for HIVnegative participants. After adjusting for age and stage, HIV infection was weakly associated with OS (HR 1.3, 95%CI 0.8-2.2]. In Uganda, cervical cancer is often incompletely treated and survival remains poor. HIV infection was not associated with cervical cancer stage at diagnosis, but may be weakly associated with shorter survival.

Bender Ignacio R, Ddungu H, **Uldrick TS**. Untangling the Effects of Chemotherapy and HIV on CD4 Counts-Implications for Immunotherapy in HIV and Cancer. JAMA Oncol. 2019 Dec 5. doi: 10.1001/ jamaoncol.2019.4634. [Epub ahead of print]

No abstract available.

Drs. Edus H. Warren (left), Global Oncology Head, and Thomas Uldrick, Global Oncology Deputy Head, in Kampala, Uganda. Photo by Fred Hutch staff.



Downing J, Niyonzima N, Guma S, Batuli M, Kiwanuka R, Atuhe I, Nalukwago Z, Mwesiga M, **Phipps W**, Ddungu H. Towards universal coveragehighlights from the 2nd Uganda Conference on Cancer and Palliative Care, 5-6 September 2019, Kampala, Uganda. Ecancermedicalscience. 2019 Nov 19;13:976. doi: 10.3332/ ecancer.2019.976. eCollection 2019.

ABSTRACT: The 2nd Uganda Conference on Cancer and Palliative Care was held in September 2019 in Kampala, Uganda under the theme: Towards Universal Coverage. It was hosted by the Uganda Cancer Institute and the Palliative Care Association of Uganda (PCAU). The conference brought together 350 delegates from eight countries. Key themes from the conference included: universal health coverage (UHC), service provision and public health; resources for achieving UHC; capacity building; human rights and engagement on the implementation of the recommendations made by the Uganda Human Rights Commission; provision of cancer and palliative care to 'hard to reach' and 'vulnerable' groups; paediatrics; health promotion and prevention; policy and advocacy and digital technology. The conference also gave opportunity to celebrate the 20th Anniversary of the work of PCAU, with a celebration dinner attended by the Minister of Health. The past few years have seen significant developments in both cancer and palliative care in Uganda, and this was evident in the presentations, and the way that provision has changed and improved since the first cancer and palliative care conference in 2017. Emphasis on UHC, along with the support of government and other stakeholders, is important in the ongoing development of cancer and palliative care services in Uganda.

McGoldrick SM, Mutyaba I, **Adams SV**, Larsen A, Krantz EM, Namirembe C, Mooka P, Nabakooza S, Ndagire M, Mubiru K, Nabwana M, Nankinga R, Gerdts S, Gordon-Maclean C, Geriga F, Omoding A, Sessle E, Kambugu J, **Uldrick TS**, Orem J, Casper C. Survival of children with endemic Burkitt lymphoma in a prospective clinical care project in Uganda. Pediatr Blood Cancer. 2019 Sep;66(9):e27813. doi: 10.1002/ pbc.27813.



Lymphoma Tumor Board at UCI-Fred Hutch Cancer Centre.

#### ABSTRACT:

PURPOSE: "Endemic" Burkitt lymphoma (BL) is a common childhood cancer in Africa. Social and treatment factors may contribute to poor survival. With the aim of improving BL outcomes in Uganda, we undertook a comprehensive project (BL Project) that provided diagnostic support, access to standard chemotherapy, nutritional evaluations, and case management. We evaluated survival of children with BL in the context of the project.

Patients and methods: Patients followed by the BL Project who consented to research were enrolled in this study. Children with a pathology diagnosis consistent with BL were eligible. Data were collected prospectively. First-line chemotherapy generally consisted of six cycles of cyclophosphamide, vincristine, low-dose methotrexate (COM). We used Kaplan-Meier and Cox regression analyses to evaluate factors associated with overall survival [OS].

RESULTS: Between July 2012 and June 2017, 341 patients with suspected BL presented to the BL Project. One hundred eighty patients with a pathology-based diagnosis were included in this study. The median age was seven years (interquartile range, 5-9), 74% lived ≥100 km from the Uganda Cancer Institute, 61% had latestage disease, 84% had ECOG performance status < 3, 63% reported B-symptoms, and 22% showed neurologic symptoms. Fewer than 10% abandoned therapy. The four-year OS rate was 44% (95% CI, 36%-53%). In a multivariate model, ECOG status was significantly associated with mortality. CONCLUSION: The BL Project reduced effects of lacking supportive care and oncology resources, and allowed patients from Uganda to receive curative intent therapy with minimal loss to follow-up. Nonetheless, OS remains unacceptably low. Improved therapeutic approaches to endemic BL are urgently needed in Africa.

Bacteremia in febrile cancer patients in Uganda. Lubwama M, **Phipps W**, Najjuka CF, Kajumbula H, Ddungu H, Kambugu JB, Bwanga F. BMC Res Notes. 2019 Jul 30;12(1):464. doi: 10.1186/s13104-019-4520-9.

#### ABSTRACT:

OBJECTIVE: The aim of this study was to determine the predominant bacterial species causing bacteremia among febrile cancer patients, and their antibacterial resistance profiles at the Uganda Cancer Institute.

**RESULTS: We enrolled in-patients** with a documented fever ( $\geq$  37.5 °C). Bacteria from positive blood cultures were identified using standard methods biochemically. Antibacterial susceptibility testing was performed with the Kirby-Bauer disc diffusion method. From a total of 170 febrile episodes, positive blood cultures were obtained from 24 [14.1%]. A positive culture was more likely to be obtained from a patient with neutropenia (P = 0.017). Of 22 (66.7%) Gram-negative bacteria isolated, half were E. coli (n = 11). Gram-negative compared to Grampositive bacteria were most likely to be isolated from patients with a hematologic malignancy (P = 0.02) or patients with neutropenia (P = 0.006). Of the isolated

Enterobacteriaceae 85% (n = 20) were resistant to three or more classes of antibiotic and 41% (n = 7) had extended spectrum beta-lactamases. Of the 11 Gram-positive bacteria isolated, the S. aureus isolate was methicillin resistant but susceptible to vancomycin. Multidrug resistant Gram-negative bacteria are the main cause of bacteremia in febrile cancer patients at the Uganda Cancer Institute. There is need for ongoing microbial surveillance, infection prevention and control, and antibiotic stewardship programs.

Murphy KJ, Conroy AL, Ddungu H, Shrestha R, Kyeyune-Byabazaire D, Petersen MR, Musisi E, Patel EU, Kasirye R, Bloch EM, Lubega I, John CC, Hume HA, Tobian AAR. Malaria parasitemia among blood donors in Uganda. Transfusion. 2020 Apr 13. doi: 10.1111/trf.15775. [Epub ahead of print]\*

#### ABSTRACT:

BACKGROUND: Malaria remains a leading transfusion associated infectious risk in endemic areas. However, the prevalence of malaria parasitemia has not been well characterized in blood donor populations. This study sought to determine the prevalence of Plasmodium in red blood cell [RBC] and whole blood [WB] units after the rainy season in Uganda.

METHODS AND MATERIALS: Between May and July 2018, blood was collected from the sample diversion pouch of 1000 WB donors in Kampala and Jinja, Uganda. The RBC pellet from ethylenediamine tetraacetic acid (EDTA) anticoagulated blood was stored at -80°C until testing. DNA was extracted and nested PCR was used to screen samples at the genus level for Plasmodium, with positive samples further tested for species identification.

RESULTS: Malaria parasitemia among asymptomatic, eligible blood donors in two regions of Uganda was 15.4%; 87.7% (135/154) of infections were with P. falciparum, while P. malariae and P. ovale

Lazarus Okoche, PCR Laboratory Manager, dyes tissue samples at the UCI - Fred Hutch Cancer Centre in Kampala, Uganda. were also detected. There were 4.3% of blood donors who had mixed infection with multiple species. Older donors (>30 years vs. 17-19 years; aPR = 0.31 [95% CI = 0.17-0.58]), females (aPR = 0.60 [95% CI = 0.42-0.87]), repeat donors (aPR = 0.44 [95% CI = 0.27-0.72]) and those donating near the capital city of Kampala versus rural Jinja region (aPR = 0.49 [95% CI = 0.34-0.69]) had a lower prevalence of malaria parasitemia.

CONCLUSIONS: A high proportion of asymptomatic blood donors residing in a malaria endemic region demonstrate evidence of parasitemia at time of donation. Further research is needed to quantify the risk and associated burden of transfusion-transmitted malaria (TTM) in order to inform strategies to prevent TTM.

Okunade K, Bashan Nkhoma K, Salako O, Akeju D, Ebenso B, Namisango E, Soyannwo O, Namukwaya E, Dandadzi A, Nabirye E, Mupaza L, Luyirika E, Ddungu H, Chirenje ZM, Bennett MI, Harding R, Allsop MJ. Understanding data and information needs for palliative cancer care to inform digital health intervention development in Nigeria, Uganda and Zimbabwe: protocol for a multicountry qualitative study. BMJ Open. 2019 Oct 31;9(10):e032166. doi: 10.1136/bmjopen-2019-032166.\*

#### ABSTRACT:

INTRODUCTION: Palliative care is a clinically and cost-effective component of cancer services in sub-Saharan Africa (SSA). Despite the significant need for palliative cancer care in SSA, coverage remains inadequate. The exploration of digital health approaches could support increases in the quality and reach of palliative cancer care services in SSA. However, there is currently a lack of any theoretical underpinning or data to understand stakeholder drivers for digital health components in this context. This project addresses this gap through engaging with key stakeholders to determine data and information needs that could be supported through digital health interventions.

METHODS AND ANALYSIS: This is a multicountry, cross-sectional, qualitative study conducted in Nigeria, Uganda and Zimbabwe. In-depth interviews will be conducted in patients with advanced cancer (n=20), caregivers (n=15), health professionals (n=20) and policy-makers (n=10) in each of the three participating countries. Data from a total of 195 interviews will transcribed verbatim and translated into English before being imported into NVivo software for deductive framework analysis. The analysis will seek to understand the acceptability and define mechanisms of patient-level data capture and usage via digital technologies.

ETHICS AND DISSEMINATION: Ethics approvals have been obtained from the Institutional Review Boards of University of Leeds (Ref: MREC 18-032), Research Council of Zimbabwe (Ref: 03507), Medical Research Council of Zimbabwe (Ref: MRCZ/A/2421), Uganda Cancer Institute (Ref: 19-2018), Uganda National Council





of Science and Technology [Ref: HS325ES] and College of Medicine University of Lagos [Ref: HREC/15/04/2015]. The project seeks to determine optimal mechanisms for the design and development of subsequent digital health interventions to support development, access to, and delivery of palliative cancer care in SSA. Dissemination of these findings will occur through newsletters and press releases, conference presentations, peer-reviewed journals and social media.

Ekdahl Hjelm T, Matovu A, Mugisha N, Löfgren J. Breast cancer care in Uganda: A multicenter study on the frequency of breast cancer surgery in relation to the incidence of breast cancer. PLoS One. 2019 Jul 11;14[7]:e0219601. doi: 10.1371/journal.pone.0219601. eCollection 2019.\*

### ABSTRACT:

BACKGROUND: Breast cancer is the most common cancer in women worldwide. Considerable funding and efforts are invested in breast cancer research and healthcare, but only a fraction of this reaches women and healthcare systems in low income countries. Surgical treatment is an essential part of breast cancer care, but access to surgery is in general very limited in low income countries such as Uganda. In this study, the previously unknown nationwide rate of breast cancer surgery was investigated.

METHODS AND FINDINGS: This was a multicenter, retrospective study, investigating breast cancer surgery in the public healthcare system in Uganda. Data were collected from operating theater registries at primary, secondary and tertiary level healthcare centres through the country, including 14 general hospitals, the 14 regional referral hospitals and the national referral hospital. Patients who underwent major surgery for breast cancer at these hospitals during 2013 and 2014 were included. The number of breast cancer procedures performed, geographical variation, level of healthcare staff performing surgery and patient characteristics were investigated. After correction for missing data, a total of 137 breast cancer procedures were performed



A group of children and a mother outside of the UCI-Fred Hutch Cancer Centre in Kampala, Uganda.

each year within the public healthcare system, corresponding to 5.7% of the breast cancer incidence in the country at that time. Most procedures (n = 161, 59.0%) were performed at the national referral hospital by qualified surgeons. Many of the patients were young; 30.1% being less than 40 years old. The proportion of male breast cancers in the study was large (6.2%).

CONCLUSIONS: The rate of breast cancer surgery in Uganda is minimal and in several parts of the country breast cancer surgery is not performed at all. More resources must be directed towards breast cancer in low income countries such as Uganda. The fact that the patients were young calls for further research, prevention and treatment specifically targeting young women in the study setting.

Jatho A, Bikaitwoha ME, Mugisha NM. Socio-culturally mediated factors and lower level of education are the main influencers of functional cervical cancer literacy among women in Mayuge, Eastern Uganda. Ecancermedicalscience. 2020 Jan 21;14:1004. doi: 10.3332/ ecancer.2020.1004. eCollection 2020.\*

BACKGROUND: Health literacy (HL) is the degree of an individual's knowledge and capacity to seek, understand and use health information to make decisions on one's health, vet information on the functional level of cervical cancer literacy in Mayuge and Uganda as a whole is lacking. We, therefore, assessed the level of functional cervical cancer literacy among women aged 18-65 years in Mayuge district in five functional HL domains; prior knowledge, oral, print, numeracy and e-health. Understanding the factors associated with cervical cancer literacy is also pertinent to cervical health communication programming, however, no study has documented this in Uganda and

particularly in Mayuge. Mayuge is a rural population-based cancer registry and one of the sites for piloting cancer control interventions in Uganda. We also assessed the factors associated with cervical cancer literacy and awareness about currently available cervical cancer preventive services.

METHODS: The study protocol was approved by the Uganda Cancer Institute research and ethic committee [UCI-REC]. In August 2017, we assessed five HL domains; cervical cancer knowledge, print literacy, oral literacy using audioclip, numeral literacy and perceived e-HL among 400 women at household levels. Correct response was scored 1 and incorrect response was scored 0 to generate the mean percentage score for each domain. The mean scores were classified as limited, basic and proficient bands based on the McCormack HL cut-offs scale for knowledge, print, oral and e-health and Weiss cut-offs in the newest vital signs (NVS) for numeracy. We used the cervical cancer literacy scores to explore the effect of selected study variables on cervical cancer literacy. We also conducted five focus group discussions (FGDs) based on the theoretical constructs of the PEN-3 model.

RESULTS: The majority (96.8%) of the participants demonstrated a limited level of cervical cancer literacy with a mean score of 42%. Women who had completed a primary level of education or lower [OR = 3.91; p = 0.044] were more likely to have limited cervical cancer literacy. The qualitative data indicated that the women had limited cervical cancer literacy coupled with limited decisional, social and financial support from their male partners with overall low locus of control. Most [92.3%] of the women were not aware of the available cervical cancer services and had no intention to screen [52.5%].

CONCLUSIONS: The women in Mayuge in general have limited cervical cancer literacy except oral HL domain. Limited cervical cancer literacy was highest among women with lower level of education and overall literacy seemed to be influenced on the higher side by socio-cultural constructs characterised by limited decisional, social and personal resources among the women with overall low locus of control. The Mayuge women further demonstrated scant knowledge about the available health services in their district and low intention to screen. Multi-strategy cervical health empowerment programme is needed to improve cervical HL using orally disseminated messages.

Mwaka AD, Mangi SP, Okuku FM. Use of traditional and complementary medicines by cancer patients at a national cancer referral facility in a low-income country. Eur J Cancer Care (Engl). 2019 Nov;28(6):e13158. doi: 10.1111/ ecc.13158. Epub 2019 Aug 23.\*

### ABSTRACT:

OBJECTIVE: The aim of this study was to describe use of traditional and complementary medicines (T&CM) and associated factors among patients with cancer.

METHODS: We conducted a cross-sectional study at the Uganda Cancer Institute [UCI] involving patients with selected solid tumours. Independent variables included age, sex, marital status, cancer site and stage. Main outcome variables were use and disclosure of use of T&CM.

RESULTS: The majority of participants were women (n = 352; 81.9%). Breast cancer [n = 312; 71.9%] was the predominant cancer type. 55.4% of participants [n =240) self-reported use of T&CM. Among them, 68.3% (140/205) reported using them to treat/cure cancer, 35.6% [72/202] for strengthening the immune system and 31.2% (63/202) for management of pain. Patients with advanced stage cancers were more likely to be users compared with those in stage one. The majority [81.9%, 195/238] of T&CM users did not disclose use to their healthcare professionals. The main reasons for nondisclosure included lack of inquiry by clinicians (79.6%, 117/147) and fear of disapproval and/or rebuke [11.6%, 17/147].

CONCLUSION: Use of T&CM by patients with cancer under biomedical care is common but often undisclosed to the healthcare professionals.

<sup>i</sup>https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 <sup>#</sup>WHO COVID-19. https://covid19.who.int/ Accessed June 23, 2020.

<sup>III</sup> Diane Mapes. Fred Hutch News Services "What happens when cancer patients get COVID-19?" May 28, 2020. https://www.fredhutch.org/en/news/centernews/2020/05/what-happens-when-cancer-patients-get-covid-19-.html Accessed June 24, 2020 .

# LOOKING AHEAD

Cancer remains an urgent global health issue. Fred Hutch has a history of driving forward innovative cancer and infectious disease research. The breakthroughs from this work should be available equitably and to ensure that Fred Hutch Global Oncology invites new collaborators and contributors to join its effort to reduce the cancer burden in Uganda and worldwide. It is especially critical to focus on the needs of cancer patients in the time of COVID-19. Global Oncology looks forward to continuing our clinical trials and research that has potential to improve the lives of cancer patients in Uganda and elsewhere.

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