SWOG Latin America Initiative
NEWSLETTER
Strengthening Relationships for Latino Cancer Patients
VOLUME ONE | ISSUE TWO | WINTER 2023

Letter from the SWOG Executive Officer for International Affairs

Dear Readers,

As we embark in the new year, we cannot help but reflect on the many accomplishments and activities of 2022. In this newsletter, we want to highlight some of the activities of the SWOG Latin America Initiative (SLAI) and our plans for the future.

During our fall SWOG group meeting in Chicago, we hosted a successful symposium and welcomed investigators from some of our sites in Latin America. Given the importance of genetic variability and diversity in cancer outcomes, we focused on genetic diversity in clinical trials from Dr. Rae and genetic predisposition in colorectal cancer and its role in health disparities—with a focus on African Americans and Latinos— from Dr. Paredes. In each symposium, we plan to learn about the activities and SWOG achievements at a SLAI site; this time we turned our attention to the Instituto Nacional de Cancerologia in Mexico, the first Latin American institution to join the initiative. In addition, we had an extraordinary round table where three research proposals by Latin American investigators were presented with an engaging discussion from members of the GI committee.

In November, in partnership with Hospital de Clínicas, Universidad de la República in Montevideo, Uruguay, we held a successful hybrid cancer control research course with Spanish-English interpretation. We were honored that many SWOG investigators and CRAB members joined us as faculty to discuss the principles of research and study design, symptom control, survivorship, social determinants of health and financial toxicity among many other topics. We are hoping that soon, some of those lectures will be widely available to SWOG members and Latin American research staff.

Chavez Mac Gregor

On the last day of the conference, a hands-on workshop took place where mentors discussed and provided input to local investigators on their research proposals. The discussions were productive, and investigators were engaged and excited to discuss their ideas and incorporate suggestions and feedback.

The SLAI team and I are grateful for the continued interest and support of this program. As we think about the future, we are hoping to soon share with you a mission statement and strategies that clearly integrate our program into SWOG's priorities and goals. This will help us to plan our path forward and ensure long-term program sustainability. Our Latin American sites and investigators face many challenges, but there are also many extraordinary opportunities to expand our reach and improve lives through cancer clinical trials and translational research beyond US borders. The mission to eradicate cancer is a collaborative, global endeavor.

Sincerely,

Mariana

Mariana Chavez Mac Gregor, MD, MS

> The mission to eradicate cancer is a collaborative, global endeavor.
>
> MARIANA CHAVEZ MAC GREGOR, MD, MS

Collaborative Group Study Status at SWOG Member Sites in Latin America

SLAI UPDATES

We are actively working on expanding the number of clinical trials relevant to our Latin American colleagues and have a list of concepts we are following for possible future international participation. Due to the additional regulatory and translation challenges of starting a trial internationally, the SLAI team encourages investigators and committees to discuss including SWOG international sites as early as possible. We are excited to grow collaborations, participate in new and relevant trials, and improve patient care!

SLAI investigator proposals

Three SLAI-investigator led proposals are making the SWOG rounds after receiving feedback in SLAI trainings 2020-2022!

Dr. Javier Retamales in Chile will be applying for an IMPACT award—with Dr. Megan Shen at the Fred Hutchinson Cancer Center as co-lead—to develop a screener for identifying areas of need in the intrapersonal, interpersonal and institutional domains for informal caregivers providing care for patients with advanced cancers in Chile.

Dr. Iván Lyra in Uruguay will be conducting an S2013 sub-study. A few questions will be incorporated into the study forms in the next revision to capture the economic impact of fixed- vs. weight-based immunotherapy dosing.

Dr. Bettina Müller in Chile has discussed and received feedback on a gastric cancer surveillance proposal (SETUP), with the prevention and epidemiology and GI committees. Dr Zev Wainberg has been working closely with her on this last committee.

SLAI-only studies

SLA-01 is a SWOG Latin America Initiative-only study that will analyze the expression of immune checkpoints in gastric cancer using samples already stored in local biobanks or laboratories. The Hope Foundation is providing support for sample shipment and SWOG biobanking, while Dr. Wistuba is providing sample analysis, free of charge. The SLAI team learned we needed to resolve some bumps in the road for studies outside of the US without federal funding. While we are still resolving some internal regulatory and logistical issues, it appears we have now received the SWOG greenlight and will be moving forward!

Current list of studies within SLAI

STUDY	ACTIVATED:	IN ACTIVATION PROCESS:
S1802	**Mexico** (first patient enrolled)	**Chile, Colombia, Uruguay**
S1827	**Mexico**	**Chile, Colombia**
S2013	**Chile** (2 pts enrolled), **Uruguay** (1 pt enrolled)	**Colombia, Mexico, Peru**
S1501		**Chile**
S1914		**Chile**
S2010		**Chile, Colombia, Mexico, Peru, Uruguay**
EA1151		**Chile, Colombia, Mexico, Uruguay**
EA8134		**Colombia, Mexico**

WANT TO LEARN MORE?

We are actively working on increasing mentorship opportunities to interested investigators at the SWOG sites in Latin America. We look forward to continuing to share exciting SLAI news in the next newsletter with the SWOG community!

To view the SWOG Latin America Symposium in full and learn more about SLAI's activities, please watch the recorded version here:

SWOG Fall 2022 Hybrid Group Meeting: SWOG Latin America Initiative Symposium - YouTube

Every project has an origin story. Most of what we at SWOG and CRAB can remember begins with **Dr. John Crowley**, CRAB co-founder and one of the early visionaries for the SLAI. Thus, it is only fitting that Dr. Crowley shares his story about how SLAI came to be. In part one, he related how collaborations in Latin America took root in SWOG, leaving readers with a notion of a future gastric prevention trial. In part two, he continues his story with the first collaborations...

The Story of the SWOG Latin America Initiative

PART TWO: THE HELICOBACTER PYLORI PHASE

Throughout 2005, Bob Greenberg, Elena Martinez, and I — with crucial input from Dave Alberts—visited possible trial sites in Latin America, held some initial meetings, and made progress on a trial design that targeted treating *Helicobacter pylori (H. pylori)*, a leading cause of gastric cancer. In winter of 2006, we held a final design conference in Antigua, Guatemala, with participation from possible collaborators from Mexico, Honduras, Nicaragua, Costa Rica, Colombia, and Chile.

In the initial grant application that Bob and I worked on in 2006-7, we planned a two-arm trial, randomizing 1400 participants to the standard 14-day treatment of three drugs or a 5-day concomitant treatment of four drugs. The NCI declined to review the trial, citing their lack of interest in studies outside of the US at that time. We needed to identify a sponsor who valued collaborations with low- and middle-income countries.

While the Bill and Melinda Gates Foundation did not generally fund cancer, they were interested in infectious diseases and low- and middle-income countries. Dr. Larry Baker, by then the SWOG chair, managed to persuade them to review our funding application. After convincing us to include a third arm and increase the sample size with no change to the budget, the Gates Foundation funded the trial in 2008. This became SWOG study S0701.

The final trial design included randomization of 1470 patients to three different arms: 1) triple therapy:

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Publications from the first *H. pylori* study:

1. Greenberg ER, Anderson GL, Morgan DR, Torres J, Chey WD, Bravo LE, Dominguez RL, Ferreccio C, Herrero R, Lazcano-Ponce EC, Meza-Montenegro MM, Peña R, Peña EM, Salazar-Martínez E, Correa P, Martínez ME, Valdivieso M, Goodman GE, Crowley JJ, Baker LH. 14-day triple, 5-day concomitant, and 10-day sequential therapies for Helicobacter pylori infection in seven Latin American sites: a randomized trial. *Lancet*. 2011 Aug 6;378(9790):507-14.
2. Morgan DR, Torres J, Sexton R, Herrero R, Salazar-Martínez E, Greenberg ER, Bravo LE, Dominguez RL, Ferreccio C, Lazcano-Ponce EC, Meza-Montenegro MM, Peña EM, Peña R, Correa P, Martínez ME, Chey WD, Valdivieso M, Anderson GL, Goodman GE, Crowley JJ, Baker LH. Risk of recurrent Helicobacter pylori infection 1 year after initial eradication therapy in 7 Latin American communities. *JAMA*. 2013 Feb 13;309(6):578-86.
3. Porras C, Nodora J, Sexton R, Ferreccio C, Jimenez S, Dominguez RL, Cook P, Anderson G, Morgan DR, Baker LH, Greenberg ER, Herrero R. Epidemiology of Helicobacter pylori infection in six Latin American countries (SWOG Trial S0701). Cancer Causes Control. 2013 Feb 24;(2):209-15.

S0701 planning meeting, Cuernavaca, Mexico, January 2009

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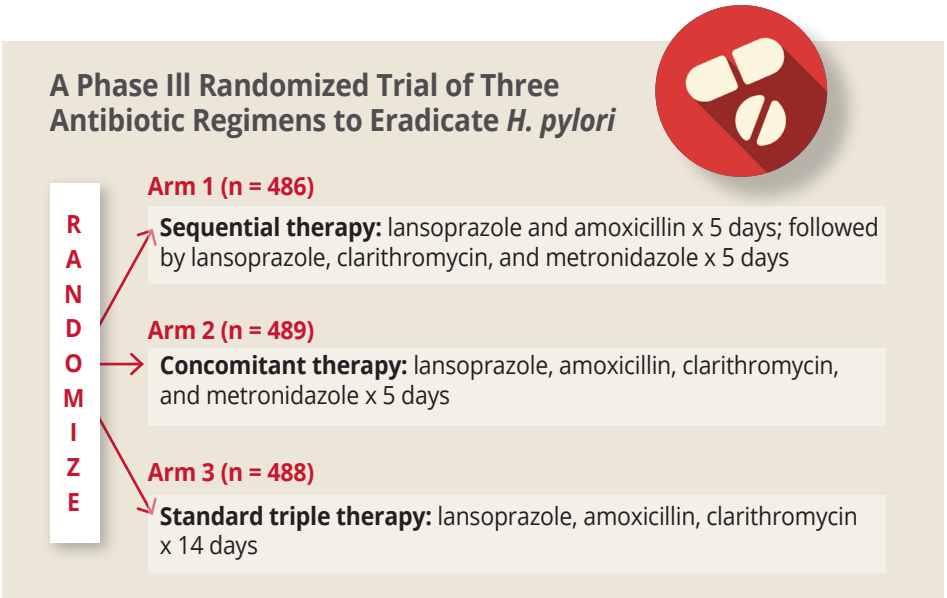
14-day lansoprazole, amoxicillin, and clarithromycin; 2) sequential: 5-day lansoprazole and amoxicillin followed by 5-day lansoprazole, clarithromycin, and metronidazole (sequential); or 3) concomitant: 5-day lansoprazole, amoxicillin, clarithromycin, and metronidazole. The primary endpoint was determined to be the *H. pylori* eradication rate at six weeks for those with infection at baseline, as measured by a urea breath test.

We identified seven performance sites in six Latin American countries: Chile, Colombia, Costa Rica, Honduras, Nicaragua, and two in Mexico. CRAB added Bob Greenberg to the payroll to provide oversight, hired Dacia Christin to organize and run the trial, and assigned Rachael Sexton as the primary statistician. CRAB developed a Spanish-language data submission program to reduce the language barrier, organized a final planning meeting in Cuernavaca, Mexico, in January 2009, and conducted a kickoff and CRA-training meeting in Antigua, Guatemala, in March 2009.

The trial was remarkably successful, with all study sites recruiting and submitting data. The first patient was enrolled in September 2009 and the last in June 2010; 1463 participants in total were enrolled. There were, of course, a multitude of challenges: the importation of urea breath test machines to seven Latin American sites from Germany, a coup in Honduras shortly before study initiation, and a centralized courier, hired to reduce paperwork in one country, who created many headaches in others. CRAB conducted monitoring visits to all sites during the trial. Final results were presented at the SWOG meeting in New Orleans in 2011.

The primary results of S0701 were published in The Lancet in 2011 and demonstrated that the six-week eradication rates justified keeping the three-drug, 14-day regimen as the standard (1). The results after one year of follow-up, published in JAMA, reinforced this conclusion (2). A descriptive paper on the epidemiology of *H. pylori* was published in 2013 (3).

Some related work regarding the prevalence of *H. pylori* in the water system of Lima, Peru, was subsequently carried out by Dr. Manuel Valdivieso, a colleague of Larry Baker's at the University of Michigan and a key player in later efforts of the SWOG Latin America Initiative.



S1316 A Case Study of a Successful SWOG Trial in Latin America

Bowel obstruction is a common problem for patients with advanced cancer and can significantly impact their quality of life. Clinicians managing these patients are often uncertain whether surgery or non-surgical management is the best treatment option. SWOG trial S1316 (link) was designed to answer this important question.

The study was activated on March 9, 2015, with an accrual goal of 220 participants. The study closed to accrual on May 15, 2020, with 221 patients registered at 30 institutions, including 56 patients to the randomized arms. Sites in Latin America were important contributors to the study, especially the randomized component.

The SLAI is proud to have participated in this study, enrolling 16 patients in this trial. Mexico's Instituto Nacional de Cancerología enrolled eight patients; Peru's Nacional de Enfermedades Neoplásicas enrolled seven patients; and Colombia's Instituto Nacional de Cancerología enrolled one patient.

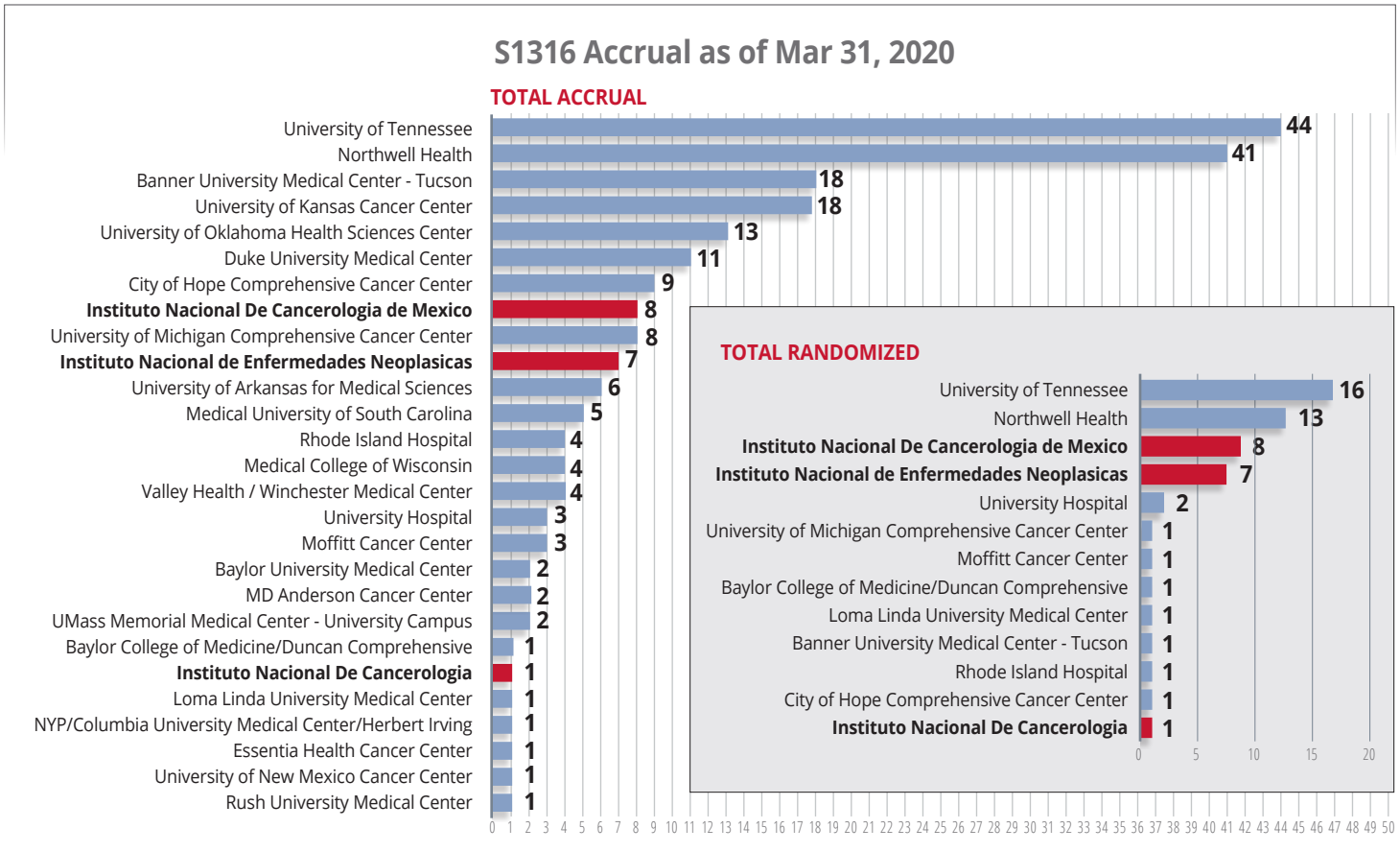
"While all of the SWOG institutes enrolling in this study did a fantastic job, the inclusion of patients from Latin American institutes improved our accrual and diversity and resulted in us completing this study faster than we otherwise would have, with greater generalizability."

DR. ROBERT KROUSE, PRINCIPAL INVESTIGATOR, PROFESSOR OF SURGERY AT THE PERELMAN SCHOOL OF MEDICINE AT THE UNIVERSITY OF PENNSYLVANIA

Dr. Robert Krouse, professor of surgery at the Perelman School of Medicine at the University of Pennsylvania, was the principal investigator.

"While all of the SWOG institutes enrolling in this study did a fantastic job, the inclusion of patients from Latin American institutes improved our accrual and diversity and resulted in us completing this study faster than we otherwise would have, with greater generalizability," said Dr. Krouse. "During the course of this study, I was able to speak with our Latin American teams multiple times and even made a trip to the region as part of the SLAI training course. These interactions left me consistently impressed with the quality of their researchers and ancillary staff as well as with their research infrastructure."

The SLAI would like to thank the three site principal investigators: Dr. Oscar Guevara (Colombia), Dr. Alberto León-Takahashi (Mexico), and Dr. Carlos Santos (Peru) for their involvement in this study as well as their teams' other clinical investigators and their lead coordinators.



Dr. Jenny Paredes, investigator at the Memorial Sloan Kettering Cancer Center and native of Colombia.

Genes and Colorectal Cancer Disparities in African American and Hispanic Patient Populations

Dr. Jenny Paredes, investigator at the Memorial Sloan Kettering Cancer Center and native of Colombia, presented a summary of her research titled "Genes and Colorectal Cancer Disparities Research in African American and Hispanic Patient Populations" at the fall SWOG Latin America Symposium. In the presentation, Dr. Paredes highlighted the discrepancies in mortality and incidence in colorectal cancer between minority populations and non-Hispanic White Americans in the United States. Many factors contribute to these discrepancies, including variations in the tumor biology and genetic composition in each population.

In earlier research at SUNY Downstate Medical Center, Dr. Paredes focused on the immunological profiles of colon tumors from African American patients. Her studies explored how differences in the genetic expression of key immunological gene and cytokine production at the systemic level may contribute to an impaired anti-tumoral response and reduced access to immunotherapies in this population as compared to non-Hispanic White Americans. Some published conclusions include observations about how colon tumors from African American patients have an increased expression of genetic coding for pro-inflammatory cytokines (such as IL-1B and IL-8), a reduction in the genetic expression of the immunotherapy targets for colon cancer, PD-L1 and CTLA4, as well as a decreased cell infiltration of cytotoxic T cells, the primary cells with anti-tumoral activity against colon cancer cells.

Dr. Paredes also shared her research experience in developing three primary colon cancer cell lines out of tumors from African American patients. These are the first in vitro models of this kind. Her research demonstrated that when these cell lines are exposed to the inflammatory cytokine IL-1B, they increase their cell proliferation and reduce their response to the chemotherapy agent 5-FU.

Finally, Dr. Paredes described her current endeavors at Memorial Sloan Kettering, where she studies the role of the intestinal microbiome and dietary fiber in the survival of bone marrow transplants for hematological malignancies. Thus far, she has observed that patients undergoing an allogenic bone marrow transplant show a reduction in three areas: their dietary fiber intake, the production of beneficial microbial metabolites, and the diversity of their intestinal microbiome. In contrast, Dr. Paredes' studies in mice models of bone marrow transplantation have shown that a fiber-rich diet results in an increase in the survival of allogenic transplantation and an augmentation in the diversity and metabolic activity of the intestinal microbiome.

Her work on cancer disparities continues. Dr. Paredes is collaborating with the SWOG member site in Mexico, the Instituto Nacional de Cancerologia, where she serves as an external advisor for studies on the microbiota and colon cancer. The SLAI has provided Dr. Paredes with the opportunity to share her work on cancer disparities, connect with other SWOG members in Latin America, and build a collaboration that has expanded her knowledge of colon cancer in Hispanic patients.

The Gastrointestinal Committee and Opportunities for SLAI Investigators

Dr. Philip Philip, SWOG gastrointestinal (GI) committee chair

Dr. Philip Philip, SWOG gastrointestinal (GI) committee chair, joined the SWOG Latin America Symposium to discuss opportunities for international participation in the SWOG GI committee. He emphasized that GI committee studies do not necessarily focus on new drugs that attract pharmaceutical interest, but they often address a patient need that would otherwise be neglected. Examples of this might be a study evaluating the effectiveness of a promising drug against the current standard of care or an intervention for a rare tumor that often inequitably affects minority and underserved populations in the US.

The GI committee is comprised of seven subcommittees: gastroesophageal, pancreatic, hepatobiliary, colon, anal and rectal, neuroendocrine, and diversity, equity, and inclusion (DEI). The DEI subcommittee focuses on writing protocols with fewer restrictions—for example, ensuring more flexible eligibility criteria. Subcommittees meet monthly on average to discuss (and re-discuss) proposals before sending vetted proposals to the GI executive committee and then the National Cancer Institute Task Force for review. The main committee meets once a month online and twice per year in person.

Dr. Philip and other GI leaders acknowledge that many SLAI sites do not always have access to drugs commercially available in the US listed in several GI protocols. In the past year, this has been a challenge for SLAI participation in protocols. Nevertheless, he encourages all interested investigators to join the GI committee and its various subcommittees, especially given that colorectal and stomach cancers are among the most common in Latin America. He told the group: "It would be nice to have more representation from SLAI [in the GI committee and subcommittees]." He stressed that committee participation is also about education; it is an opportunity to learn from other experts with different foci and to observe and participate in making proposed concepts more robust. He also offered his committee's expertise in supporting focused discussion on diseases of relevance in Latin America, such as gastric cancer.

Dr. Mauricio Cuello's Team in Uruguay Hosted the SLAI Training Course on Cancer Control

The Hospital de Clínicas Dr. Manuel Quintela and Universidad de la República hosted the SWOG Latin America Initiative (SLAI) clinical trials training course from 9 to 11 November 2022 in Montevideo, Uruguay.

Our co-partner in designing and implementing the conference was Dr. Mauricio Cuello, associate professor and academic director of the Hospital de Clínicas. SWOG group chair Dr. Charles Blanke and SWOG executive officer for international affairs Dr. Mariana Chavez MacGregor led discussions from online. SWOG investigators Drs. Mauricio Cuello and Iván Lyra partnered with SLAI project manager Dacia Christin in moderating the many guest speakers.

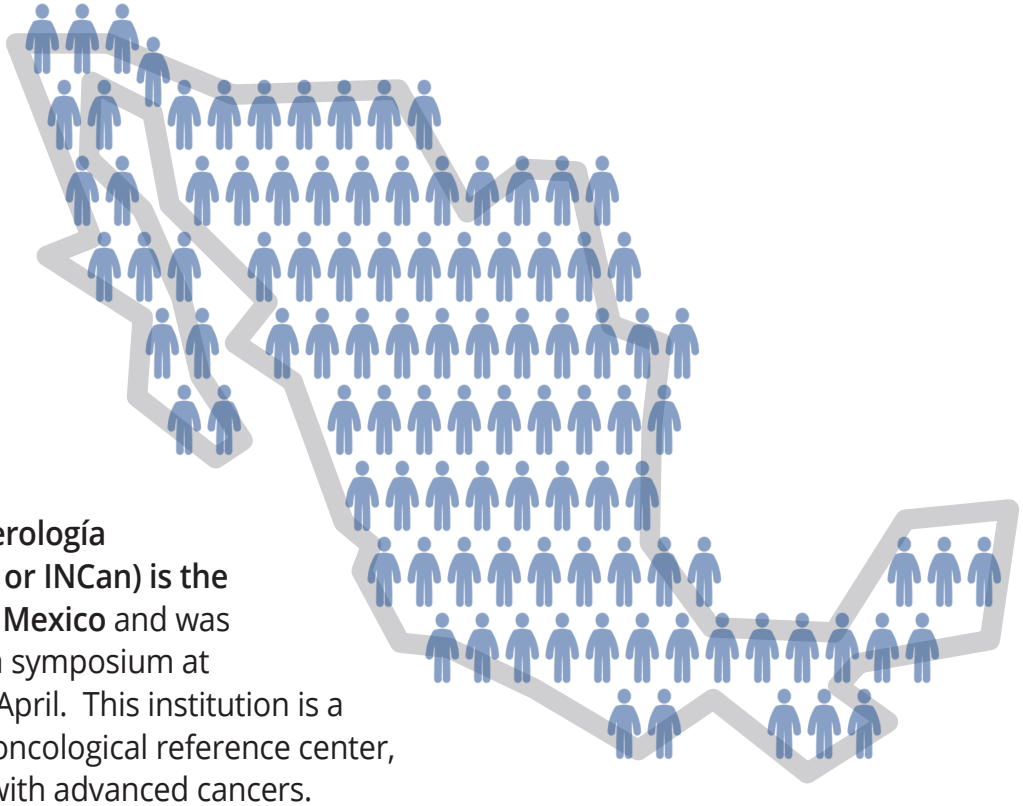
The training was entitled "Research in Cancer Control," and physician scientists and clinical operations specialists from both Montevideo and the United States presented on topics such as the cancer burden in Uruguay, Uruguayan cancer registries, the basics of biostatistics and study design, and a host of cancer-prevention related topics.

The hybrid format of the conference allowed in-person and remote translated presentations in Spanish and English, which included talks by numerous SWOG principal investigators and leading biostatisticians. The conference ended with a selected group of early-stage Uruguayan scientists presenting research proposals, which included in-person feedback from seasoned SWOG investigators Dr. Mauricio Cuello, Dr. John Crowley, Dr. Irene Tami-Maury, Dr. Lynn Henry, Ms. Rachael Sexton, and former SWOG executive officer and current ASCO chief medical officer Dr. Julie Gralow.

The conference was graciously funded by The Hope Foundation for Cancer Research via its ongoing support to the SWOG Latin America Initiative.

WANT TO LEARN MORE?

Check out the LinkedIn post with a link to the agenda here: https://www.linkedin.com/posts/cancer-research-and-biostatistics_crab-swog-latinamerica-activity-6980995192858324992-or7H



Spotlight on Mexico

Instituto Nacional de Cancerología (National Cancer Institute, or INCan) is the SWOG main member site in Mexico and was featured at the Latin America symposium at the SWOG group meeting in April. This institution is a public hospital and national oncological reference center, whose patients often arrive with advanced cancers.

Dr. Paula Cabrera has served as the SWOG principal investigator at the institute since 2009. Dr. Gabriela Mora, the head CRA, regularly shares information with CRAs at other SLAI sites from SWOG group meetings. She frequently translates SWOG protocols and amendments and distributes them, reducing time spent on translation at other SLAI sites.

Dr. David Cantú, director of research at INCan and SWOG investigator, presented INCan's activities in person at the fall group meeting. Although developed countries have been experiencing an improvement in survival for many cancers, he underlined that cancer mortality is rising in many low- and middle-income countries, Mexico notwithstanding. Dr. Cantú is excited to expand INCan's access to clinical trials like SWOG's, because this increases knowledge about the cancer landscape in Mexico, as well as safeguards patients' access to timely treatments, thereby increasing quality of care and often survival for patients. He views narrow eligibility criteria as one of the biggest barriers to patient recruitment.

How does INCan initiate a SWOG trial? First, the SWOG team at INCan identifies a study "champion" to secure protocol support from the corresponding department. This champion will actively recruit patients after protocol activation. SWOG champions exist in the breast, radiation oncology, lung, urology, gastroenterology, and gynecology departments. Even if interested, other factors like access to study drugs—whether commercial or standard of care—can be a barrier to INCan's participation in a SWOG trial.

If there is sufficient institutional interest and capacity, the protocol is translated for submission to INCan's investigational and ethics committees. These approvals take four to six weeks. If specimen shipping is mandated, COFEPRIS, the country's regulatory agency, must also provide approval, which can take a year or more and has hindered participation in more than one study.

> "INCan has a large patient population with locally advanced disease who could benefit [from these collaborative group trials]. If INCan can open three of these studies in the next few months, it would be exciting!"
>
> **DR. PAULA CABRERA,**
> SWOG PRINCIPAL INVESTIGATOR AT INSTITUTO NACIONAL DE CANCEROLOGÍA

INCan was the first Latin American institution to become a SWOG member, in 2010, and has recruited 224 participants to six collaborative group studies thus far. Among SWOG's top recruiters in 2020-2021, INCan enrolled 60 patients to S1714. Dr. Marytere Herrera will serve as study principal investigator to SLA01, a retrospective study aiming to characterize immune checkpoints in gastric cancer tissues in Latin America. Currently, S1802 and S1827 are activated at INCan, while S2010, S2013, EA8134, and EA1151 are in the process of activation. Dr. Cabrera said eagerly, "INCan has a large patient population with locally advanced disease who could benefit [from these collaborative group trials]. If INCan can open three of these studies in the next few months, it would be exciting!"