INTERNATIONAL THYROID ONCOLOGY GROUP

WINTER 2024

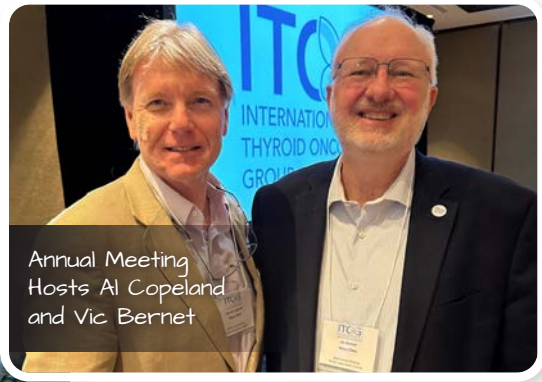
NEWSLETTER

2024 ANNUAL MEETING

THE "GO TO" ITOG 2024 ANNUAL MEETING

The International Thyroid Oncology Group (ITOG) held its annual meeting from April 10–12th, 2024, at the Sawgrass Marriott in Ponte Vedra Beach, Florida, with 112 attendees (84 in person, 28 virtual). Hosted by ITOG members Vic Bernet and Al Copland of the Mayo Clinic Jacksonville, and organized by Mabel Ryder and Christine Spitzweg, the event offered a blend of scientific exploration, collaborative discussion, and engaging social activities.

The meeting started with two engaging meetings: the Corporate Leadership Council, led by Laura Boucai, and the Board of Directors meeting, chaired by the ITOG President Greg Randolph. After subsequent afternoon committee meetings, members received an insightful tour of the key facilities at the Mayo Clinic campus in Jacksonville including the Doris and J. Wayne Weaver Simulation Center, and a model of future expansion plans. The evening concluded with a welcome reception which included food, drinks, camaraderie and a pleasant ocean breeze at the Cabana Beach Club by the Atlantic Ocean.



Annual Meeting Hosts Al Copeland and Vic Bernet

The scientific program comprised the second day of the meeting and started with keynote addresses by Dr. Lucile Adams-Campbell on health equity and Dr. Michael Story on the Mayo Clinic Florida's planned heavy ion facility and its applications to oncology. The day continued with focused sessions on medullary, differentiated, and oncocytic thyroid cancers. The evening banquet featured a historical overview of ITOG by Dwight Vicks and a heartfelt Rick Abrams Memorial Lecture by Dr. Dawn Mussallem, who shared her inspiring journey overcoming significant health and personal challenges.

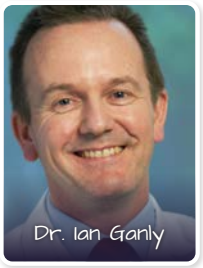
Friday's sessions began with a keynote speech on artificial intelligence by John Halamka of Mayo Clinic Rochester. Discussions then focused on cutting-edge topics that included anaplastic thyroid cancer, immunotherapies, neoadjuvant therapies, and pediatric thyroid cancer. The meeting concluded with updates on current and potential future ITOG clinical trials and a rich brainstorming discussion on strategies for ITOG growth.

The 2024 ITOG meeting was widely regarded as a success that fostered scientific innovation, collaboration, and enjoyment in the scenic Florida setting. The 2025 ITOG meeting will be at the University of Michigan hosted by ITOG members Frank Worden and Tom Giordano.

OUR MISSION

To catalyze a cure for the most challenging thyroid cancers through the collaborative efforts of our unique multidisciplinary team of leading physicians, scientists, and advocates to design, coordinate, and prioritize state-of-the-art clinical trials and correlative science.

ITOG INVESTS $100,000 IN ONCOCYTIC RESEARCH



Oncocytic cell carcinomas (previously called Hurthle cell carcinoma or HCC) is a rare form of thyroid cancer that comprises only 2% of all thyroid cancers. This cancer shows a wide spectrum of biological behavior that is determined by the extent of vascular invasion. The most aggressive form is called widely invasive oncocytic carcinoma.

Dr. Ian Ganly, surgeon scientist at Memorial Sloan Kettering Cancer Center (MSKCC), has conducted extensive research on this rare cancer. His landmark publication in **Cancer Cell** in 2018 revealed that HCC was a unique cancer characterized by recurrent somatic mutations, rare chromosomal alterations, and recurrent mitochondrial DNA mutations (Cancer Cell. 2018, Aug;34:256-270). His research aims to identify and use the genomic alterations that occur in this cancer as a target to develop new therapeutic strategies and through the creation of new immunotherapy agents.

Specifically, his research focuses on mTOR signaling, a key pathway in cancer development. Recent in vitro and in vivo experiments that used the drug Rapamycin to target the mTOR pathway confirmed that mTOR is a key driver of HCC growth and provided evidence for use of mTOR inhibitors to treat this cancer. These results were published in the journal **Molecular Cancer Therapeutics** (Molecular Cancer Therapeutics. 2022, Feb;21:382-394). In addition, the team at MSKCC have recently completed a clinical trial on 34 patients that used the combination of Everolimus, an mTOR inhibitor, with Sorafenib, a VEGF inhibitor, and found improved oncological outcomes. This trial supports the use of mTOR inhibitors as the treatment of choice for the treatment of patients with metastatic HCC.

Dr Ganly has also completed a large metabolic profiling project to determine the principal metabolic alterations in these cancers in the hope to identify a metabolic pathway that can be similarly targeted with drugs. Analysis of this project has revealed that these cancers show a switch from the metabolic pathway called the Krebs cycle to aerobic glycolysis to an increase in biosynthesis of unsaturated fatty acids, and an increase in the lysine degradation pathway as a means to produce energy. These novel findings are a major breakthrough in our understanding of this cancer and are published in the high impact journal **Science Advances** (Sci Adv. 2022;8(25): eabn9699). We are now exploring novel drugs that may inhibit these pathways to prevent cancer growth.

Furthermore, he examines and compares the immune signature of patients with HCC to patients with other cancers and other types of thyroid cancer. This important work has revealed that HCC have an immunosuppressed microenvironment that is mediated by the major loss of heterozygosity (LOH) in HCC which results from the major chromosomal alterations. The team hypothesizes that immunotherapy in combination with targeted therapy drug, such as Everolimus or Lenvatinib , will provide the best approach to exploit the immunological vulnerability of HCC. Dr. Ganly has recently published the metabolic and immunologic results in the high impact journal Science Advances (Sci Adv. 2022;8(25): eabn9699). Dr. Ganley is excited to report that a multi-institution randomized clinical trial is planned on this topic.

With the help of ITOG, Dr Ganly's lab is developing new cell lines from organoid and mouse models to study this rare cancer. Dr. Ganly's team have successfully created the first four patient derived xenograft (PDX) mouse models of HCC that have ever been created. This creation will provide a platform to study new drug treatments for HCC not only in Dr Ganly's laboratory, but also in other national and international laboratories. He has used these models already to confirm that the mTOR drug treatment is effective in treating HCC.

Table 1. ITOG Completed Studies.

Name	Number	Drug	Status
The Combination Targeted Therapy With Pembrolizumab and Lenvatinib in Progressive, Radioiodine-Refractory (RAIR) Differentiated Thyroid Cancers (DTC): A Phase II Study	NCT02973997	Pembrolizumab and Lenvatinib	Completed. Results published
An Open-Label, Single-Arm, Multicenter, Phase 2 Trial of Lenvatinib for the Treatment of Anaplastic Thyroid Cancer (ATC)	NCT02657369	Lenvatinib	Completed. Results published
Phase II Study of XL184 (Cabozantinib) in Combination With Nivolumab and Ipilimumab (CaboNivolpi) in Patients With Radioiodine-Refractory Differentiated Thyroid Cancer Whose Cancer Progressed After One Prior VEGFR-Targeted Therapy	NCT03914300	Cabozantinib, Ipilimumab, Nivolumab	Completed accrual.
Randomized Double-Blind Phase II Study of Radioactive Iodine (RAI) in Combination With Placebo or Selumetinib for the Treatment of RAI-Avid Recurrent/Metastatic Thyroid Cancers	NCT02393690	Selumetinib	Completed accrual.
Phase II Study of Cabozantinib in Patients With Radioiodine-Refractory Differentiated Thyroid Cancer Who Progressed on Prior VEGFR-Targeted Therapy	NCT01811212	Cabozantinib	Completed. Results published
A Phase 1/2 Study of Oral Selpercatinib (LOXO-292) in Patients With Advanced Solid Tumors, Including RET Fusion-Positive Solid Tumors, Medullary Thyroid Cancer, and Other Tumors With RET Activation (LIBRETTO-001)	NCT03157128	Selpercatinib	Recruiting. Some results published
Randomized Phase II Study of Sorafenib With or Without Everolimus in Patients With Radioactive Iodine Refractory Hurthle Cell Thyroid Cancer	NCT02143726	Sorafenib and Everolimus	Completed accrual.

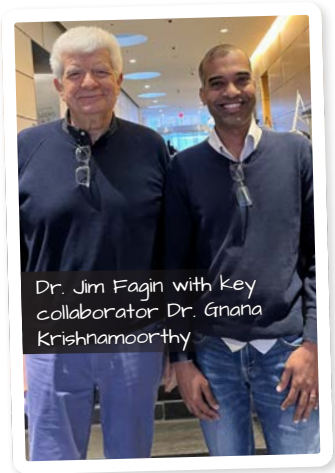
Table 2. Current ITOG Clinical Trials.

Name	Number	Drug	Status
Neoadjuvant Treatment With Selpercatinib in RET-Altered Thyroid Cancers	NCT04759911	Selpercatinib	Recruiting at MD Anderson Cancer Center and University of Michigan Health System
Restoration of Radioiodine Uptake With Selpercatinib in RET Fusion-Positive Radioiodine-Refractory Thyroid Cancer: A Phase 2 Study Performed in Collaboration With the International Thyroid Oncology Group (ITOG)	NCT05668962	Selpercatinib	Recruiting at Massachusetts General Hospital.
A Phase 1 Trial of concurrent Intensity Modulated Radiation Therapy (IMRT) and Dabrafenib/ Trametinib in BRAF Mutated Anaplastic or Poorly Differentiated Thyroid Cancer	COH 21308	Dabrafenib, Trametinib, and Intensity Modulated Radiation Therapy	Recruiting at City of Hope. Soon to open at Ohio State University and MD Anderson Cancer Center.

Table 3. Current ITOG Registries.

Multi-Institutional Medullary Thyroid Cancer MTC Collaborative Registry	Collect MTC patient clinical data into REDCap repository for analysis.	Collection occurring at four ITOG member institutions.
Acquired Resistance Registry	Collect information on patients that progress on standard kinase inhibitor therapy into a REDCap repository for analysis.	Based at Royal North Shore in Australia with 10 ITOG member institutions active.

ITOG SELECTS JAMES A. FAGIN, MD FOR THE ROBERT F. GAGEL ITOG DISCOVERY AWARD


Dr. Jim Fagin with key collaborator Dr. Gnana Krishnamoorthy

The Robert F. Gagel ITOG Discovery Award is a $100,000 award that is granted over a two-year period for research and innovation with direct and tangible translational implications toward developing novel or improved treatments for thyroid cancer. Dr. Jim Fagin was chosen to receive The Gagel Award for his submission "Leveraging therapeutic vulnerabilities induced by cGAS-STING activation in ATC." The overarching goal of his project is to co-opt a pathway that plays a fundamental role in coordinating how our body fights infections to boost the immune response against anaplastic thyroid cancers (ATC), the most aggressive endocrine cancer.

In acceptance of the award, Dr. Fagin stated: "It is a particularly meaningful one to me for several reasons. First, because it honors Bob Gagel, a pioneer in the field of endocrine oncology and without him ITOG would not exist. Second, because it allows my group to continue to make inroads in understanding mechanisms of response and resistance to therapies for the most lethal types of thyroid cancer. I cannot overemphasize the gratification that my team and I feel when we make discoveries that are incorporated into new treatments for cancer patients. We have been incredibly fortunate to have had that experience, and it definitely keeps us motivated. Finally, because ITOG and the conference that it sponsors has become the most exciting thyroid cancer venue by far that brings translational scientists and clinical trialists together to find new treatments for our patients in a collaborative spirit. Having idealistic patient advocates by our side keeps our focus on the prize."

One of the first defense mechanisms against infections by viruses or bacteria is triggered by the presence of DNA in the cytoplasm. In normal cells, DNA is present only in the nucleus. When foreign DNA from a microorganism enters the cell cytoplasm, there is a DNA sensor called cGAS, which in turn generates a messenger molecule called cGAMP. cGAMP then activates a protein called stimulator of interferon genes (STING), and interferon is a potent stimulator of the immune response and recruits immune cells to the site of infection.

Many cancer types, including ATC, have mutations in genes that disrupt the integrity of DNA and the ability to repair damaged DNA. When that happens, DNA can sometimes be present in the cytoplasm in the form of extrachromosomal DNA. The cancer cell responds to this as if it were being attacked by a microorganism, and illegitimately triggers the cGAS-STING pathway that generates an immune response that exhausts the body's ability to combat cancer cells. We have evidence that oncogene-targeted therapies that reactivate the cGAS-STING pathway target ATC cancer. We believe that further understanding of these mechanisms will enable us to create new therapies to create durable treatments for this devastating disease.

ITOG INCREASES COLLABORATION WITH EUROPE

We are pleased to report that our relationship with the European Thyroid Association (ETA) has become closer thanks to the excellent work of Laura Fugazzola and Lindsay Bischoff. As a result, ITOG is listed as an ETA-affiliated society on their website and has been invited to create an ITOG-ETA Symposium at the ETA's 2026 Annual Meeting in Porto, Portugal. In addition, Dr. Ian Ganly represented ITOG at the 2024 ETA Annual Meeting in Athens, Greece from September 7th-10th where he delivered his lecture entitled, "The neoantigen landscape and tumor immune microenvironment of oncocytic cell cancer." In his talk Ian explained his research on the immune system and how it related to aggressive forms of oncocytic thyroid cancer. We are grateful for his tireless efforts in research against these advanced cancers and his contribution to this international meeting, and look forward to future collaboration with the ETA.

ITOG NEW MEMBERS 2024

Amy Chen, M.D.
Surgical Oncology
Emory University

Aime Franco, Ph.D.
Endocrinology
University of Pennsylvania,
Perelman School of Medicine

Ian Ganly, M.D., Ph.D
Surgical Oncology
Memorial Sloan-Kettering Cancer Center

Dana Hartl, M.D., Ph.D.
Surgical Oncology
Gustave Roussy

Megan Haymart, M.D.
Endocrinology
University of Michigan

Priyanka Iyer, M.B.B.S.
Endocrinology
University of Texas MD Anderson

Joanna Klubo-Gwiezdzinska, M.D., Ph.D., M.H.Sc.
Endocrinology and Clinical Research
NIH

Anupam Kotwal, M.D.
Endocrinology
University of Nebraska School of Medicine

Stephan Lai, M.D., Ph.D.
Surgical Oncology
The University of Texas MD Anderson

Inigo Landa, Ph.D.
Basic Science
Harvard Brigham and Women's Hospital

Wayne Miles, Ph.D.
Basic Science
Ohio State University

Irene Min, M.D.
Endocrinology, Radiology
Houston Methodist

Fabian Pitoia, M.D., Ph.D.
Endocrinology
University of Buenos Aires

Nikita Pozdeyev, M.D.
Endocrinology
University of Colorado School of Medicine

Cristina Romei, Ph.D.
Endocrinology
University of Pisa

Mara Roth, M.D.
Endocrinology
University of Washington School of Medicine

Marika Russell, M.D.
Surgical Oncology
Massachusetts Eye and Ear

Fernanda Vaisman, M.D.
Endocrinology
Brazilian National Cancer Institute

Jonathan Wadsley, MA, MRCP, FRCR
Clinical Oncology
Weston Park Cancer Centre, UK

Bo Wang, Ph.D.
Neuroscience Endocrinology
Fujian Medical University

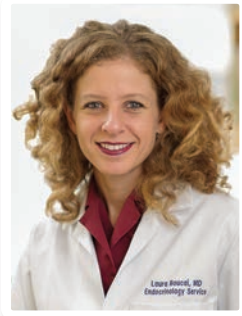
Jennifer Wang, M.D., Ph.D.
Surgical Oncology
The University of Texas MD Anderson


Mabel Ryder welcomes new member Inigo Landa

NEW OFFICERS ELECTED TO THREE-YEAR TERMS

We are pleased to announce that the ITOG Board unanimously voted to re-elect President Greg Randolph to a second term. His outstanding leadership and incredible energy has grown the size of ITOG, increased core initiatives and expanded its reach. We are thrilled to have Greg continue his great work. Our utmost thanks to outgoing Secretary Mabel Ryder and Protocol Chair Bryan Haugen for their devotion and insight over the past 3 years. ITOG is better because of them.

In addition to President Randolph, the ITOG Board elected Laura Boucai as the new Secretary and Frank Worden as the new Protocol Chair. The Board also voted to expand the Executive Committee to include the Chair of the Correlative Science Committee, Alan Ho. Dwight Vicks will continue as Chief Financial Officer.



LAURA BOUCAI

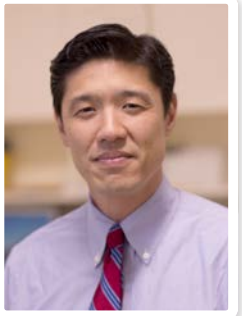
Secretary

Dr. Laura Boucai received her medical degree from Universidad de Buenos Aires, Facultad de Medicina, Argentina, in 2002. She completed her internal medicine residency at Weill Cornell Medical Center and her endocrinology fellowship at Albert Einstein College of Medicine in New York where she joined the faculty after training. In 2012, Dr. Boucai was recruited as a faculty member to join a multidisciplinary team with expertise in thyroid cancer at the Memorial Sloan Kettering Cancer Center. She is currently an associate member at Memorial Sloan Kettering Cancer Center in New York and an associate professor of clinical medicine at Weill Cornell Medical College. Her research is focused on thyroid cancer biology, where she studies the genomic and transcriptomic landscape of thyroid cancer in an attempt to find new therapeutic strategies for the most advanced disease.

FRANCIS WORDEN

Protocol Chair

Dr. Francis Worden received his medical degree from the Indiana University School of Medicine in 1993. Prior to attending medical school, he worked as a registered pharmacist at a large community hospital in Indianapolis. In 1997, Dr. Worden completed a combined residency in internal medicine and pediatrics at the Detroit Medical Center and completed a medical oncology/hematology fellowship at the University of Michigan. In July of 2000, Dr. Worden joined the faculty at the University of Michigan Rogel Cancer Center, where he works as a clinical investigator with the multidisciplinary head and neck oncology team and the multidisciplinary lung cancer team. Dr. Worden's research interests include organ preservation in head and neck cancer and endocrine oncology.



ALAN L. HO

Correlative Science Committee Chair

Dr. Alan L. Ho received his combined MD and PhD from Washington University at St. Louis School of Medicine in 2003. He completed his internal medicine residency training at Weill Cornell Medical Center and his medical oncology fellowship at Memorial Sloan Kettering Cancer Center (MSKCC). He joined the MSKCC head and neck medical oncology service in 2009 and was recently appointed their chief of service. Furthermore, he is a translational clinical researcher who focuses on developmental therapeutics for head and neck. He has built translational research programs in head and neck squamous cell carcinomas, salivary gland cancers, and thyroid cancers. Within MSKCC, he serves as the chair of the Investigational New Drug (IND) committee. In addition to serving as an ITOG Board member, he co-leads the Head and Neck Working Group in the Experimental Therapeutics and Rare Tumor Committee of the Alliance cooperative group, chairs the head and neck subsection of the International Clinical Trials in Rare Cancers Initiative, and serves as a member of the NCI Head and Neck Steering Committee.

YOU CAN HELP

DONATE NOW

We are grateful for your generosity and ask you to continue to help us catalyze a cure for thyroid cancer by donating at itog.org or contacting Dwight Vicks at dwight@itog.org.

When Jean Vicks learned of her metastatic thyroid cancer, she turned her fear into action. She inspired leading medical experts to create the organization known as the International Thyroid Oncology Group.