

INTERNATIONAL THYROID ONCOLOGY GROUP

Winter 2020

Dr. Robert Gagel Receives Jean Vicks Inspiration Award

During the ITOG General Membership meeting on July 30th, 2020, the Board of Directors was pleased to present Dr. Robert Gagel with the Jean Vicks Inspiration Award for his significant contributions to the International Thyroid Oncology Group (ITOG). Named for co-founder Dwight Vicks' wife Jean, who bravely faced medullary thyroid cancer for thirteen years, the Jean Vicks Inspiration Award honors outstanding ITOG members for their commitment and contribution to the organization.

Robert Gagel, MD, is a professor of medicine at the University of Texas MD Anderson Cancer Center, and an adjunct professor in the Departments of Medicine and Cell Biology at Baylor College of Medicine. Dr. Gagel's research on the development of strategies to prevent and treat medullary thyroid carcinoma has been trailblazing over his 40+ year career.

As one of the founders of ITOG, Dr. Gagel, along with Barry Nelkin, invited the original attendees to the first ITOG meeting at the Multiple Endocrine Neoplasia (MEN) Conference in 2003. Dr. Gagel was elected the first ITOG chair and worked diligently to launch the organization, establish the organizational structure and recruit the best talent. His kind and respectful demeanor provided outstanding leadership that was vital in establishing the collaborative culture essential to the mission of ITOG. Thus, it was only fitting that the \$100,000 grant available to ITOG members for compelling research that will lead to better thyroid cancer treatments was named The Robert F. Gagel Discovery Award.

Currently, as the principal investigator at the Gagel Laboratory in the MD Anderson Cancer Center, Dr. Gagel studies the molecular mechanisms causative for hereditary and sporadic medullary thyroid cancer using in vitro cell culture models of medullary thyroid carcinoma, elucidating the role of the RET proto-oncogene in the development of medullary thyroid carcinoma. His research team has also characterized the role of the calcium-sensing receptor in human disease and defined mechanisms for alternative RNA processing of the calcitonin gene. More recently, they demonstrated that RET, upon activation, is translocated to the nucleus where it interacts with the transcription factor ATF4 which, in turn, leads to its downregulation and an inhibition of apoptosis. It is now clear that this is the major mechanism by which RET activation leads to cellular transformation. Dr. Gagel's current research projects focus on the role of the RET proto-oncogene in the genesis of bone metastasis in medullary thyroid carcinoma. Future goals for his laboratory include the identification of other nuclear factors that interact with RET and whether this information can be used therapeutically to treat medullary thyroid carcinoma.

"I'm honored to be working with such a wonderful group of people," Dr. Gagel said upon receiving the award. "We have come a long way, but there is still so much more to be done."

Dr. Gagel is only the third recipient of the Jean Vicks Inspiration Award. The first was awarded to Elizabeth and Michael Ruane in 2014 and the second to Dr. Samuel Wells in 2017.



Former ITOG Chair Lori Wirth, ITOG Chair Manisha Shah, Jean Vicks Inspiration Award winner Bob Gagel, and ITOG Board member Andrew Gianoukakis



Jean Vicks, one of the inspirations for ITOG

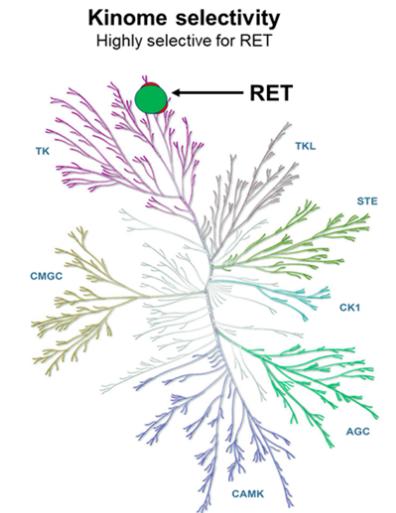
ITOG's Collaborative Research Leading to Major Breakthrough in Treatment of Thyroid Cancer

It is with great pleasure to share that Dr. Lori Wirth, Dr. Eric Sherman, Dr. Bruce Robinson et al. (NEJM, Aug 27 2020) found that a phase 1-2 trial of selpercatinib, a selective RET-inhibitor, showed evident and durable efficacy in the treatment of patients with RET-altered thyroid cancer. Several ITOG members across the world have made significant contributions to this multicenter pivotal trial that led to FDA approval of selpercatinib in patients with RET-altered thyroid cancer in May 2020.

The RET proto-oncogene encodes a transmembrane tyrosine kinase receptor crucial for intracellular growth signaling, mutations to which enable constitutive receptor activity and subsequent tumor growth and metastasis. Although 70% of medullary thyroid cancers are positive for RET mutations, there were no selective RET kinase inhibitors approved by the FDA until now. Furthermore, the efficacy of approved multi-targeted kinase inhibitors is limited by their systemic adverse effects, which is attributed to their non-RET targets. These are two of many challenges that illustrate the need for a selective RET kinase inhibitor.

In both RET-mutant medullary and RET fusion-positive thyroid cancer patients with and without previous treatment of multitargeted kinase inhibitors, vandetanib or cabozantinib, selpercatinib (pictured) showed marked efficacy with little toxicity. Specifically, patients previously treated had a response rate of 69% and 1-year progression free survival of 82%, and patients not previously treated had a response of 73% and 92%, respectively. Selpercatinib shows promise in ITOG's collaborative efforts to develop and conduct safe and effective therapies for thyroid cancer.

As Dr. Manisha Shah, Chair of ITOG, expressed, "The timeline of three years from the first patient in clinical trial to the FDA approval of this cancer drug is unprecedented in the history of drug development for thyroid cancer."



ITOG Board of Directors Vote to Move Forward on Tumor Registry Partnership and Development

A strength of ITOG is its multidisciplinary team members' routine care of patients with advanced and rare malignancies. Gathering information about these populations and combining it into a central resource in the form of a patient registry would allow our organization to analyze these diseases on a larger scale. The primary objective of an ITOG registry would be to characterize the natural history of and current practice patterns for the care of patients with advanced thyroid malignancies, with an emphasis on specific driver mutations, to allow for further critical analysis of this cohort and for consideration in creating future trials. A registry taskforce was created for the purpose of determining the feasibility of developing such a registry and recently reported its findings and recommendations to the ITOG Board of Directors. Additionally, the taskforce held a plenary session at the 2019 ITOG Annual Meeting in New York to further explore some of the salient issues surrounding registry development with the membership.



ITOG Board member Nifa Busaidy with Tumor Registry Co-Chairs Libby Grubbs and Julie Ann Sosa

Initial taskforce investigations included working with a third-party vendor for creation and management of the registry, both with nonprofit groups such as AACR and in the private sector. These approaches proved cost prohibitive. Partnering with an ITOG member-affiliated institution to create a novel registry or join an existing registry was identified as more feasible. Participating in a current registry managed by one of its members allows ITOG to utilize preexisting platforms and avoid the costs and time burden associated with a build from the ground up.

The BOD voted on moving forward with partnering with a current registry and has chosen, as an initial effort, to work with the Medullary Thyroid Cancer (MTC) Registry managed by two of its member institutions, The University of Texas MD Anderson Cancer Center and The University of California-San Francisco. The registry, helmed by ITOG members Drs. Elizabeth Grubbs and Julie Ann Sosa, is in its eighth year and has yielded 22 publications and generated funding including an FDA RO1 and SPORE grant, as well as industry support. Opportunities for ITOG will include utilization of curated data from the registry to inform scholarship or clinical trial design and the ability to build out and foster collaboration among ITOG institutions and investigators. Initially, the registry will work with an ITOG Registry Oversight Committee and partner with 2-3 member institutions within the first two years with a minimum requirement of each institution providing >25 registrants per year. ITOG will support its member institutions' registry contributions.

Trial Update

OSU 17277: Clinical Trial of Dabrafenib, Trametinib, and Radiation Therapy in Treating Patients with BRAF Mutated Anaplastic Thyroid Cancer

Based on laboratory research conducted at The Ohio State University, Dr. Manisha H. Shah has launched an early phase clinical trial of combination therapy—dabrafenib, trametinib, and intensity modulated radiation therapy (IMRT)—in patients with BRAF mutated anaplastic thyroid cancer (ATC). Given the rarity of ATC, this trial is nearly impossible to conduct at a single center, and ITOG's role in the design and implementation of this multicenter trial is vital. MD Anderson Cancer Center and Memorial Sloan Kettering Cancer Center are set to open this trial that is now ongoing at The Ohio State University. This trial is also supported by R01 grant of the National Cancer Institute and has potential to develop a new safe and effective therapy for patients with this rare cancer. <https://clinicaltrials.gov/ct2/show/NCT03975231>



Dr. Manisha H. Shah

NCI 10240: Phase II Study of Cabozantinib in combination with Nivolumab and Ipilimumab (CaboNivoIpi) in Patients with Radioiodine-Refractory Differentiated Thyroid Cancer

To build upon the success observed during the 1st ITOG clinical trial (Dr. Shah and team published it in *Journal of Clinical Oncology* in 2017), this trial is developed to examine if triple combination therapy—immunotherapy and multikinase inhibitor—will demonstrate high effectiveness and safety for patients with advanced differentiated thyroid cancer (DTC) whose cancer progressed while on standard of care therapy. Led by ITOG investigator Dr. Bhavana Konda at The Ohio State University, this trial is open at several ITOG centers. ITOG is catalyzing the conduction and completion of this trial, which is desperately needed for patients with DTC. This trial is also supported by the UM1 grant of the National Cancer Institute. <https://clinicaltrials.gov/ct2/results?cond=&term=NCT03914300&cntry=&state=&city=&dist=>



Dr. Bhavana Konda

Dr. Bryan Haugen Shares Preliminary Results

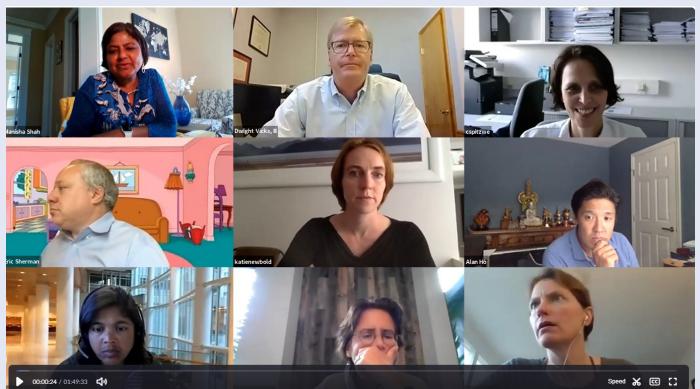
As a leader for conducting investigator-initiated ITOG-ACCRU 1504 clinical trial examining role of combination of immunotherapy and tyrosine kinase inhibitor therapy in differentiated thyroid cancer, Dr. Bryan Haugen presented preliminary results of this trial at the international conferences American Society of Clinical Oncology [ASCO] Annual Meeting and European Society for Medical Oncology [ESMO] Annual Virtual Congress) in 2020. ITOG philanthropy funded correlative science studies for this trial.



Dr. Bryan Haugen

ITOG Goes Virtual

The 2020 ITOG Annual Meeting, which was scheduled to be hosted by ITOG Members Sophie Leboulleux and Martin Schlumberger in Paris in May, was cancelled due to the COVID-19 pandemic. Drs. Leboulleux and Schlumberger put together an exciting agenda featuring ITOG members and prominent guests from around the world. Although the rapid development of COVID-19 did not provide adequate time to convert to a virtual annual meeting, ITOG members collaborate virtually on a regular basis to continue the important work of ITOG and prepare for the virtual 2021 Annual Meeting. ITOG plans to re-establish in-person meetings as soon as it is determined safe to do so.



ITOG Elects New Board Members

Andrew Gianoukakis

Professor of Medicine in the Geffen School of Medicine at UCLA, Dr. Gianoukakis is a clinician, educator and clinical researcher who serves as program director of the Harbor-UCLA Endocrinology and Metabolism training program. Dr. Gianoukakis heads the thyroid unit at Harbor-UCLA Medical Center and directs the Thyroid Nodule Aspiration and Thyroid Oncology clinics, as well as directs a research team performing phase II-III clinical thyroid cancer trials and studies. He has been a member of the International Thyroid Oncology Group (ITOG) since 2012 and has served as chair of ITOG's Membership Committee since 2013. Dr. Gianoukakis was a co-host of the 2018 ITOG Annual Meeting. Additionally, Dr. Gianoukakis serves as secretary of the Southern California Thyroid Cancer Consortium (SCThyCC), and as an advisory board member of the National Graves' Disease and Thyroid Foundation (GDATF) and the Thyroid Cancer Survivors Association (ThyCa).



Andrew Gianoukakis, MD
Endocrinology
University of California Los Angeles
Hospital: Harbor-UCLA

Yariv Houvras

Associate Professor of Research in Surgery at Weill Cornell Medicine, Dr. Houvras is a physician-scientist with a clinical focus on treating patients with advanced thyroid cancers. He completed training in Hematology and Medical Oncology at Dana Farber Cancer Institute and joined the faculty at Weill Cornell Medical College in 2011. Dr. Houvras participated in clinical trials for tyrosine kinase inhibitor (TKI) therapy for patients with advanced thyroid cancer. He leads a cancer genetics lab at Weill Cornell that uses a model organism, zebrafish, to identify new drugs and drug targets. Dr. Houvras was the first ITOG member to win the prestigious Robert F. Gagel Discovery Award, a \$100,000 grant to facilitate bringing research to treatments in thyroid cancer. The first chair of the ITOG Website Committee, this is Dr. Houvras' second time serving on the ITOG Board.



Yariv Houvras, MD Medical Oncology
Weill Cornell Medical College

Kate Newbold

Dr. Kate Newbold is a consultant oncologist at the Royal Marsden NHS in London, England. Dr. Newbold manages thyroid cancer from early to advanced stages administering radioiodine, systemic therapies and external beam radiotherapy. She has been involved in clinical research for 20 years. Dr. Newbold is fully integrated into the national and European thyroid cancer research networks (NCRI, ETA-CRN and EORTC endocrine tumor working group).



Kate Newbold, MD Medical Oncology
The Royal Marsden NHS
Foundation Trust

Mabel Ryder

An endocrinologist at the Mayo Clinic in Rochester, Minnesota, Dr. Ryder has clinical expertise in endocrine oncology as well as prior laboratory experience in advanced thyroid cancer. Her depth and range of expertise will help facilitate ITOG's mission to improve the treatment of patients with advanced disease through collaborative efforts. Dr. Ryder has been a strong advocate for clinical trials through ITOG and has supported patient enrollment, serving on committees for protocol and trial development. Dr. Ryder's prior work on tumor microenvironment and immune-based therapies will help to develop and promote similar novel trials through ITOG's efforts.



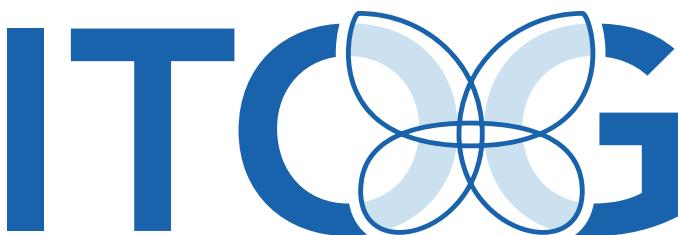
Mabel Ryder, MD Endocrinology
Mayo Clinic (Rochester)

Christine Spitzweg

Dr. Spitzweg is a professor of medicine and endocrinology at the Department of Internal Medicine IV, University Hospital Munich, Ludwigs-Maximilians-University (LMU) in Munich, Germany. After completing her training in Munich she spent three years at the Mayo Clinic in Rochester, MN, as a postdoctoral research fellow. She is a clinical scientist with a special focus on advanced thyroid cancer and endocrine oncology. Her basic research aims at investigation of expression/regulation of the sodium iodide symporter (NIS) in and outside of the thyroid gland, the role of NIS as a novel theragnostic gene in the management of non-thyroidal and thyroidal cancer, as well as thyroid hormone regulation of mesenchymal stem cell biology and angiogenesis. She has chaired the research committee of the American Thyroid Association (2011-2013) and was a member of the Board of Directors of the ATA (2014-2018). She has been a member of ITOG since 2017 and serves on the thyroid cancer registry committee and the membership committee.



Christine Spitzweg, MD Endocrinology
University Hospital Munich,
Ludwig-Maximilians



YOU CAN HELP.

ITOG is a 501(c)-3 corporation funded by philanthropy. You can help catalyze a cure for thyroid cancer by donating at www.itog.org/donation or contacting Dwight Vicks at dwight@itog.org.