MARCH 2021

The Life Raft Group is pleased to present the members of the LRG 2021 Medical Advisory Board. Members will play a crucial role in offering expert opinions on research and medical developments. Comprised of experts from leading academic and medical institutions around the world, the goal of the Medical Advisory Board is to share scientific and research expertise to provide strategic direction on LRG initiatives that ensure the overall survival and well-being of gastrointestinal stromal tumor (GIST) patients.

Our distinguished members are profiled in this issue, followed by their responses to two timely questions that affect the treatment of GIST patients.

The Life Raft Group Medical Advisory Board Profiles

Dr. Suzanne George
Dana-Farber Cancer Institute
Boston, Massachusetts, USA

Suzanne George, MD, is the Clinical Research Director of the Center for Sarcoma and Bone Oncology at Dana-Farber Cancer Institute and an Associate Professor of Medicine at Harvard Medical School. She also serves as senior physician to the affiliate staff in the Division of Adult Oncology at Brigham and Women's Hospital.

Dr. George’s areas of expertise include soft tissue sarcoma, bone sarcomas, and gastrointestinal stromal tumor (GIST), with a specific focus on sarcoma management and clinical investigation of developmental therapeutics. In her current role, she works extensively with a multidisciplinary team, treating and providing consultation to many patients with sarcoma from all over the world. She also is actively involved in clinical research at Dana-Farber Cancer Institute, working with a team of investigators to develop and execute new clinical trials focusing on therapy for metastatic soft tissue sarcoma.

Dr. George holds memberships with several professional organizations, including the Connective Tissue Oncology Society, the American Society of Clinical Oncology, the American College of Surgical Oncology, and the World Sarcoma Network. She also serves on the scientific advisory boards for the Desmoid Tumor Research Foundation and Leiomyosarcoma Direct Research. Additionally, she is Vice-Chair of the Alliance for Clinical Trials in Oncology and an editorial board member for Journal of Clinical Oncology.

Dr. George also is involved in several international initiatives, including the Gynecological Sarcoma Group, a collaboration between the National Cancer Institute, the European Organization for Research and Treatment of Cancer, and the United Kingdom International Clinic Trials in Rare Cancer Initiative.

Dr. George’s profile continues on next page
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She also is a contributing member to the Sarcoma and GIST Scoring Committee, an international expert panel established to develop guidelines for the definition of survival endpoints in clinical trials.

Dr. George is a member of the NCCN Soft Tissue Sarcoma Panel and serves as a liaison to the NCCN Cervical/Uterine Cancer Panel. She received her medical degree from the University of Massachusetts Medical School. She completed an internship at University of North Carolina Hospitals and a residency in internal medicine at Tufts New England Medical Center. She went on to complete a hematology and oncology fellowship at New England Medical Center.

Dr. Michael C. Heinrich
Knight Cancer Institute
Oregon Health & Science University
School of Medicine
Portland, Oregon, USA

Dr. Michael Heinrich is a medical oncologist at the Knight Cancer Institute and Professor of Medicine and Cell/Developmental Biology at Oregon Health and Science (OHSU) School of Medicine. His research, like much of the work at the Knight Cancer Institute, revolves around a basic, yet complex premise. You have to understand what is broken in order to fix it. That’s why Dr. Heinrich is intently focused on identifying the molecular targets that cause cancer, which is essential to the development of better and less toxic therapies. He is recognized internationally for groundbreaking research discoveries that have improved care for patients with gastrointestinal stromal tumors, and his research has implications for many types of cancer.

Dr. Heinrich's research includes both preclinical identification of novel molecular targets and testing of new agents in the laboratory and the clinic. This includes both genomics research using high-throughput genotyping to identify oncogenic mutations and testing of new compounds in cellular and biochemical assays. His laboratory is particularly expert in the analysis of inhibitors of oncogenic receptor tyrosine kinases such as KIT, PDGFRA and FLT3.

Dr. Heinrich earned his medical degree in 1984 from Johns Hopkins University School of Medicine in Baltimore. He completed both his residency training and hematology and medical oncology fellowship at OHSU.

Dr. Sameer Rastogi
All India Institute of Medical Services
New Delhi, India

Dr. Sameer Rastogi is a faculty member in the Department of Medical Oncology at All India institute of Medical Sciences (AIIMS), New Delhi, a leading tertiary care center in North India. Currently, he is running a dedicated sarcoma and gastrointestinal stromal tumor (GIST) medical oncology clinic in AIIMS New Delhi. His other interests are endocrine cancers and melanoma.

Dr. Rastogi’s profile continued on next page
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Over the years he has gained extensive experience with GIST and has many GIST patients on treatment currently. His areas of interest are mutational testing in GIST, wildtype GIST and newer medicines including avapritinib and ripretinib. A group of patients who received treatment from him have formed a sarcoma support group called Sachin Sarcoma Society which is currently one of the leading support groups for sarcoma/GIST patients in India.

Dr. Rastogi did his Medical Oncology fellowship at Tata Memorial Centre, Mumbai and has various publications to his credit including articles in prestigious journals. He has received various international awards like the Young investigator Award from SIOP (International Society of Pediatric Oncology) and the Clinical Oncology Society of Australia (COSA) Asia Pacific award.

Dr. Peter Reichardt
Helios Klinikum Berlin-Buch
Berlin, Germany

Dr. Peter Reichardt is Assistant Professor and Head of the Department of Oncology and Palliative Care at the Helios Klinikum Berlin-Buch in Berlin, Germany, and is the Director of the Cancer Center Berlin-Buch and the Sarcoma Center Berlin-Brandenburg.

Dr. Reichardt has led and conducted multiple clinical trials in bone sarcomas, soft tissue sarcomas and gastrointestinal stromal tumours in the adjuvant, advanced, and refractory settings.

Dr. Reichardt is a co-author of the current European Society for Medical Oncology (ESMO) guidelines for the management of GIST, soft tissue and bone sarcomas and a member of the ESMO Sarcoma Faculty. He is Chairman of the German Sarcoma Foundation, a member of the Medical Board of the MAX Foundation, and a member of the Life Raft Group’s Global GIST Advisory Team. Dr. Reichardt has contributed to numerous publications on soft tissue sarcoma and GIST management in leading oncology journals.

He trained in internal medicine and haematology/oncology at the University of Heidelberg and at the MD Anderson Cancer Center, Houston, TX, USA. From 1992 to 2007, he was a consultant at the Charité University Hospital in Berlin.

Dr. Gary Schwartz
Herbert Irving Comprehensive Cancer Center
Columbia University
New York City, NY, USA

Dr. Schwartz is a board-certified medical oncologist and internist and chief of Columbia University Medical Center’s Division of Hematology and Oncology.

He is actively involved in translational and clinical research. The lab, which he directs, focuses on the identification of new targeted agents for cancer therapy, especially in the treatment of sarcoma and melanoma. However, these agents are not disease specific and hold promise in the treatment of all solid-tumor malignancies. These laboratory studies
Dr. Jason Sicklick is an NIH and FDA R01 funded investigator, Professor of Surgery, Executive Vice Chair of Research in the Department of Surgery, and Co-Leader of the Sarcoma Disease Team at Moores Cancer Center UC San Diego Health. He is a board-certified general surgeon and surgical oncologist specializing in the treatment of complex retroperitoneal and abdominal sarcomas, including gastrointestinal stromal tumors (GIST), as well as hepatobiliary oncology. In 2016, Dr. Sicklick was named the GIST Clinician of the Year by the Life Raft Group, the largest GIST patient advocacy group in the world. In 2018, Dr. Sicklick was selected as a James IV Association of Surgeons fellow. This highly prestigious international traveling fellowship is designed to promote communication and collaboration in the international surgical community. In 2018 he also received the RARE Champion of Hope in Medical Care & Treatment Award from the Global Genes-Allies in Rare Disease, the largest global non-profit advocacy organization for individuals and families fighting rare and genetic diseases. In addition, he received the 2019 Excellence in Mentoring Award from the UC San Diego Health Systems International.

Dr. Sicklick is an active member of the National Comprehensive Cancer Network (NCCN) Soft Tissue Sarcoma Committee and GIST Subcommittee, and the Trans-Atlantic Australasian Retroperitoneal Sarcoma Working Group, amongst 11 national/international committees he currently serves on. Dr. Sicklick is on the Editorial Boards of Annals of Surgical Oncology, Journal of Gastrointestinal Surgery and Journal of Surgical Research. He has published in prestigious journals such as Nature Medicine, Nature, Gastroenterology, Cancer Research, Annals of Surgery, JAMA Surgery, Archives of Surgery, and Annals of Surgical Oncology. He is a member of the numerous societies including the American Society of Clinical Oncology.
Dr. Sicklick’s profile continued:

College of Surgeons, Society for Surgery of the Alimentary Tract (SSAT), the Society for University Surgeons (SUS), Surgical Biology Club II (SBC2), the Association of Academic Surgery (AAS), the Society of Surgical Oncology (SSO), American Society of Clinical Oncology (ASCO), American Association for Cancer Research (AACR), and Connective Tissue Oncology Society (CTOS). He previously served a Cancer Liaison Physician to the American College of Surgeons’ (ACS) Commission on Cancer. In addition, he is active on committees in the ACS, SUS, SSAT, AHPBA, and SSO.

Dr. Sicklick has been featured in many lay press articles, including stories in ABC News, National Geographic, the Los Angeles Times, and the San Diego Union Tribune. His translational and clinical research focus is on molecular mechanisms of GIST, as well as precision medicine approaches to cancer therapy.

He received his medical degree from the UCLA School of Medicine, completed his general surgery residency at The Johns Hopkins Hospital where he was the Administrative Chief Resident, and completed a fellowship in surgical oncology at Memorial Sloan Kettering Cancer Center where he was the Chief Administrative Fellow. He joined the UC San Diego Division of Surgical Oncology at Moores Cancer Center in 2010.

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**Dr. Jonathan Trent**
Sylvester Comprehensive Cancer Center
University of Miami
Miami, Florida, USA

Dr. Trent is currently the Associate Director for Clinical Research, the Director of the Bone and Soft-tissue Sarcoma Group and Medical Director of the Precision Medicine Initiative at the Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine.

Dr. Trent’s interests are in the clinical and translational research of sarcomas, direct care of sarcoma patients, and education about sarcoma. As Associate Director for Clinical Research, his goal is to help Sylvester Faculty develop clinical trials that provide clinically effective and scientifically exciting therapy to cancer patients of South Florida and beyond.

The major focus of his clinical, educational and research efforts are with gastrointestinal stromal tumor (GIST), chondrosarcoma, and other sarcomas. The major efforts of Dr. Trent’s research focus on understanding the mechanisms of action and resistance of imatinib in GIST and other sarcomas while striving toward improved therapeutic options. His work involves the use of novel preoperative/postoperative clinical trials, prospectively acquired tumor tissue, cell lines, archival tissue, as well as collaborations with disciplines such as the genomics facility, surgical oncology, pathology, radiology and interventional radiology.

Dr. Trent earned his MD and PhD in cancer biology from The University of Texas Health Science Center where he also completed a residency in internal medicine. He then completed a fellowship in medical oncology at The University of Texas MD Anderson Cancer Center while serving as chief fellow. Prior to joining the University of Miami, Sylvester Comprehensive Cancer Center, he held an appointment as associate professor of medicine in the Department of Sarcoma Medical Oncology, Division of Cancer Medicine at the University of Texas MD Anderson Cancer Center in Houston.
The Life Raft Group Medical Advisory Board Commentary

Our Medical Advisory Board were presented with two questions. Their responses shed light on two major issues: The importance of mutational/biomarker testing, and future promising diagnostic tools and potential treatments.

What do you believe is the importance of biomarker (mutational) testing for GIST patients?

**Dr. George:** I think mutational testing can inform prognosis and help to guide therapy.

**Dr. Heinrich:** This is the most important factor in optimizing and individualizing medical treatment. I believe that every patient that is being considered for medical treatment of their GIST, either in the localized or the advanced disease settings, should first undergo mutational testing.

**Dr. Rastogi:** I think mutational testing is indispensable for the treatment of GIST patients. As we are moving forward, we are understanding that GIST is not a single disease and not all mutational subtypes behave in the same way or respond in a similar way to drugs. Mutational testing helps us to tailor treatments and also gives us insight about the biology of the disease.

**Dr. Reichardt:** It is important for prognosis, prediction, treatment allocation and should be considered mandatory.

**Dr. Schwartz:** This is an absolutely critical part of the analysis of any patient with newly diagnosed GIST. At a time of "precision medicine", it allows the personalization of the treatment with the selection of a drug that has the best chance of inhibiting the target. It should also be a part of the process for assessing disease progression. With the development of second and third generation drugs, an understanding of the acquired secondary or tertiary mutations will similarly allow an improvement in precisely defining the optimal drug therapy.

**Dr. Sicklick:** Therapy directed by genomic testing has been proven to be cost-effective and associated with improved outcomes as compared with the empirical imatinib approach and should be offered as standard of care to all GIST patients.

**Dr. Trent:** It should be required for any GIST patient on therapy.

What new treatments/diagnostic tools do you foresee for GIST patients in the near future?

**Dr. George:** Recently approved kinase inhibitors will continue to integrate into the paradigm of management of GIST - both ripretinib for advanced GIST after three lines of therapy and avapritinib for GIST which harbors mutation in exon 18 of PDFRA.

**Dr. Heinrich:** I predict that we will continue to develop improved kinase inhibitors that can be used as a single agent or part of combination treatment approaches. Although results to date have been disappointing, I do believe that we will develop effective immunotherapy treatments for advanced GIST.

**Dr. Rastogi:** Regarding treatment, I think cabozantinib is a very promising new drug. I also feel that avapritinib should be explored more in non PDGFRA D842V mutations. Regarding diagnostic tools, liquid biopsy and single cell RNA sequencing both seem to have future implications in terms of reducing tissue requirements. However, we need more data for both of them.

**Dr. Reichardt:** Combination therapies and a new treatment algorithm.
**Dr. Schwartz:** We need to better understand the tumor microenvironment (TME) as well as the activation of complimentary pathways that would bypass the inhibition of KIT signaling. This can be done through single cell RNAseq assessment (TME) or assessment of phospho-protein activation. The latter will require the development of technology to inform us on protein kinase activation on small amounts of tissue. Assays are underway to make this feasible. There are other opportunities in cell free DNA which will allow for better tumor monitoring and for determination of acquired mutations precluding the need for tumor acquisition through biopsies. Another area of interest is exosomes and their role in the cancer biology of GIST. More to come on this.

**Dr. Sicklick:** I see broader genomic sequencing panels guiding individualized combination therapies for patients with GIST whose tumors often harbor concomitant alterations in additional genes or pathways. With rare exceptions, we rarely see a single drug cure GIST.

**Dr. Trent:** ctDNA should be performed on all patients at progression.

"The Life Raft Group is excited to collaborate with our Medical Advisory Board to address the vital issues affecting the survival and well-being of GIST patients."

Norman J. Scherzer, Executive Director

The Life Raft Group welcomes commentary and discussion on all articles and prints such commentaries uncensored.

**Invitation to Collaborate**

In our Life Raft Group GIST Patient Registry we have identified over 700 examples of patients being prescribed off-label treatment, with over 400 patients being prescribed an off-label drug at least once, with many of these patients receiving significant benefit (six months or greater PFS).

We would like to expand this data in order to see if further insights can be found, and invite physicians and researchers to collaborate with us on a project examining this in more detail. If you would like to collaborate or learn more, please contact lrgscience@liferaftgroup.org
LRG SCIENCE

Patient Powered Real World Evidence

Interested in Submitting an Article to LRG Science?

LRG Science is based on a foundation of Real World Evidence and Real World Data collected from: The LRG Patient Registry, Global Surveillance Team, our LRG Medical Advisory Board and our collaborative efforts such as the Pediatric & SDH-Deficient GIST Consortium.

We welcome content from other sources of Real World Evidence, and invite submissions of articles, editorials, case studies or breaking news for future issues, most especially, although not limited to gastrointestinal stromal tumor, SDH-deficiency and sarcoma.

To inquire about authoring an LRG SCIENCE article, providing commentary on an article, or to subscribe to our LRG SCIENCE mailing list, please contact Mary Garland, Director of Communications at mgarland@liferaftgroup.org.