



Liquid Biopsies in Oncology Drug and Device Development Part 2

Renaissance Downtown Hotel
Washington, DC
October 10, 2017

Workshop Cochairs

Julia A. Beaver, MD, Director (acting), Division of Oncology Products I, Office of Hematology and Oncology Products (OHOP), Center for Drug Evaluation and Research (CDER), FDA

Julia A. Beaver, MD, is the Director (acting) of the Division of Oncology Products 1, OHOP, FDA. Beaver graduated magna cum laude from Princeton University and then earned her medical degree from the University of Pennsylvania School of Medicine. She completed a residency in internal medicine at Johns Hopkins University School of Medicine, followed by a fellowship in medical oncology at The Johns Hopkins Sidney Kimmel Cancer Center. At the FDA, she was previously Clinical Team Leader of the Breast and Gynecologic Malignancies Group 1 and subsequently Associate Director in DOP1 prior to assuming her role as acting Director. She is also an Assistant Professor of Oncology, part-time, at Johns Hopkins University where she is a member of the Breast Cancer Group and sees patients at Johns Hopkins Oncology at Sibley Memorial Hospital.

Gideon M. Blumenthal, MD, Deputy Director (acting), Office of Hematology and Oncology Products (OHOP), Center for Drug Evaluation and Research (CDER), FDA

Gideon M. Blumenthal, MD, is acting deputy office director of the Office of Hematology and Oncology Products (OHOP). Blumenthal is a medical oncologist and serves as the associate director of precision therapeutics in OHOP. He is board certified in internal medicine, medical oncology, and hematology by the American Board of Internal Medicine. He earned his undergraduate degree from Washington University in St Louis and his medical degree from University of Maryland School of Medicine. He completed an internal medicine residency at University of Maryland, followed by a hematology/oncology fellowship at the National Cancer Institute. Blumenthal previously worked as a medical officer, clinical team leader in thoracic oncology and head and neck cancer, and scientific liaison for lung cancer at FDA. He was an associate investigator on several phase 1 and phase 2 clinical trials as a fellow and then as an adjunct attending physician in the thoracic malignancy branch of the NCI. Blumenthal serves as the OHOP scientific liaison to the American Society for Clinical Oncology, is a member of the Foundation for the NIH Biomarker Consortium Cancer Steering Committee, and served on the White House Cancer Moonshot Liquid Biopsy Blood Profiling Atlas in Cancer (Blood-PAC) committee. His research has focused on investigating novel intermediate endpoints and biomarkers to better inform oncology drug and diagnostic development and clinical trial design.

Reena Philip, PhD, Director, Division of Molecular Genetics and Pathology (DMGP), Office of In Vitro Diagnostics and Radiological Health (OIR), Center for Devices and Radiological Health (CDRH), FDA

Reena Philip, PhD, currently holds the position of Director in the Division of Molecular Genetics and Pathology in the Office of In Vitro Diagnostic Devices and Radiological Health, at Center for Devices and Radiologic Health at the FDA. At the FDA, she has been involved in many diverse activities including premarket clearance/approval, manufacturer assistance, post market regulatory compliance actions, and the development of FDA Guidance on In Vitro Companion

Diagnostic Devices. In addition, she has been an ongoing participant in FDA multi-center reviews in companion diagnostics.

Carlos L. Arteaga, MD, AACR President, 2014-2015; Director, Harold C. Simmons Comprehensive Cancer Ctr., UT Southwestern Medical Ctr.

Carlos L. Arteaga, MD, obtained his medical degree at the University of Guayaquil in Ecuador. He trained in Internal Medicine and Medical Oncology at Emory University and the University of Texas Health Sciences Center San Antonio, respectively. He joined Vanderbilt in 1989 where he served as Associate Director for Translational/Clinical Research, Director of the Center for Cancer Targeted Therapies and the Breast Cancer Program of the Vanderbilt-Ingram Cancer Center (VICC). He has over 300 publications in the areas of signaling by growth factor receptors and oncogenes in breast tumor cells, development of targeted therapies and biomarkers of drug action and resistance, and investigator-initiated clinical trials in breast cancer. Since 2002, he directed the NCI-funded Vanderbilt Breast Cancer SPORE where he co-led several investigator-initiated clinical trials. His research is or has been funded by the National Cancer Institute, the American Cancer Society, the Department of Defense Breast Cancer Research Program, Stand Up 2 Cancer (SU2C), the Susan G. Komen for the Cure Foundation, and the Breast Cancer Research Foundation. He is member of the American Society of Clinical Investigation (1998) and the Association of American Physicians (2005). He served in the NCI Board of Scientific Counselors (1999-2004), NCI Parent Subcommittee A for review of Cancer Centers (2004-2008), the Breast Core Committee of the Eastern Cooperative Oncology Group (ECOG) and the Board of Directors of the American Association for Cancer Research (2004-2007). Arteaga is the recipient of the 2003 AACR Richard & Hinda Rosenthal Award, a 2007-2017 ACS Clinical Research Professor Award, the 2009 Gianni Bonadonna Award from the American Society of Clinical Oncology (ASCO), the 2011 Brinker Award for Scientific Distinction from the Komen Foundation, and the 2015 Prize for Scientific Excellence in Medicine from the American-Italian Cancer Foundation. He was elected Fellow of the American Association for the Advancement of Science (AAAS) in 2013 and Fellow of the AACR Academy in 2015, and serves in the Scientific Advisory Board of the Komen Foundation. He chaired the AACR Special Conference 'Advances in Breast Cancer Research' (2003-11) and has served as AACR cochair of the annual San Antonio Breast Cancer Symposium since 2009. He was Deputy Editor of Clinical Cancer Research (2005-2013) and is member of the Editorial Board of Cancer Cell, Cancer Discovery and six other peer-reviewed journals. He serves in the advisory boards of several academic Breast Cancer Programs and NCI-designated Cancer Centers. He served as the 2014-2015 President of the American Association for Cancer Research, the largest cancer research organization in the world. In 2017, after a national search, he was appointed as Director of the Harold C. Simmons Cancer Center and Associate Dean for Oncology Programs at UT Southwestern Medical Center.

Pasi Jänne, MD, PhD, Director, Lowe Center for Thoracic Oncology; Scientific Director, Belfer Institute for Applied Cancer Science; Senior Physician, Dana-Farber Cancer Institute; and Professor of Medicine, Harvard Medical School

Pasi Jänne, MD, PhD, is the Director of the Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute and a Professor of Medicine at Harvard Medical School. He is also the Director of the Belfer Center for Applied Cancer Science at the Dana-Farber Cancer Institute. After earning his MD and PhD from the School of Medicine at the University of Pennsylvania, Jänne completed his internship and residency in Medicine at Brigham and Women's Hospital, Boston. He subsequently completed fellowship training at Dana-Farber Cancer Institute/Massachusetts General Hospital combined program in medical oncology in 2001. In 2002 he earned a Masters Degree in clinical investigation from Harvard University.

Jänne's research combines laboratory based studies, with translational research and clinical trials of novel therapeutic agents in patients with lung cancer. His main research interests center around understanding and translating the therapeutic importance of oncogenic alterations in lung cancer. He has made seminal therapeutic discoveries, including being on one of the co-discoverers of EGFR mutations, and findings from his work has led to the development of several clinical trials. In addition, he led the first-in man clinical trial of the mutant selective EGFR inhibitor osimertinib which was approved by the Food and Drug Administration in 2015. Jänne has received several awards for his research, including from Uniting Against Lung Cancer, American Lung Association, and the Bonnie J. Addario Lung Cancer Foundation. He is an elected member to the American Society of Clinical Investigation (2008), American Association of

Physicians (2016) and the Finnish Academy of Science and Letters (2016). In 2017 he was awarded an American Cancer Society Clinical Research Professorship. He is also the recipient of the 2010 American Association for Cancer Research (AACR) Richard and Hinda Rosenthal Memorial Award and a member of the 2010 AACR Team Science Award, and is an active member of the AACR's Regulatory Science and Policy subcommittee.

Workshop Speakers and Panelists

J. Carl Barrett, PhD, AstraZeneca

J. Carl Barrett, PhD, is vice-president of translational science in the Oncology Innovative Medicines Division at AstraZeneca Pharmaceuticals. His responsibility is to develop and execute biomarker strategy and translational sciences efforts to support compound development from research through early and full development in oncology. Barrett's longstanding research interests focus on the discovery of the critical genetic and epigenetic changes in the cancer cell, in particular the discovery of genes involved in breast cancer (BRCA1) and in the processes of cellular senescence and cancer metastasis. He has made significant contributions to the identification of molecular defects in cancers and the role of the biosystem in the carcinogenesis process.

From 2005-2011, Barrett was the global head of Oncology Biomarkers and Imaging in Novartis Oncology Translational Medicine. Prior to joining Novartis, Barrett was the founding director of the NCI Center for Cancer Research (CCR), which is the NCI intramural center for translation medicine and novel technologies. Prior to joining NCI, Barrett was the scientific director at the National Institute of Environmental Health Sciences where his efforts focused on integrating new approaches to toxicology by utilization of molecular approaches of toxicogenomics, molecular toxicology and the Environmental Genome Project. Trained as a chemist at the College of William and Mary, Barrett received his PhD degree in biophysical chemistry from Johns Hopkins University. He has published over 600 research articles and reviews in leading scientific journals and books. He is a member of the Johns Hopkins University Society of Scholars, an elected member of the Ramazini Foundation, an honorary member of the Japanese Cancer Association and a recipient of multiple NIH awards and Keynote lectures.

Maximilian Diehn, MD, PhD, Stanford Univ.

Max Diehn, MD, PhD, is an Assistant Professor of Radiation Oncology at Stanford University. He has co-appointments in the Stanford Cancer Institute and Institute for Stem Cell Biology and Regenerative Medicine. His laboratory research has focused on development and application of methods for detection of circulating tumor DNA, lung cancer biology, and the intersection of cancer and stem cell biology. Diehn is a board-certified radiation oncologist and clinically specializes in treatment of thoracic malignancies. He also leads an active clinical trials program that includes interventional and translational investigator-initiated studies. He has made significant research contributions in number of areas, including in cancer stem cell biology and cancer genomics. His group developed a next generation sequencing-based method for detection of circulating tumor DNA called CAPP-Seq. Further development and clinical application of liquid biopsy approaches are major ongoing research efforts in his laboratory.

Diehn received his undergraduate degree at Harvard College and his MD and PhD degrees at Stanford University. He then completed internal medicine internship and radiation oncology residency at Stanford. Diehn's graduate and postdoctoral work focused on genomics, cancer biology, and stem cell biology. He subsequently joined the faculty of Stanford University and is the CRK Faculty Scholar and Assistant Professor of Radiation Oncology. He has received numerous awards including the V Foundation Scholar Award, the Sidney Kimmel Scholar Award, the Doris Duke Clinical Scientist Development Award, and the NIH Director's New Innovator Award. He was elected into the American Society for Clinical Investigation in 2016.

Daniel A. Haber, MD, PhD, Massachusetts General Hospital

Daniel A. Haber, MD, PhD, is Director of the Massachusetts General Hospital Cancer Center and the Kurt J. Isselbacher Professor of Oncology at Harvard Medical School. His laboratory interests have focused on the area of cancer genetics, including the etiology of the pediatric kidney cancer Wilms tumor, genetic predisposition to breast cancer, and targeted cancer therapies. His laboratory reported that lung cancers with activating mutations in the epidermal growth factor receptor (EGFR) are uniquely sensitive to tyrosine kinase inhibitors that target this receptor. This observation has had important implications for the genotype-directed treatment of non-small cell lung cancer, and more broadly for strategies to identify critical genetic lesions in cancers that may serve as an "Achilles heel" and be suitable for molecular targeting. In collaboration with Mehmet Toner's laboratory, Haber's laboratory has recently established the application of a novel microfluidic technology for quantifying and purifying Circulating Tumor Cells (CTCs) from the blood of patients with various epithelial cancers. This new application has potentially profound implications for early diagnosis of cancer and for noninvasive molecular profiling of cancers during the course of therapy.

Haber received his MD and PhD degrees at Stanford in 1983, completed an internal medicine residency at MGH, clinical oncology training at the Dana-Farber Cancer Institute, and a postdoctoral research fellowship at MIT. He joined the faculty of Harvard Medical School in 1991. Haber's numerous awards include a MERIT Award from the National Cancer Institute, the Doris Duke Distinguished Clinical Scientist Award, and a Dream Team Award from Stand Up To Cancer. He received the Richard and Hinda Rosenthal Memorial Award from the American Association for Cancer Research (AACR). He was appointed to the Howard Hughes Medical Institute in 2008 and elected to the Institute of Medicine in 2009 and the American Academy of Arts and Sciences in 2011.

Anne-Renee Hartman, MD, GRAIL, Inc.

Anne-Renee Hartman, MD, is the Vice President of Clinical Development at GRAIL, Inc. and a medical oncologist by training. Prior to GRAIL, Anne-Renee was the Senior Vice President of Clinical Development at Myriad Genetics, Inc. At Myriad, Anne-Renee led the development of several commercialized diagnostics in oncology, including hereditary cancer testing, companion diagnostics for PARP therapy selection, and diagnostic and prognostic assays for melanoma, lung, and prostate cancer. Anne-Renee was previously an Assistant Professor of Medicine at The Dana-Farber Cancer Institute and Harvard Medical school, specializing in breast cancer genetics. She completed her oncology fellowship at Stanford University where she helped set up the cancer genetics clinic. Anne-Renee holds a Bachelor's degree in Molecular Biology from Princeton University, an MD from the University of Michigan, and completed her residency in Internal Medicine at the University of Chicago.

David Hyman, MD, Memorial Sloan Kettering Cancer Center

David Hyman, MD, is Chief of Early Drug Development at Memorial Sloan Kettering Cancer Center. He leads a large multidisciplinary group of researchers and physicians to conduct a variety of early phase clinical studies including first-in-human studies, novel combinations of investigational therapy, and histology-independent, molecularly selected "basket" studies. Under his direction, this service enrolls approximately 300 patients each year to a clinical trial portfolio of 35-40 early phase studies. In addition to conducting first-in-human studies, Hyman's personal research has focused on the development of genomically selected targeted therapies. In particular, Hyman has helped to pioneer the use of multi-histology, genomically selected, "basket" studies which select patients based on the mutations harbored in their cancer rather than where the cancer came from. Hyman led the first-in-kind basket study that evaluated vemurafenib in BRAFV600 mutant cancers and published his initial findings in the New England Journal of Medicine. Hyman currently serves as Global Principal Investigator on three additional multi-national basket studies evaluating targeted therapy for patients whose tumors harbor AKT1, ERBB2, or NTRK1/2/3 alterations. Hyman has published extensively on the design and conduct of precision medicine and basket studies as well as their utility and limitations in multiple journals including Cell, Cancer Discover, JCO and PLOS Medicine. Hyman's translational research is focused on understanding how the consequences of pathway inhibition vary as a function of tumor cell lineage and the complement of co-mutations within tumor cells.

Raghu Kalluri, MD, PhD, UT MD Anderson Cancer Ctr.

Raghu Kalluri, MD, PhD, was born in St. Louis, Missouri. He received his B.S. in Chemistry and Genetics, then earned his PhD in Biochemistry and Molecular Biology from the University of Kansas Medical Center, and then received his MD degree from Brown University Medical School. Kalluri was a postdoctoral fellow and a research associate at the University of Pennsylvania Medical School and performed research in areas of immunology and organ fibrosis. In 1997, Kalluri moved to Harvard Medical School as an Assistant Professor of Medicine and as a faculty based in the Department of Medicine at the Beth Israel Deaconess Medical Center. In 2000, he was named Associate Professor and the Director of the Center for Matrix Biology. In 2006, this program became the Division of Matrix Biology and Kalluri was appointed the Chief of the Division and promoted to Professor of Medicine at Harvard Medical School. He held appointments in the Department of Biological Chemistry and Molecular Pharmacology at HMS, Harvard MIT Division of Health Sciences and Technology, Harvard Stem Cell Institute and was a research fellow of the HMS Peabody Society. In 2012, Kalluri moved to The University of Texas MD Anderson Cancer Center as the Chairman and Professor of the Department of Cancer Biology and the Director of the Metastasis Research Center. Kalluri currently holds the RE Bob Smith Distinguished Chair for Cancer Biology and previously held the Olla S. Stribling Distinguished Chair in Cancer Research and the Rebecca and Joseph Brown Endowed Chair at MD Anderson Cancer Center. In 2015 Kalluri received the Jacob Henle Medal from the Georg-August University in Germany to honor his contribution to medical research. He is the recipient of several mentorship and teaching awards from the Beth Israel Deaconess Medical Center and Harvard Medical School. He is also the recipient of research excellence awards for his work on basement membranes and extracellular matrix as related to fibrosis and cancer progression. He is a fellow of the American Society of Clinical Investigation and the American Association for the Advancement of Science (AAAS). Kalluri has published over 287 peer-reviewed manuscripts. Kalluri has trained 73 postdoctoral fellows, 11 graduate students, and 56 undergraduate students, and fifty-one of his trainees hold academic positions around the world. Kalluri teaches 1st year core courses for graduate students and medical students. He serves on science and health advisory panels in the USA and European Union and on the editorial boards of several academic journals representing biology and medicine. His laboratory is broadly interested in the study of cell/tissue microenvironment and its impact on cancer progression and metastasis, and tissue injury and repair.

Scott Kopetz, MD, PhD, UT MD Anderson Cancer Ctr.

Scott Kopetz, MD, PhD, received his medical degree from Johns Hopkins School of Medicine after an undergraduate degree in Electrical and Biomedical Engineering at Vanderbilt University. He obtained his residency training in Internal Medicine at Duke University Medical Center, followed by a medical oncology fellowship at M. D. Anderson Cancer Center. He subsequently completed a PhD at MD Anderson in cancer biology with thesis focus on mechanisms of chemotherapy resistance in colorectal cancer.

Kopetz is currently Deputy Chair of the Department of Gastrointestinal Medical Oncology and Program Leader of the GI Program of the Cancer Center Support Grant at MDACC. Kopetz is well versed in multidisciplinary care of and translational research for GI cancer patients. His laboratory is funded by multiple NIH-funded grants, including 3 current R01 grants. He serves on the NCI GI Steering Committee, Colon Cancer Task Force, and is Vice-Chair for Colon Cancer in the NSABP/RTG/GOG (NRG) Cooperative Group. Kopetz is Co-Leader of the Colorectal Cancer Moonshot at MD Anderson, a multi-disciplinary effort to improve the survival of this disease beyond incremental advances. He has authored over 200 peer-reviewed articles in respected scientific journals such as Nature Medicine, Journal of Clinical Oncology, Lancet, Nature Reviews Cancer, Cancer Research, Clinical Cancer Research, and JAMA, and is a senior editor for Clinical Cancer Research, and editorial board member on Journal of Clinical Oncology and JNCI. Kopetz has developed a translational and clinical trial program in BRAF-mutated colorectal cancer, which has resulted in addition of combination therapy with a BRAF inhibitor to the current treatment guidelines. He also co-lead the clinical trial resulting in the FDA-approval of nivolumab for mismatch repair deficient tumors. He also is a leader in the development and implementation of circulating tumor DNA into clinical management, including interrogation of mechanisms of resistance, evaluation of minimal residual disease, and integration into clinical trial designs. Further research efforts include leadership in the development of the Consensus Molecular Subtypes, an RNA- based methodology for CRC classification that is now being widely integrated in retrospective and clinical trial efforts.

C. Ola Landgren, MD, PhD, Memorial Sloan Kettering Cancer Ctr.

C. Ola Landgren, MD, PhD, is Professor of Medicine and Chief Attending Physician of the Myeloma Service at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York, NY. Landgren is one of the world leaders in the field of early treatment strategies and molecular- and cell-based monitoring of minimal residual disease (MRD) detection in multiple myeloma and its precursor states. He leads a translational research program at MSKCC designed to discover new treatment paradigms integrating modern therapy and novel MRD assays. Landgren has designed and led the definitive study showing that all multiple myeloma patients are preceded by a precursor stage. As part of his ongoing research program, he is studying molecular mechanisms underlying the trajectory from precursor to full-blown multiple myeloma with the goal to develop treatment strategies aiming to delay, prevent, and ultimately define a cure for multiple myeloma.

Landgren has published over 250 peer-reviewed publications and he is a frequently invited speaker at national and international hematology conferences. He serves on several research committees and editorial boards for scientific journals.

Eunice Lee, PhD, FDA

Eunice Lee, PhD, is currently Chief of the Molecular Pathology and Cytology Branch in the Office of In Vitro Diagnostics and Radiological Health of the Center for Devices and Radiological Health at the FDA. The Molecular Pathology and Cytology Branch is responsible for reviewing regulatory submissions for a variety of devices with oncology indications, including genomic assays, whole slide imaging systems, and companion diagnostics. Eunice graduated magna cum laude from Bryn Mawr College and received a PhD from the Massachusetts Institute of Technology. She completed fellowships at the National Institutes of Health and Stanford University, and has worked at the National Cancer Institute.

Meijuan Li, PhD, FDA

Meijuan Li, PhD, graduated from the Division of Biostatistics, University of Minnesota in December 2008 with a doctorate in Biostatistics. Her PhD thesis focuses on non-parametric Bayesian survival analysis. She joined CDRH as a statistical reviewer in DBS. She was as a team leader from 2011 to 2015, and became the branch chief of DSBII/DBS in 2015. Her branch covers all in vitro diagnostic devices and some in vivo diagnostic and therapeutic devices submitted to CDRH. Li has extensive regulatory statistical review experience including many cutting edges genetic/genomic diagnostic devices such as next generation sequencing, copy number variation, digital pathology. She is the leading statistical expert in companion diagnostic devices. Li has published numerous manuscripts in areas including Bayesian statistics, survival analysis, missing data, and personalized medicine. She has been manuscript referee for several statistical journals. Li also serves as an editorial board member for two different statistical journals. In addition, Li serves as a FDA technical contact for a few Clinical & Laboratory Standards Institute (CLSI) standards. Li is also a coauthor of CLIS EP-19 guidance for Clinical Laboratory Measurement Procedures. Li had over 10 years of working experience in quantitative genetics and molecular biology prior to starting her PhD in biostatistics. Li holds a joint patent on biomarkers associated with maize drought tolerance.

Nicholas C. Turner, MD, PhD, Royal Marsden Hospital Inst. of Cancer Res.

Nicholas C. Turner, MD, PhD, is a Consultant Medical Oncologist who specialises in the treatment of breast cancer, and Professor of Oncology at the Breast Cancer Now Research Centre at the Institute of Cancer Research (ICR). Turner read Natural Sciences at Cambridge University before qualifying in 1997 from the University of Oxford Medical School. He completed a PhD at The Institute of Cancer Research in 2006. He is Breast Theme Lead for The Royal Marsden NIHR Biomedical Research Centre, a member of the NCRI Breast Cancer Clinical Studies Group, and Breast Domain Lead of the Genomics England Clinical Interpretation Partnerships. He sits on the organising committees of many international conferences on breast cancer, was the executive chair of the IMPAKT 2015 breast cancer conference, and is a scientific editor of the journal Cancer Discovery. Professor Turner is Chief Investigator of a number of national and international

trials of precision therapy in breast cancer. His research interests include the development of new therapies for breast cancer and using liquid biopsies to deliver more precise treatment for breast cancer.

P. Mickey Williams, PhD, NCI

Mickey Williams, PhD, directs the Molecular Characterization Laboratory, established by the National Cancer Institute (NCI), Division of Cancer Treatment and Diagnosis (DCTD), to focus on development of state of the art genomic technologies for clinical research. Laboratory goals are to assist in the development and application of well-characterized and validated clinical assays to support cancer patient management. One of several ongoing projects is the development and implementation of massively parallel sequencing assays for selection of patients for early stage clinical trials. He is Co-Scientific Principal Investigator for the NCI-MATCH Trial. He cochairs the clinical laboratory network supporting this large precision medicine trial.

Williams has been active in the use of molecular technologies for drug-target discovery. During his thirteen years at Genentech, he developed novel assays to support clinical studies and discover new therapeutic targets. He was the author of the first quantitative “real-time” PCR papers and contributed to the development of this powerful technology. Prior to joining FNLCR in 2010, he was a senior research group leader at Roche Molecular Diagnostics. While at Roche, he led the research effort and managed two large multi-national clinical assay studies: The MILE Study (microarray innovations in leukemia), and a collaboration with the LLMPP (leukemia and lymphoma molecular profiling project). He also initiated 2 projects that have subsequently been approved by the FDA as IVD kits. He has published over 50 manuscripts and is an inventor on over 30 issued U.S. Patents. Williams received his PhD from the University of Virginia.