AML

The Boston Society Acute Myeloid Leukemia MEDICAL SYMPOSIUM

October 4, 2019

Broad Institute of MIT and Harvard
Cambridge, MA

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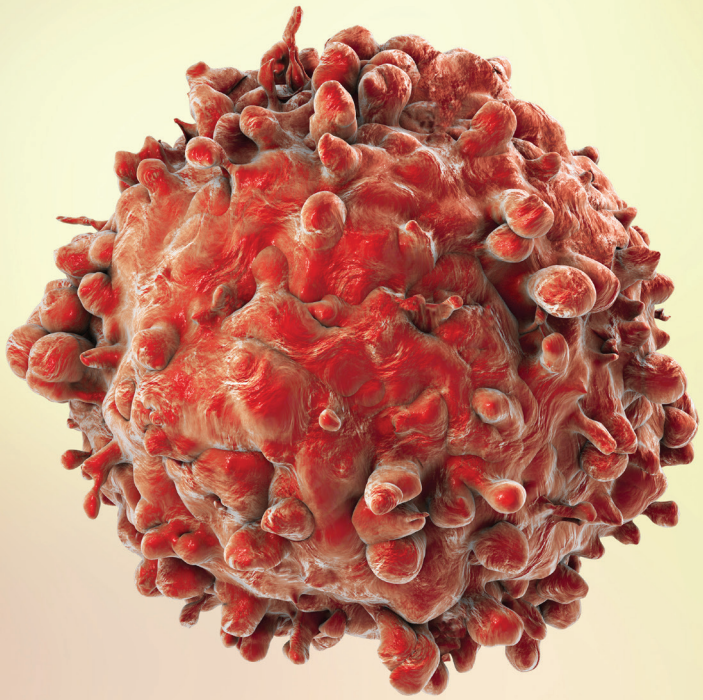

Organized by: The Boston Society

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2019 AML SPONSORS

AGIOS is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic diseases through scientific leadership in the field of cellular metabolism and adjacent areas of biology.

BIOCRATES provides quantitative metabolomics kits and services. Our kits feature both polar molecules and lipids, and it is possible to quantitate over 600 molecules with our newest kit. We also have specialty kits and services for all of your metabolomics needs. Quantitative metabolomics allows for the development of sums and ratios of metabolites, which expands the potential for discovery of new biomarkers, signatures of health or disease, or probing into a drug's mechanism of action. We feature coverage of important metabolic pathways for many different disease areas, and our newest kit is especially relevant for microbiome research.

PFIZER At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety, and value in the discovery, development, and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments, and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments, and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us.

THE MASSACHUSETTS SOCIETY OF CLINICAL ONCOLOGISTS (MSCO) is a statewide organization representing oncologists and physicians who provide care for cancer patients. Founded in 1985, the Society is dedicated to improving cancer care and treatment and is recognized by the Massachusetts Medical Society and the American Society of Clinical Oncology as the voice for cancer physicians and their patients in the state.

ORGANIZERS' WELCOME

Welcome to the 2019 Acute Myeloid Leukemia Medical Symposium.
Our organizers have gathered an excellent group of speakers for the first annual AML symposium. The program is arranged to incorporate extensive audience participation and discussion. We encourage attendees to take full advantage of the opportunity to engage in discussion in order to receive the maximum benefit from the AML experience.
Thank you for your participation.

ORGANIZING COMMITTEE

Presiding Chairs

Academic Chair: Daniel J. DeAngelo, Dana Farber Cancer Institute
Chair: Bikash Verma, MedTherapy Biotech

Committee Members

Andrew Brunner, DF/HCC/Mass General
Gwen Nichols, Leukemia and Lymphoma Society
David Sykes, Mass General/Harvard
K. Gary Vanasse, NIBR
Patrick A. Zweidler-McKay, ImmunoGen

AML 2019 SYMPOSIUM AGENDA

Friday, October 4

7:00 - 8:00 REGISTRATION
8:00 - 8:10 **Conference Opening**
Bikash Verma, MedTherapy Biotech

SESSION I: The Current Landscape – Updates

8:10 - 8:15 **Session Introduction**
Bikash Verma, MedTherapy Biotech

8:15 - 8:40 **Current Landscape for the Treatment of Patients with Acute Myeloid Leukemia**
Daniel DeAngelo, Dana Farber Cancer Institute

8:40 - 8:50 **Q & A**

8:50 - 9:15 **Application of Clinical and Functional Genomics to Pediatric AML**
Kimberly Stegmaier, Harvard Medical School

9:15 - 9:25 **Q & A**

9:25 - 9:45 Break

SESSION II: State of the Art Research and Treatment Updates

9:45 - 9:50 **Session Introduction**
Dan DeAngelo, DFCI

9:50 - 10:15 **Optimizing CAR T Cell for AML: What can we learn from experience in ALL**
Terry Fry, Children's Hospital Colorado

10:15 - 10:25 **Q & A**

10:25 - 10:50 **Defining a Role for BH3 Mimetics in High Risk Myeloid Malignancies**
Jacqueline Garcia, Dana Farber Cancer Center

10:50 - 11:00 **Q & A**

11:00 - 11:25 **Epigenetic Targets of R-2-hydroxyglutarate in IDH Mutant Tumors: Beyond TET2**
Julie-Aurore Losman, Dana Farber Cancer Center

11:25 - 11:35 **Q & A**

11:35 - 1:05 **Lunch & Networking Hour**

1:05 - 1:30 **State of the Art Research and Treatment Updates:**
Advances in the Management of TP53 Mutant Acute Myeloid Leukemia
David Sallman, Moffitt Cancer Center

1:30 - 1:40 **Q & A**

1:40 - 2:05 **Emerging Immune-based Therapies in AML**
Mikael Rinne, Novartis Institutes for Biomedical Research

2:05 - 2:15 **Q & A**

SESSION III: On the Horizon

2:15 - 2:20 **Session Introduction**
Andrew Brunner, Mass General Hospital/Harvard Medical School

2:20 - 2:45 **Recent Drug Approvals in Acute Myeloid Leukemia**
Kelly Norsworthy, FDA

2:45 - 2:55 **Q & A**

2:55 - 3:15 Break

3:15 - 3:40 **LLS Children's Initiative**
Gwen Nichols, The Leukemia and Lymphoma Society

3:40 - 3:50 **Q & A**

3:50 - 4:15 **Enabling Genomic Actionability in the Clinic**
Jeffrey Venstrom, Foundation Medicine

4:15 - 4:25 **Q & A**

4:25 - 4:30 Closing Remarks
4:30 - 6:00 Evening Reception hosted by The Boston Society

ABSTRACTS

SESSION I: The Current Landscape – Updates

Application of Clinical and Functional Genomics to Pediatric AML

Kimberly Stegmaier, Dana Farber Cancer Institute

Overall survival has improved to over 90% for children with acute lymphoblastic leukemia (ALL) treated in the United States. Survival rates for children with acute myeloid leukemia (AML), however, have lagged at only 65-70%. Moreover, while recent years have witnessed the FDA approval of eight new drugs for adults with AML, only one of these, gemtuzumab ozogamicin, was also FDA-approved for children. Next-generation sequencing efforts have demonstrated that pediatric and adult AML are distinct entities and thus each requires a focused discovery effort. Our laboratory is taking a two-pronged approach to address this problem. First, we have collaboratively led a multi-institutional precision medicine clinical genomics study for children with high-risk acute leukemias, including AML, known as the LEAP (LEukemiA Precision-based Therapy). This study seeks to determine the feasibility to identify actional alterations with a matched targeted therapy for pediatric patients with acute leukemia. Second, we are applying functional genomics approaches to identify new therapeutic targets and novel drug combinations for children with AML. Early results from both of these studies will be discussed.

SESSION II: State of the Art Research and Treatment Updates

Epigenetic Targets of R-2-hydroxyglutarate in IDH Mutant Tumors: Beyond TET2

Julie-Aurore Losman, Dana Farber Cancer Center

Acute Myeloid Leukemia (AML) is the most common leukemia in adults in the United States, with an estimated incidence of 12,000 new cases per year. Even in younger adults (age <65), the 5-year survival rate of patients with AML is only 40%. Mutations in Isocitrate Dehydrogenase (IDH1 and IDH2) are present in ~20% of cases of de novo normal karyotype AML and in 10-20% of cases of secondary AML that result from leukemic transformation of myelodysplastic syndrome (MDS) or myeloproliferative neoplasm (MPN). Mutant IDH transforms cells by producing R-2-hydroxyglutarate (R-2HG), an oncometabolite that can dysregulate the activity of a number of cellular enzymes, including TET2, a myeloid tumor suppressor that regulates the methylation state of DNA. It is not known if R-2HG has other pathogenic targets besides TET2 in AML. However, the phenotypes of IDH mutant and TET2 mutant myeloid diseases are quite different, suggesting that inhibition of other pathways by R-2HG contributes to mutant IDH-mediated transformation. We performed an unbiased positive-selection CRISPR-Cas9 genetic screen and identified two H3K4 histone lysine demethylases, KDM5A and KDM5C, as potential novel pathogenic targets of R-2HG in IDH mutant AML. I will present our data supporting a role for inhibition of KDM5 histone lysine demethylases in IDH mutant AML and will discuss strategies we are undertaking to validate the in vivo relevance of these findings in AML and in other IDH mutant tumor contexts.

State of the Art Research and Treatment Updates: Advances in the Management of TP53 Mutant Acute Myeloid Leukemia

David Sallman, Moffitt Cancer Center

Advancements in genomic techniques such as next generation sequencing (NGS) have dramatically enhanced our knowledge of the underlying genetic alterations in acute myeloid leukemia (AML) with significant prognostic and therapeutic implications. TP53 mutant patients represent a molecular cohort with very poor outcomes and lack of disease modifying therapy. The clonal burden

of TP53 is intimately associated with outcomes in this patient group and novel therapies targeting this mutation are urgently needed. Although combination therapy of hypomethylating agents with venetoclax has brought forth a paradigm change in the management of AML, TP53 mutant patients still have poor outcomes secondary to TP53 mutant driven resistance. The treatment landscape of these patients is encouraging with therapies that directly target the mutant protein and immunotherapies demonstrating the greatest potential. Specifically, the combination of APR-246, a p53 reactivator, with azacitidine has been well tolerated and has significantly improved response rates in TP53 mutant myelodysplastic syndrome (MDS) and oligoblastic AML patients. Ideally, future translational data will further elucidate the underpinnings driving the poor outcomes for this molecular subgroup to lead to additional novel therapeutic strategies.

Emerging Immune-based Therapies in AML
Mikael Rinne, Novartis Institutes for Biomedical Research

Allogeneic stem cell transplant and donor lymphocyte infusion promote graft versus leukemia effects and highlight the importance of the immune system for the cure of patients with acute myeloid leukemia (AML). Evasion of the host immune system is increasingly recognized as a key mechanism in both cancer development and drug-resistant disease progression. Although therapeutically targeting immune pathways has changed the treatment paradigm for solid and lymphoid tumors, immune-based therapies have yet to be approved for AML. Major challenges include the lack of identification of clinically validated antigen targets on primitive leukemic stem cells that may address the impact of clonal heterogeneity in AML and the observation that most subtypes of AML appear to present as immunologically "cold" tumors. Herein, we present an overview of the most recent advances in immunotherapy for AML, exclusive of CAR-T therapy. Topics reviewed include the use of immunomodulatory approaches that promote more effective application of checkpoint inhibitors (anti-PD-1/PD-L1, anti-TIM3 and CTLA-4), the discovery of novel antigens that enable the use of antibody drug conjugates and biologics that promote cell death via antibody-dependent cell cytotoxicity, and utilizing CD3-engaging bispecific antibodies to recruit cytotoxic, anti-tumor T cells. Despite concerns regarding heterogeneous antigen expression and immune-related toxicities, immune-based therapies have the potential to serve as a backbone for the development of next generation combination regimens for patients with AML, particularly for older patients unfit for induction chemotherapy and for those with minimal residual disease.

SESSION III: On the Horizon

Recent Drug Approvals in Acute Myeloid Leukemia
Kelly Norsworthy, FDA

Since 2017, eight new drugs have been approved by the FDA for patients with Acute Myeloid Leukemia (AML). Several of the drugs were approved based on novel clinical trial endpoints and in distinct patient populations. New safety concerns also emerged, such as differentiation syndrome, which has required unique monitoring and treatment considerations. This talk will feature a discussion of the recent drug approvals for AML, highlighting requirements for FDA approval, clinical endpoints used, and key safety concerns. The speaker will briefly touch upon novel endpoints, minimal residual disease, and opportunities to engage with the FDA early in development.

BIOGRAPHIES

Daniel J. DeAngelo, MD, PhD, Harvard Medical School: Daniel J. DeAngelo, MD, PhD is a professor of medicine at Harvard Medical School and the Chief of the Division of Leukemia at Dana-Farber Cancer Institute in Boston, Massachusetts. Dr. DeAngelo earned his MD and PhD in molecular genetics from Albert Einstein College of Medicine of Yeshiva University in Bronx, New York. He completed his internship and residency at Massachusetts General Hospital in Boston and clinical fellowships in Medical Oncology and Hematology at the Dana-Farber Cancer Institute and Brigham and Women's Hospital, both in Boston.

Dr. DeAngelo's clinical research focuses on optimizing therapy for adult leukemias, myelodysplastic syndromes and myeloproliferative disorders. He serves on the leukemia core committee for the Cancer and Leukemia Group B (CALGB) and is principal and co-investigator of several ongoing clinical protocols. He has a particular interest in the treatment of young adults with leukemia, particularly acute lymphoblastic leukemia.

Dr. DeAngelo is actively involved in a number of professional societies such as the American Society of Hematology and the American Society of Clinical Oncology. In addition, he serves as a member of the NCCN CML and ALL guidelines committee. Dr DeAngelo has authored or coauthored more than 200 original peer-reviewed manuscripts, review articles, and book chapters and has presented his work nationally and internationally.

Terry Fry, MD, University of Colorado School of Medicine: Dr. Fry is a Professor of Pediatrics, Hematology and Immunology, Co-Director of the Human Immunology and Immunotherapy Initiative, Director of Cancer Immunotherapy at the University of Colorado School of Medicine and holds the Robert and Kathleen Clark Endowed Chair in Pediatric Cancer Therapeutics at the Children's Hospital Colorado. He arrived at Children's Hospital Colorado in 2018 after serving as Head of the Hematologic Malignancies Section in the Pediatric Oncology Branch at the NIH where he led efforts in Cellular Immunotherapy for pediatric leukemia. Prior to the NIH, Dr. Fry was Chief of Blood and Marrow Transplantation at Children's National Medical Center in Washington, DC. Dr. Fry's research focuses on the preclinical and clinical development of chimeric antigen receptor T cells for pediatric cancers. He serves on the Committee for Scientific Affairs for the American Society of Hematology, Vice Chair for Biology in the Cellular Therapy Committee of the Children's Oncology Group and was recently elected into the American Society for Clinical Investigation.

Jacqueline S. Garcia, MD, Harvard Medical School: Dr. Jacqueline S. Garcia is an Instructor in Medicine at Harvard Medical School. She is a clinical/translational investigator in the Adult Leukemia Program at the Dana-Farber Cancer Institute and an attending physician at the Brigham & Women's Hospital. She graduated from University of Illinois at Chicago College of Medicine and completed her internship and residency training in Internal Medicine at the University of Chicago. She next completed Hematology and Oncology Fellowship training at Stanford University. Dr. Garcia's research focus is on the design and execution of scientifically-based early phase clinical studies and proof-of-concept studies in high risk myeloid malignancies, particularly for patients with relapsed or refractory acute myeloid leukemia. She is the overall Principal Investigator of several investigator-initiated clinical studies and is the local site PI for several important industrially-sponsored studies for patients with acute myeloid leukemia and myelodysplastic syndrome.

Julie-Aurore Losman, MD, Dana-Farber Cancer Institute: Julie-Aurore Losman is an Assistant Professor in the Division of Molecular and Cellular Oncology at the Dana-Farber Cancer Institute and an Attending Physician in the Division of Hematology at the Brigham and Women's Hospital. She completed her MD/PhD training at Columbia University's College of Physicians and Surgeons and her clinical training in internal medicine at John's Hopkins Hospital. She then entered the tri-institutional Hematology/Oncology Fellowship Program at Dana-Farber Cancer Institute/Brigham and Women's Hospital/Massachusetts General Hospital. After completing her clinical training, she began her post-doctoral research fellowship in the laboratory of Dr. Gary Gilliland at Brigham and Women's Hospital. Dr. Gilliland left Harvard to become a Vice President at Merck about a year later, and she switched her postdoctoral training to Dr. William G. Kaelin, Jr.'s laboratory at Dana-Farber. In 2014, she started her own laboratory at Dana-Farber. Her research focuses on understanding the link between aberrant cellular metabolism and epigenetic dysregulation in leukemia, with the goal of identifying novel therapeutic targets to treat patients with cancer.

Gwen Nichols, MD, The Leukemia & Lymphoma Society: Gwen Nichols received her BA from Williams College. Dr. Nichols received her MD with Honors from the State University of New York. She trained in internal medicine at the University of Chicago, and did her hematology-oncology fellowship at Memorial Sloan-Kettering Cancer Center where she served as Chief Fellow. She did post-doctoral research and was a Leukemia Service attending at MSKCC before being recruited to Columbia University as Director of the Hematologic Malignancies Program. At Columbia she was a PI on numerous clinical trials, ran an active translational research laboratory, and was an Advisory Dean of Students. Committee service included numerous grant review committees, the SWOG Leukemia Committee, the Education Committee of ASCO, and she continues to serve on the Scientific Advisory Board for the International Waldenstrom's Macroglobulinemia Foundation. She was chosen "Physician of the Year" at Columbia, and received the Humanism in Medicine Award. Dr. Nichols joined Roche in 2007 and led the MDM2 franchise. In 2013 she became the Translational Medicine Group Head for Molecularly Targeted Therapeutics and Oncology Site Head for the Roche Innovation Center in New York. As of March 2017, Dr. Nichols joined the Leukemia and Lymphoma Society as their Chief Medical Officer, where she oversees the mission including research, patient access, education, public policy and advocacy.

Kelly Norsworthy, MD, FDA: Dr. Norsworthy is a Medical Oncologist and Hematologist and serves as Scientific Liaison for Acute Myeloid Leukemia (AML) in the Division of Hematology Products at the U.S. Food and Drug Administration (FDA). She is a Clinical Reviewer on the leukemia team in DHP and Co-Chair of the Acute Leukemia/MDS focus group in FDA's Oncology Center of Excellence. Her interests include differentiation therapies for the treatment of AML, the optimal diagnosis and management of differentiation syndrome, assessment of clinical trial endpoints for AML and relationship to overall survival, and development of novel therapeutics for AML, myelodysplastic syndrome (MDS), and myeloproliferative neoplasms.

Dr. Norsworthy received her Bachelor of Science degree in Mathematics from the University of Maryland, College Park, and following graduation, worked as a biostatistician at the National Institutes of Health, Critical Care Medicine Department. She received her M.D. from the University of Maryland School of Medicine, where she also completed residency training in Internal Medicine, and served as Chief Resident of the Internal Medicine training program. She completed her fellowship training in Hematology and Medical Oncology at Johns Hopkins Hospital.

Dr. Norsworthy remains clinically active, practicing inpatient leukemia part-time as an Adjunct Assistant Professor of Oncology at Johns Hopkins Hospital.

Mikael Rinne, MD, PhD, NIBR: Mikael Rinne is a Senior Clinical Program Leader at Novartis Institutes for BioMedical Research (NIBR) where he oversees several programs in AML and MDS. Mikael received his M.D., Ph.D. from Indiana University before a Neurology residency at Brigham and Women's and Massachusetts General Hospitals, followed by a Neuro-Oncology fellowship at Dana-Farber Cancer Institute and Massachusetts General Hospital. He was a post-doctoral fellow in the cancer program at the Broad Institute and a Neuro-Oncologist at the Dana-Farber Cancer Institute before joining NIBR in 2016.

David Sallman, MD, Moffitt Cancer Center: Dr. Sallman is an Assistant Member in the Department of Malignant Hematology at Moffitt Cancer Center in Tampa, Florida. He is board certified in medical oncology, hematology, and internal medicine. Dr. Sallman's clinical interests are myelodysplastic syndromes (MDS), acute myeloid leukemia (AML), and myeloproliferative neoplasms. His research interests focus on the development of novel targeted therapeutic strategies (phase 1 and 2 clinical trials) for patients with MDS and AML, based on the underlying mutational drivers of each disease. Dr Sallman has authored or co-authored numerous articles, books, book chapters, and abstracts and serves as reviewer for multiple journals. In 2017, he received the Young Investigator Grant from the MDS Foundation, and in 2016, he won the Best Abstract Award at the Moffitt Research Symposium. Dr. Sallman earned his medical degree from the University of South Florida College of Medicine. He completed an internal medicine residency at Massachusetts General Hospital before completing a hematology/oncology fellowship at Moffitt Cancer Center.

Kimberly Stegmaier, MD, Dana-Farber Cancer Institute: Dr. Stegmaier is Professor of Pediatrics at Harvard Medical School and the Ted Williams Chair at Dana-Farber Cancer Institute, has advanced the application of genomics to drug and protein target discovery for pediatric malignancies, including leukemia. She is the Vice Chair for Pediatric Oncology Research, Co-director of the Pediatric Hematologic Malignancy Program, and an attending physician providing clinical care in Pediatric Oncology at the Dana-Farber Cancer Institute and Boston Children's Hospital. Dr. Stegmaier is also an Institute Member of the Broad Institute of Harvard and MIT. She has served as a Council Member with the Society for Pediatric Research from 2013-2016 and now as the Chair for the American Association for Cancer Research (AACR) Pediatric Cancer Working Group. Dr. Stegmaier is the recipient of numerous awards, such as the Joanne Levy, MD, Memorial Award for Outstanding Achievement from the American Society of Hematology, the Society for Pediatric Research Young Investigator Award, a Stand Up to Cancer (SU2C) Innovative Research Grant, the A. Clifford Barger Excellence in Mentoring Award from Harvard Medical School, the 2016 E. Mead Johnson Award for Research in Pediatrics, an NCI Outstanding Investigator R35 Award, and the 2017 St. Baldrick's Foundation Robert J. Arceci Innovation Award. Dr. Stegmaier received her undergraduate degree from Duke University where she graduated valedictorian, medical degree from Harvard Medical School, and trained in Pediatrics and Pediatric Hematology/Oncology at Boston Children's Hospital and Dana-Farber Cancer Institute.

Thank you to all of our Organizers, Speakers, Sponsors and Delegates! Without your dedication, support and participation AML 2019 would not be possible. We greatly value your comments regarding AML 2019 as well as thoughts or suggestions for improving future conferences. Please take the time to fill out our survey when we send it to you next week.

Sincerely,

The Boston Society