AML

The Boston Society
Acute Myeloid Leukemia
MEDICAL SYMPOSIUM

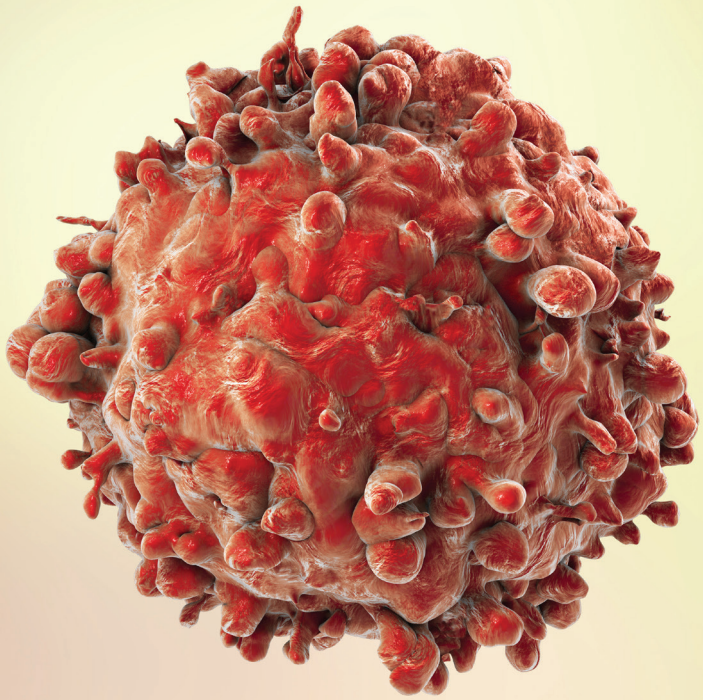
HARVARD MEDICAL SCHOOL

Massachusetts Society of Clinical Oncologists

VIRTUAL EVENT

Friday, October 22, 2021

2021



Organized by: The Boston Society

www.bostonsociety.org

ORGANIZERS' WELCOME

Welcome to the 2021 Acute Myeloid Leukemia Medical Symposium.
Our organizers have gathered an excellent group of speakers for the this year's 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

Committee Members

Andrew Brunner, DF/HCC/Mass General
Gwen Nichols, Leukemia and Lymphona Society
Daniel Pollyea, Univ. of Colorado School of Medicine
Patrick A. Zweidler-McKay, ImmunoGen

AML 2021 SYMPOSIUM AGENDA

Friday, October 22

11:50 - 12:00 **Conference Opening and Session I Introduction**
Daniel DeAngelo, Dana Farber Cancer Institute

SESSION I: The Current Landscape – Updates

12:00 - 12:15 **Transplant in the Context of MDS Patients**
Corey Cutler, Dana Farber Cancer Institute

12:15 - 12:20 **Q & A**

12:20 - 12:30 **Precision Medicine for Pediatric Acute Myeloid Leukemia**
Yana Pikman, Harvard Medical School/DFCI

12:30 - 12:35 **Q & A**

12:35 - 1:00 Break

1:00 - 1:25 PLENARY LECTURE
Innovation in the Industry for Bringing New Therapies
Vas Narasimhan, Novartis

1:25 - 1:30 **Q & A**

SESSION II: State of the Art Research and Treatment Updates

1:30 - 1:35 **Session Introduction**
Patrick A. Zweidler-McKay, ImmunoGen

1:35 - 1:45 **Update in CAR-T and Other Cell Therapies for AML**
Gail Roboz, Cornell

1:45 - 1:50 **Q & A**

1:50 - 2:00 **SARS-CoV-2 Infections in Malignancy, Particularly any Preliminary Data in Hematologic Malignancy**
Vivek Naranbhai, Harvard Medical School/DFCI

2:00 - 2:05 **Q & A**

2:05 - 2:20 **Manipulating the Microenvironment for AML Therapies (GMI 1271)**
Dan DeAngelo, Dana Farber Cancer Institute

2:20 - 2:25 **Q & A**

2:25 - 2:35 **NK Cell Therapies for AML**
Rizwan Romee, Dana Farber Cancer Institute

2:35 - 2:40 **Q & A**

2:40 - 2:50 **Immunomodulatory Therapeutic Strategies - PD1/PDL1, CD47, CD70**
David Sallman, Moffitt Cancer Center

2:50 - 2:55 **Q & A**

2:55 - 3:15 Break

SESSION III: On the Horizon

3:15 - 3:20 **Session Introduction**
Gwen Nichols, Leukemia and Lymphona Society

3:20 - 3:30 **Updates in MDS Treatment**
Andy Brunner, Mass General Hospital

3:30 - 3:35 **Q & A**

3:35 - 3:45 **FDA Perspective on New Therapy Development for AML**
Lori Ehrlich, FDA

3:45 - 3:50 **Q & A**

3:50 - 4:00 **From Disney to Doxorubicin: Childhood Cancer Perspective From a Medical Dad**
Andrew Herber, The Mayo Clinic

4:00 - 4:05 **Q & A**

4:05 - 4:10 Closing Remarks

ABSTRACTS

SESSION I: The Current Landscape - Updates

A Multi-Center Biologic Assignment Trial Comparing Reduced Intensity Allogeneic Hematopoietic Cell Transplantation to Hypomethylating Therapy or Best Supportive Care in Patients Aged 50-75 with Advanced Myelodysplastic Syndrome Blood and Marrow Transplant Clinical Trials Network Study 1102

Corey Cutler, Dana Farber Cancer Institute

Background: Recent advances in treatment of myelodysplastic syndrome (MDS) have improved survival and quality of life (QOL), and reduced transfusion burden in patients with MDS. However, allogeneic hematopoietic cell transplantation (HCT) remains the only curative therapy for MDS and is widely used in younger MDS patients. While transplantation outcomes among selected older individuals with MDS are similar to those in younger individuals with MDS, early transplantation for older individuals is infrequently offered since the relative benefits of HCT over non-HCT therapy in older patients with advanced MDS have not been well defined. To define these benefits, we conducted a multi-center, biologic assignment trial among older individuals with advanced MDS.

Methods: The study was an open-label, multicenter, biologic assignment trial in patients aged 50-75 with higher risk de novo MDS (IPSS Intermediate-2 (Int-2) or High-Risk) who were candidates for reduced-intensity conditioning (RIC) allogeneic HCT, comparing outcomes of those with a suitable HLA-matched donor to those without a donor. The trial was conducted by the Blood and Marrow Transplant Clinical Trials Network (BMT CTN 1102, NCT02016781). Eligible subjects were enrolled prior to a formal donor search, and before or after MDS treatment was initiated. Biological assignment to the Donor or No Donor arm was based on high-resolution HLA typing of eligible family members and a search of the unrelated donor registries. Subjects were initially assigned to the No Donor arm and re-assigned to the Donor group when a suitable donor was identified. Subjects who died or whose 90-day donor search ended without identifying a suitable donor remained in the No Donor arm. Subjects in the Donor arm were expected to undergo RIC HCT within 6 months of enrollment. Subjects underwent RIC HCT or non-HCT therapy according to institutional standards. The primary analysis compared three-year overall survival (OS) between arms using adjusted survival estimates to account for the potential bias resulting from biological assignment. The sample size was selected to provide at least 80% power to detect a difference of 15% in 3-year OS. Between January 2013 and November 2017, 384 subjects (Donor n=260, No Donor n=124) were enrolled at 34 centers. The study groups were well balanced for age, gender, KPS, IPSS risk, MDS disease duration and responsiveness to hypomethylating therapy. The median follow-up time for surviving patients was 34.2 months (range: 2.3-38 months) in the Donor arm and 26.9 months (range: 2.4-37.2 months) in the No Donor arm.

Results: In an intent-to-treat analysis, adjusted OS at 3 years from study enrollment in the Donor arm was 47.9% (95% CI: 41.3%-54.1%) compared with 26.6% (95% CI: 18.4%-35.6%) in the No Donor arm (p=0.0001, absolute difference 21.3% (95% CI: 10.2%-31.8%)). A sensitivity analysis excluding subjects assigned to the No Donor arm who died or withdrew prior to the end of the 90-day search window showed no effect on outcome (Adjusted OS: 48.0% vs. 28.1%, p=0.0004). Leukemia-free survival (LFS) at 3 years was greater in the Donor arm (35.8%, 95% CI: 29.8%-41.8%) compared with the No Donor arm (20.6%, 95% CI: 13.3%-29.1%, p=0.003), with no changes in the sensitivity analysis. The OS and LFS benefit was seen across all subgroups tested.

There were no clinically significant differences in QOL between Donor and No Donor arms as measured by the FACT-G, the MOS-SF36 Physical and Mental Component Scores and the EQ-5D utility score at all time points.

The overall non-compliance rate for the trial was 26.3%. Reasons for non-compliance included the use of myeloablative conditioning or failure to proceed to RIC transplant in the Donor arm, and the use of alternative donors in the No Donor arm. In an as-treated analysis, comparison of the HCT and No HCT arms demonstrated a significant advantage in 3-year OS (47.4% vs. 16.4%, $p<0.0001$) and LFS (39.3% vs. 10.9%, $p<0.0001$) for subjects who underwent HCT.

Conclusions: We observed a significant OS advantage in older patients with Int-2 and High IPSS risk de novo MDS who are RIC HCT candidates and have a matched donor, when compared with those without a donor. The benefit of having a matched donor was seen across subgroups, including those who were of Medicare age (>65) and below. HCT should be offered to all individuals between the ages of 50-75 with Int-2 and High IPSS risk MDS in whom a suitable donor can be identified.

SESSION II: State of the Art Research and Treatment Updates

NK Cell Therapies for AML

Rizwan Romee, Dana Farber Cancer Institute

NK cell hold great promise for cancer immunotherapy. Recent work including from our group has led to the identification of memory-like NK cells with enhanced anti-leukemia activity. We are currently evaluating allogeneic memory-like NK cells in combination with novel immunomodulatory agents in several malignancies including patients with AML and MDS relapsed after haploidentical donor transplantation. We are seeing massive expansion and prolonged persistence of adoptively transferred memory-like NK cells in an immune compatible environment. This approach is also safe and associated with promising activity. We have optimized lentivirus based transduction of the memory-like NK cells and have generated a TCR-like CAR against NPM1 mutated AML. NPM1 NK cell CAR show potent and tumor specific activity in vitro and in vivo. Further, transcriptomics and proteomics analysis of the transduced cell show upregulation of key gene pathways in repones to the tumor target engagement. Efforts are on to initiate a phase 1 trial of our NPM1 NK cell CAR in patients with advanced NPM1 mutated AM.

SESSION III: On the Horizon

Updates in MDS Treatment

Andrew Brunner, Mass General Hospital

Higher-risk myelodysplastic syndromes encompass a spectrum of blood cancers with ineffective clonal hematopoiesis and poor overall survival. Current therapies including the hypomethylating agents azacitidine or decitabine; for some patients allogeneic stem cell transplant, the only curative therapy in MDS, is also an option. There are a number of emerging treatments that seek to change this paradigm, and as such it is important to consider the different ways in which MDS care can improve. Among these, improving the response rate, prolonging the durability of responses, and improved and tolerable maintenance therapies are all considerations for clinical trial design. New approaches to MDS will hopefully provide more tailored therapy that matches the variation in clinical needs across individual MDS patients.

From Disney to Doxorubicin: Childhood Cancer Perspective from a Medical Dad

Andrew Herber, The Mayo Clinic

As a hospitalist PA working only a few steps away from

the Mayo Eugenia Children's Hospital childhood cancer was only something I thought happened to other families... well, until the day it wasn't. My son Nathan was diagnosed with high risk T Cell Lymphoblastic Lymphoma on September 26th, 2018, a mere 2 weeks after spending his 4th birthday at Disney World. If you ever watch a child fight cancer, it will change your life forever, especially if that child is your son.

BIOGRAPHIES

Andrew Brunner, MD, Mass General Hospital: Dr. Brunner is a member of the Leukemia Program at Massachusetts General Hospital and an Assistant Professor at Harvard Medical School. His research focuses on identifying novel therapies and treatment strategies for patients with myelodysplastic syndromes and other myeloid neoplasms including secondary AML.

Lori Ehrlich, MD, PhD, FDA: Dr. Lori Ehrlich is a pediatric hematologist/oncologist serving as a clinical team leader in the FDA's Division of Hematologic Malignancies I in the Office of Oncologic Diseases. She joined the FDA in 2014 and reviews drugs for malignant hematology indications with a focus on acute leukemias and pediatric drug development. Dr. Ehrlich completed her residency and fellowship training as a pediatric hematologist/oncologist at the Children's Hospital of Philadelphia. She received her medical degree and doctorate from the University of Pittsburgh School of Medicine.

Andrew Herber, Mayo Clinic: Andy Herber works as a Physician Assistant at in Hospital Medicine at Mayo Clinic in Rochester, MN for the past 16 years. He is an Assistant Professor of Medicine in the Mayo College of Medicine and an Associate in the Division of Hospital Medicine. In addition to seeing patients, Andy serves as the NPPA Education Lead for Mayo Clinic. He is a course director for three Hospital Medicine CME courses, been a PA preceptor for 15 years, and also is faculty at the Mayo Clinic Simulation Lab. He is a nationally recognized speaker and has won numerous education awards. He is a father of three boys, one of which completed treatment for High Risk Lymphoblastic Lymphoma in March of this year. He serves on the Board of Trustees for the Leukemia and Lymphoma Society in MN and is a childhood cancer advocate.

Vivek Naranbhai, MD, PhD, Harvard Medical School/DFCI: Dr. Naranbhai is a hematology-oncology fellow and immunogeneticist at Massachusetts General Hospital, the Dana-Farber Cancer Institute and Harvard Medical School. He is also a research associate and senior scientist at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) University of KwaZulu Natal. His work spans immunology, genetic epidemiology and bioinformatics in malignant and infectious diseases.

He obtained an MBChB (summa cum laude), Honours in Medical Microbiology (summa cum laude) and PhD (Immunology) concurrently at the Nelson R Mandela School of Medicine, South Africa working on Natural Killer cell responses in HIV. He then had an early leadership opportunity as the deputy-director of the Vaccine and Pathogenesis Programme at CAPRISA where he was involved in studies of Tenofovir gel for preventing HIV acquisition in women and demonstrated a link between systemic immune activation and HIV acquisition. As a Rhodes Scholar in Oxford, UK, he pursued a second PhD/DPhil in genetics of immune-mediated disease in the laboratory of Dr Adrian Hill. He was a postdoctoral scholar in the laboratory of Mary Carrington at the National Cancer Institute and completed internal medicine residency at Massachusetts General hospital, followed by fellowship in Hematology-Oncology at Massachusetts General Hospital. He is currently a postdoctoral fellow in the laboratory of John Iafrate where he works on immunology and genomics of cancer. His recent work involves elucidating features of antigen presentation that predict responses to immune-checkpoint blockade, and studying immune responses to COVID vaccination in patients with cancer. Together with Justin Gainor and John Iafrate, he co-leads the CANVAX study, a study of COVID vaccination in patients with Cancer.

His long term interests are in the basic immunobiology of infectious and malignant disease, and its translation to enhancing clinical care in resource-constrained settings.

Vas Narasimhan, MD, MPP, Novartis: Dr. Vas is the CEO of Novartis. He is also an elected member of the National Academy of Medicine. Since becoming CEO of Novartis in 2018, Vas has led a strategic and cultural transformation to build a leading medicines company powered by advanced therapy platforms and data science. He leads a company of more than 100,000 associates that does business in approximately 155 countries and that reached 769 million patients with its medicines in 2020. He continues to champion access and global health priorities, including through a commitment by Novartis to expand access to innovative medicines in low- and middle-income countries by at least 200% by 2025.

Vas received his M.D. from Harvard Medical School and his master's degree in public policy from the John F. Kennedy School of Government at Harvard University. Among many roles at Novartis, Dr. Narasimhan has previously served as Global Head of Biopharmaceuticals & Oncology Injectables at Sandoz International and Global Head of Drug Development and Chief Medical Officer.

Yana Pikman, MD, Harvard Medical School/DFCI: Dr. Pikman is an Assistant Professor of Pediatrics at Harvard Medical School and an attending physician and investigator within the Dana-Farber/Boston Children's Cancer and Blood Disorders Center. She received her A.B. degree in Biology at Barnard College and completed her M.D. degree at Harvard Medical School. Dr. Pikman completed pediatric residency training in the Boston Combined Residency Program at Boston Children's Hospital/Boston Medical Center, followed by pediatric hematology/oncology fellowship training at Boston Children's Hospital/Dana-Farber Cancer Institute. Dr. Pikman's translational research laboratory focuses on the implementation of clinical genomics and targeted therapies for treatment of pediatric acute leukemia.

Gail J. Roboz, MD, Cornell University: Dr. Roboz is an internationally known expert in developmental therapeutics and novel clinical trials for acute leukemias, myelodysplastic syndrome, and myeloproliferative disorders. She is the principal investigator on numerous investigator-initiated, cooperative group, and industry-sponsored clinical trials in these areas and has authored many related manuscripts and abstracts. Dr. Roboz serves on the Leukemia Core Committee for the Alliance clinical trials in oncology and is the Weill Cornell Principal Investigator for the MDS Clinical Research Consortium. She chairs the clinical committee of the European Leukemia Net (ELN) working group on minimal residual disease in acute myeloid leukemia. She also serves on the Scientific Advisory Board of the Aplastic Anemia and MDS International Foundation. Dr. Roboz has played an active role as a chair, speaker and panelist at numerous national and international conferences and is the recipient of prestigious honors and awards in the field.

Rizwan Romee, MD, Harvard Medical School/DFCI: Dr. Rizwan Romee is an associate professor of medicine at Harvard Medical School and director of the haploidentical donor transplant program at Dana Farber Cancer Institute (DFCI), Boston. He is also the principal investigator of the Romee Lab for NK Cell Gene Manipulation and Therapy at DFCI. The research focus of his laboratory is genetic manipulation of the human Natural Killer (NK) cells to enhance their anti-tumor function and simultaneously modulate the highly immune suppressive tumor microenvironment (TME). His work at Washington University helped describe human memory-like NK cells with enhanced anti-tumor activity and he led a first in human clinical trial of these cells in patients with relapsed and refractory AML demonstrating safety and promising activity. He is currently leading translational NK cell program at DFCI evaluating memory-like NK cells in combination with novel immune-modulatory agents in patients with advanced malignancies including AML and MDS relapsed after stem cell

transplantation, MRD+ multiple myeloma (in combination with CD38 ARM) and head and neck cancer (in combination with CTLA-4 blockade/ipilimumab and IL-15 super-agonist).

David Sallman, MD, Moffitt Cancer Center: Dr. Sallman is an assistant member in the Department of Malignant Hematology at Moffitt Cancer Center and assistant professor in the Department of Oncologic Sciences at the University of South Florida, both in Tampa. He earned his medical degree from the University of South Florida College of Medicine and completed an internal medicine residency at Massachusetts General Hospital before completing a hematology/oncology fellowship at Moffitt Cancer Center. 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. Specifically, he studies the genetic drivers of myeloid diseases to improve prognostication for patients and to allow for more personalized treatment. He has published significantly on this topic, including recently in highly regarded journals such as Leukemia and Haematologica, and these works are the foundation of clinical trials/translational studies designed to improve the quality of life and survival of patients with MDS. He is the principal investigator for multiple ongoing studies focused on higher-risk MDS. Furthermore, his recent work has focused on TP53-mutant MDS, where he and his team identified and validated that the clonal burden of TP53 mutation is strongly concordant with patient outcomes and are intimately tied with the clinical trajectory of these patients. Additionally, they have identified that serial next-generation sequencing has significant prognostic value and can be an early biomarker of outcome with novel agents. He has been the lead principal investigator for a phase 1b/2 clinical trial of APR-246 in combination with azacitidine for the treatment of TP53-mutant MDS and AML patients, a proposal that was developed at American Society of Hematology Clinical Research Training Institute. This trial has been one of the highest impact studies in high-risk MDS, and the data from this trial support the registrational, randomized phase 3 trial that ideally will lead to the first molecularly targeted approval for MDS. This work has led to funding support from Moffitt Cancer Center and the Edwards P. Evans Foundation of the MDS Clinical Research Consortium and an Dresner Foundation Early Career Award to support his career goals as an innovative clinical/translational investigator in MDS.

Dr Sallman has authored or coauthored numerous articles, books, book chapters, and abstracts and serves as reviewer for multiple journals. He received the Young Investigator Grant from the MDS Foundation in 2017 and he won the Best Abstract Award at the Moffitt Research Symposium in 2016.

Thank you to all of our Organizers, Speakers, Sponsors and Delegates! Without your dedication, support and participation AML 2021 would not be possible. We greatly value your comments regarding AML 2021 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