

Meet The Professors: Acute Myeloid Leukemia Edition, 2017

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists and other healthcare providers involved in the treatment of acute myeloid leukemia (AML).

OVERVIEW OF ACTIVITY

AML is the most common form of leukemia among adults, and in 2016 an estimated 19,950 cases will be diagnosed and 10,430 individuals will die from this disease. Despite the frequency of AML and its associated morbidity and mortality, standard treatment algorithms for this disease have largely remained unchanged. Historically, front-line management has included induction chemotherapy with cytarabine and an anthracycline in an effort to reduce leukemic burden and induce disease remission followed by consolidation strategies using various doses and sequences of similar agents with or without stem cell transplantation depending on the patient's ability to tolerate intensive therapy.

Much dismay has been expressed over the lack of progress in the management of this challenging disease, but in truth a number of recent scientific and therapeutic advances indicate that the future may be much brighter for patients with AML. Significantly, recent progress in molecular diagnostics has not only led to improvements in risk stratification but has also raised the potential hope that effective targeted therapeutic interventions may soon become available. Specifically, molecular diagnostics have led to the identification of several novel genetic markers, including FLT3-ITD, NPM1, CEBPA, c-KIT and others, the presence or absence of which appear to inform patient outcomes. As a result, a number of these have been incorporated into available risk stratification models and clinical practice Guidelines, including those developed by the National Comprehensive Cancer Network.

An array of other targeted and novel therapeutics are being investigated across a variety of AML subsets and clinical situations. These, in addition to the significant strides that have been made to date, provide reason for hope that new treatments will be approved in the near future and that their incorporation into standard care will improve outcomes for patients with this disease. To offer optimal patient care, clinicians need educational interventions designed to increase their knowledge of recent advancements and appropriately counsel

them regarding how those new strategies can be safely and effectively integrated into current protocol and off-protocol treatment algorithms for patients with AML.

LEARNING OBJECTIVES

- Consider age, performance status and disease-related factors to guide the selection of appropriate patients for treatment with induction therapy and/or allogeneic stem cell transplantation.
- Appreciate the clinical and prognostic significance of specific cytogenetic and molecular abnormalities, and employ this information in treatment decision-making for patients with AML.
- Recognize the importance of genetic testing in the treatment of AML.
- Assess available research evidence with existing and emerging FLT3 inhibitors, and use these data to inform decisions concerning clinical care and protocol opportunities.
- Appreciate the recent FDA breakthrough designations for and available data with midostaurin and venetoclax in preparation for their potential availability in the clinic.

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Successful completion of this CME activity enables the participant to earn up to 2.75 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the

CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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Consulting Agreements: Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc; **Contracted Research:** Astellas Pharma Global Development Inc, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc.

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COMMUNITY ONCOLOGISTS — The following community oncologists (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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No relevant conflicts of interest to disclose.

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No relevant conflicts of interest to disclose.

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Speakers Bureau: Takeda Oncology.

MODERATOR — **Dr Love** is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Agendia Inc, Amgen Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheragnostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacy-clics LLC, an AbbVie Company, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate Inc.

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Hardware/Software Requirements:

A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

- A phase 3 open-label, multicenter, randomized study of ASP2215 versus salvage chemotherapy in patients with relapsed or refractory acute myeloid leukemia (AML) with FLT3 mutation. NCT02421939**
- A phase 3 open-label randomized study of quizartinib (AC220) monotherapy versus salvage chemotherapy in subjects with tyrosine kinase 3 - internal tandem duplication (FLT3-ITD) positive acute myeloid leukemia (AML) refractory to or relapsed after first-line treatment with or without hematopoietic stem cell transplantation (HSCT) consolidation. NCT02039726**
- Cancer Genome Atlas Research Network. **Genomic and epigenomic landscapes of adult de novo acute myeloid leukemia.** *N Engl J Med* 2013;368(22):2059-74.
- Chou et al. **The prognostic impact and stability of isocitrate dehydrogenase 2 mutation in adult patients with acute myeloid leukemia.** *Leukemia* 2011;25(2):246-53.
- Cortes JE et al. **Final results of a phase 2 open-label, monotherapy efficacy and safety study of quizartinib (AC220) in patients ≥ 60 years of age with FLT3-ITD positive or negative relapsed/refractory acute myeloid leukemia.** *Proc ASH* 2012;Abstract 48.
- Dang L et al. **IDH mutations in glioma and acute myeloid leukemia.** *Trends in Mol Med* 2010;16:387-97.
- DiNardo C et al. **A phase 1b study of venetoclax (ABT-199/GDC-0199) in combination with decitabine or azacitidine in treatment-naïve patients with acute myelogenous leukemia who are \geq to 65 years and not eligible for standard induction therapy.** *Proc ASH* 2015;Abstract 327.
- Dombret H et al. **International phase 3 study of azacitidine vs conventional care regimens in older patients with newly diagnosed AML with $>30\%$ blasts.** *Blood* 2015;126(3):291-9.
- Foran JM et al. **North American Leukemia, Intergroup phase III randomized trial of single agent clofarabine as induction and post-remission therapy, and decitabine as maintenance therapy in newly-diagnosed acute myeloid leukemia in older adults (age ≥ 60 years): A trial of the ECOG-ACRIN Cancer Research Group (E2906).** *Proc ASH* 2015;Abstract 217.
- Frohling S et al. **Prognostic significance of activating FLT3 mutations in younger adults (16 to 60 years) with acute myeloid leukemia and normal cytogenetics: A study of the AML Study Group Ulm.** *Blood* 2002;100(13):4372-80.
- Kantarjian HM et al. **Multicenter, randomized, open-label, phase III trial of decitabine versus patient choice, with physician advice, of either supportive care or low-dose cytarabine for the treatment of older patients with newly diagnosed acute myeloid leukemia.** *J Clin Oncol* 2012;30(21):2670-7.
- Konopleva M et al. **A phase 2 study of ABT-199 (GDC-0199) in patients with acute myelogenous leukemia (AML).** *Proc ASH* 2014;Abstract 118.
- Levis M et al. **Results of a first-in-human, phase I/II trial of ASP2215, a selective, potent inhibitor of FLT3/Axl in patients with relapsed or refractory (R/R) acute myeloid leukemia (AML).** *Proc ASCO* 2016;Abstract 7003.
- Levis M et al. **Results from a randomized trial of salvage chemotherapy followed by lestaurtinib for patients with FLT3 mutant AML in first relapse.** *Blood* 2011;117(12):3294-301.
- Litzow MR. **More flitting about FLT3.** *Blood* 2005;106:3331-2.
- Lo-Coco F et al. **Retinoic acid and arsenic trioxide for acute promyelocytic leukemia.** *N Engl J Med* 2013;369 (2):111-21.
- Marcucci G et al. **Adding KIT inhibitor dasatinib (DAS) to chemotherapy overcomes the negative impact of KIT mutation/over-expression in core binding factor (CBF) acute myeloid leukemia (AML): Results from CALGB 10801 (Alliance).** *Blood* 2014;124:8.
- Pan R et al. **Selective BCL-2 inhibition by ABT-199 causes on-target cell death in acute myeloid leukemia.** *Cancer Discov* 2014;4(3):362-75.
- Popplewell LL, Forman SJ. **Is there an upper age limit for bone marrow transplantation?** *Bone Marrow Transplantation* 2002;29(4):277-84.
- Prensner JR, Chinnaiyan AM. **Metabolism unhinged: IDH mutations in cancer.** *Nat Med* 2011;17(3):291-3.
- Röllig C et al. **Addition of sorafenib versus placebo to standard therapy in patients aged 60 years or younger with newly diagnosed acute myeloid leukaemia (SORAML): A multicentre, phase 2, randomised controlled trial.** *Lancet Oncol* 2015;16(16):1691-9.
- Souers AJ et al. **ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets.** *Nat Med* 2013;19(2):202-8.

Select Publications

Stone RM et al. **The multi-kinase inhibitor midostaurin (M) prolongs survival compared with placebo (P) in combination with daunorubicin (D)/cytarabine (C) induction (ind), high-dose C consolidation (consol), and as maintenance (maint) therapy in newly diagnosed acute myeloid leukemia (AML) patients (pts) age 18-60 with FLT3 mutations (mut): An international prospective randomized (rand) P-controlled double-blind trial (CALGB 10603/RATIFY [Alliance]).** *Proc ASH 2015*;Abstract 6.

Uy G et al. **Addition of sorafenib to chemotherapy improves the overall survival of older adults with FLT3-ITD mutated acute myeloid leukemia (AML) (Alliance C11001).** *Proc ASH 2015*;Abstract 319.

Walter RB et al. **Impact of pretransplantation minimal residual disease, as detected by multiparametric flow cytometry, on outcome of myeloablative hematopoietic cell transplantation for acute myeloid leukemia.** *J Clin Oncol* 2011;29(9):1190-7.

Wolach O, Stone RM. **How I treat mixed-phenotype acute leukemia.** *Blood* 2015;125(16):2477-85.