Year in Review

On Demand — Significance and Relevance of Recent Data Sets and Publications in the Management of Acute Leukemias

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists, hematology-oncology fellows and other healthcare professionals involved in the treatment of acute leukemias.

OVERVIEW OF ACTIVITY

The treatment of acute leukemias remains a challenge for many healthcare professionals and patients despite recent gains made in the management of this group of diseases. Determining which treatment approach is most appropriate requires careful consideration of patient-specific characteristics, physician expertise and available health-system resources. Published results from ongoing trials continually lead to the emergence of new therapeutic targets and regimens, thereby altering management algorithms. In order to offer optimal patient care, including the option of clinical trial participation, the practicing cancer clinician must be well informed of these advances.

To bridge the gap between research and patient care, this video program features a one-on-one discussion with leading hematology-oncology investigator Dr Richard M Stone. By providing information on the latest clinical developments in the context of expert perspectives, this CME activity assists medical oncologists, hematologists, hematology-oncology fellows and other healthcare professionals with the formulation of evidence-based and current therapeutic strategies.

LEARNING OBJECTIVES

- Evaluate the clinical relevance of recent pivotal research evidence specific to acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and acute promyelocytic leukemia (APL) as published in peer-reviewed journals and/or presented at major oncology conferences.
- Review current data on recent treatment advances and updated practice standards, including FDA approvals, in acute leukemias, and integrate this information into current clinical care.
- Identify the clinical and prognostic significance of specific cytogenetic and molecular abnormalities, and use this information to develop, adapt or refine current diagnostic testing algorithms for patients with AML.
- Consider demographic and disease-related factors to guide the identification of patients with AML appropriate for treatment with induction therapy and/or stem cell transplantation.
- Determine an evidence-based approach to the management of AML in elderly patients, considering the role of single-agent or combination therapy.
- Assess available research evidence with existing and emerging FLT3-inhibiting agents, and use this information to guide clinical care and protocol opportunities for appropriate patients with AML.
- Use the results of emerging clinical research in the optimization of treatment for young adult and adult patients with newly diagnosed and recurrent ALL.
- Appraise existing efficacy and safety data from trials leading to the approval of chimeric antigen receptor (CAR) T-cell therapy in young adult patients with relapsed/refractory B-cell precursor ALL, and recall the scientific rationale supporting the ongoing investigation of novel applications of this treatment approach.
- Understand the biological and clinical presentations associated with a diagnosis of APL, and develop an evidence-based approach to the management of low/intermediate- and high-risk disease in the up-front and relapsed settings.
- Identify the mechanisms of action of and recall new data with promising investigational agents in acute forms of leukemia, and refer appropriate patients for participation in ongoing trials using these approaches.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2 Medical Knowledge 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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HOW TO USE THIS CME ACTIVITY

This CME activity consists of slide and video components. To receive credit, the participant should review the slide presentations, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/YIROnDemand18/Leukemia/CME**.

CONTENT VALIDATION AND DISCLOSURES

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

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Consulting Agreements: AbbVie Inc, Actinium Pharmaceuticals Inc, Agios Pharmaceuticals Inc, Amgen Inc, Argenx, Arog Pharmaceuticals Inc, Astellas Pharma Global Development Inc, Celator Pharmaceuticals Inc, Celgene Corporation, Fujifilm, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Juno Therapeutics, Karyopharm Therapeutics, Merck, Novartis, Orsenix, Otsuka America Pharmaceutical Inc, Pfizer Inc, Rafael Pharmaceuticals Inc, Roche Laboratories Inc, Seattle Genetics; **Contracted Research:** Novartis.

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later
Adobe Flash Player 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: October 2018

Expiration date: October 2019

Select Publications

Abaza Y et al. **Long-term outcome of acute promyelocytic leukemia treated with all-*trans*-retinoic acid, arsenic trioxide, and gemtuzumab.** *Blood* 2017;129(10):1275-83.

Borthakur G et al. **Phase II study of CPX-351 (cytarabine:daunorubicin) liposome injection in patients (pts) with newly diagnosed acute myeloid leukemia (AML) at high risk for induction mortality.** *Proc ASH* 2017;**Abstract 892**.

Cortes J et al. **Quizartinib, an FLT3 inhibitor, as monotherapy in patients with relapsed or refractory acute myeloid leukaemia: An open-label, multicentre, single-arm, phase 2 trial.** *Lancet Oncol* 2018;19(7):889-903.

Cortes J et al. **Quizartinib significantly prolongs overall survival in patients with FLT3-internal tandem duplication–mutated (mut) relapsed/refractory AML in the phase 3, randomized, controlled QUANTUM-R trial.** *Proc EHA* 2018;**Abstract LB2600**.

Cortes JE et al. **A phase 2 randomized study of low dose ara-c with or without glasdegib (PF-04449913) in untreated patients with acute myeloid leukemia or high-risk myelodysplastic syndrome.** *Proc ASH* 2016;**Abstract 99**.

DiNardo CD et al. **Durable remissions with ivosidenib in IDH1-mutated relapsed or refractory AML.** *New Engl J Med* 2018;378(25):2386-98.

DiNardo CD et al. **Durable response with venetoclax in combination with decitabine or azacitidine in elderly patients with acute meyloid leukemia (AML).** *Proc ASCO* 2018;**Abstract 7010**.

DiNardo CD et al. **Mutant isocitrate dehydrogenase (mIDH) inhibitors, enasidenib or ivosidenib, in combination with azacitidine (AZA): Preliminary results of a phase 1b/2 study in patients with newly diagnosed acute myeloid leukemia (AML).** *Proc ASH* 2017;**Abstract 639**.

Gill H et al. **Long-term outcome of relapsed acute promyelocytic leukemia treated with oral arsenic trioxide-based reinduction and maintenance regimens: A 15-year prospective study.** *Cancer* 2018;124(11):2316-26.

Gökbuget N et al. **Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia.** *Blood* 2018;131(14):1522-31.

Jongen-Lavrencic M et al. **Molecular minimal residual disease in acute myeloid leukemia.** *N Engl J Med* 2018;378(13):1189-99.

Kantarjian H et al. **Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia.** *N Engl J Med* 2017;376(9):836-47.

Kantarjian HM et al. **Inotuzumab ozogamicin versus standard therapy for acute lymphoblastic leukemia.** *N Engl J Med* 2016;375(8):740-53.

Lancet JE et al. **CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia.** *J Clin Oncol* 2018;[Epub ahead of print].

Maude SL et al. **Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia.** *N Engl J Med* 2018;378(5):439-48.

Olson NE et al. **Tumor gene signature associated with neurotoxicity in R/R B-ALL patients treated with JCAR015, a CD19-directed CAR T cell product.** *Proc ASCO* 2018;**Abstract 7007**.

Park JH et al. **Long-term follow-up of CD19 CAR therapy in acute lymphoblastic leukemia.** *N Engl J Med* 2018;378(5):449-59.

Perl AE et al. **Selective inhibition of FLT3 by gilteritinib in relapsed or refractory (R/R) AML: A multicentre, first-in-human, open-label, phase 1-2 study.** *Lancet Oncol* 2017;18(8):1061-75.

Platzbecker U et al. **Minimal-residual disease guided treatment with azacitidine in MDS/AML patients at imminent risk of relapse: Results of the prospective RELAZA2 trial.** *Proc ASH* 2017;**Abstract 565**.

Pratz K et al. **Preliminary results from a phase 1 study of gilteritinib in combination with induction and consolidation chemotherapy in subjects with newly diagnosed acute myeloid leukemia (AML).** *Proc ASH* 2017;**Abstract 722**.

Ravandi F et al. **Phase 2 study of combination of cytarabine, idarubicin, and nivolumab for initial therapy of patients with newly diagnosed acute myeloid leukemia.** *Proc ASH* 2017;**Abstract 815**.

Rollig C et al. **The addition of sorafenib to standard AML treatment results in a substantial reduction in relapse risk and improved survival. Updated results from long-term follow-up of the randomized-controlled Soraml trial.** *Proc ASH* 2017;**Abstract 721**.

Shah BD et al. **Outcomes of patients treated with prior blinatumomab in ZUMA-3: A study of KTE-C19, an anti-CD19 chimeric antigen receptor (CAR) T cell therapy, in adult patients with R/R ALL.** *Proc ASCO* 2018;**Abstract 7006**.

Select Publications

Shah NN et al. **CD4/CD8 T-cell selection enhances CD22 CAR-T cell transduction and in-vivo CAR-T expansion: Updated results on phase I anti-CD22 CAR dose expansion cohort.** *Proc ASH* 2017;**Abstract 809**.

Stein EM et al. **Enasidenib in mutant *IDH2* relapsed or refractory acute myeloid leukemia.** *Blood* 2017;130(6):722-31.

Stein EM et al. **Ivosidenib or enasidenib combined with standard induction chemotherapy is well tolerated and active in patients with newly diagnosed AML with an IDH1 or IDH2 mutation: Initial results from a phase 1 trial.** *Proc ASH* 2017;**Abstract 726**.

Stone RM et al. **Midostaurin plus chemotherapy for acute myeloid leukemia with a FLT3 mutation.** *N Engl J Med* 2017;377(5):454-64.

Wang ES et al. **Low relapse rate in younger patients ≤ 60 years old with newly diagnosed FLT3-mutated acute myeloid leukemia (AML) treated with crenolanib and cytarabine/anthracycline chemotherapy.** *Proc ASH* 2017;**Abstract 566**.

Wei A et al. **Phase 1/2 study of venetoclax with low-dose cytarabine in treatment-naïve, elderly patients with acute myeloid leukemia unfit for intensive chemotherapy: 1-year outcomes.** *Proc ASH* 2017;**Abstract 890**.

Xuan L et al. **Effect of sorafenib on the outcomes of patients with FLT3-ITD acute myeloid leukemia undergoing allogeneic hematopoietic stem cell transplantation.** *Cancer* 2018;124(9):1954-63.

Zhu HH et al. **Oral arsenic plus retinoic acid versus intravenous arsenic plus retinoic acid for non-high-risk acute promyelocytic leukaemia: A non-inferiority, randomised phase 3 trial.** *Lancet Oncol* 2018;19(7):871-9.