

Acute Leukemias™

U P D A T E

Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

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Acute Leukemias™

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Acute Leukemias Update

A Continuing Medical Education Audio Series

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 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 medical oncologist must be well informed of these advances. To bridge the gap between research and patient care, this issue of *Acute Leukemias Update* features one-on-one discussions with leading hematology-oncology investigators. By providing information on the latest clinical developments in the context of expert perspectives, this CME activity assists medical oncologists, hematologists and hematology-oncology fellows with the formulation of evidence-based and current therapeutic strategies.

LEARNING OBJECTIVES

- Appraise current data on recent therapeutic advances and changing practice standards, including FDA approvals, in acute forms of leukemia, and integrate this information into clinical care.
- Recognize the clinical and prognostic significance of specific cytogenetic and molecular abnormalities, and use this information in treatment decision-making for patients with acute forms of leukemia.
- Consider age, performance status and disease-related factors in the identification of patients with acute lymphoblastic leukemia who are appropriate for targeted agents or chemotherapy.
- Counsel patients regarding the incidence and manifestation of side effects and toxicities associated with newly approved and investigational agents and regimens in the treatment of acute forms of leukemia.
- Identify the proposed mechanisms of action of and recall new data with investigational agents demonstrating promising activity in acute forms of leukemia, and refer appropriate patients for participation in trials evaluating these approaches.

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Interview with Daniel Pollyea, MD, MS

Tracks 1-23

- | | | | |
|-----------------|------------------------------------------------------------------------------------------------------------|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Track 1 | Overview of acute myeloid leukemia (AML) in older patients | Track 14 | Similarities and differences among midostaurin, quizartinib and gilteritinib |
| Track 2 | Are older patients with AML receiving treatment? | Track 15 | Recently FDA-approved IDH1/2 inhibitors enasidenib and ivosidenib for patients with AML |
| Track 3 | Case: An 83-year-old woman with AML receives azacitidine with venetoclax on a clinical trial | Track 16 | Recognition and management of differentiation syndromes in patients with AML treated with IDH or FLT3 inhibitors |
| Track 4 | Durable responses to venetoclax in combination with azacitidine or decitabine in elderly patients with AML | Track 17 | Clinical experience with enasidenib in patients with AML and IDH2 mutations |
| Track 5 | Efficacy of venetoclax alone and in combination with hypomethylating agents (HMAs) for AML | Track 18 | Case: A 48-year-old man with relapsed/refractory AML and an IDH1 mutation receives ivosidenib |
| Track 6 | Management of treatment-associated tumor lysis syndrome (TLS) | Track 19 | Case: A 28-year-old man with Philadelphia chromosome-negative B-cell acute lymphoblastic leukemia (ALL) receives the bispecific T-cell engaging antibody blinatumomab |
| Track 7 | Biologic synergy of venetoclax and an HMA in AML | Track 20 | Challenges in using pediatric-inspired induction chemotherapy for adults with high-risk Philadelphia chromosome-negative ALL |
| Track 8 | Mechanism of action of venetoclax in AML | Track 21 | Mechanism of action and side effects of blinatumomab |
| Track 9 | Therapeutic targeting of AML stem cells | Track 22 | Current role of chimeric antigen receptor (CAR) T-cell therapy in ALL |
| Track 10 | Activity and tolerability of azacitidine/venetoclax in AML | Track 23 | Case: A 38-year-old woman with acute promyelocytic leukemia receives all-trans retinoic acid and arsenic trioxide |
| Track 11 | Quality of life with venetoclax | | |
| Track 12 | Liposomal cytarabine/daunorubicin (CPX-351) for secondary AML | | |
| Track 13 | Incidence of FLT3 mutations in AML; outcomes with approved and investigational FLT3 inhibitors | | |

Interview with Jorge E Cortes, MD

Tracks 1-20

- | | | | |
|----------------|-----------------------------------------------------------------------------------------------------------------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Track 1 | Potential undertreatment of AML in elderly patients | Track 5 | Case: A 68-year-old man with a history of previously treated Hodgkin lymphoma presents with secondary AML and an IDH1 mutation |
| Track 2 | Safety and preliminary efficacy of venetoclax in combination with an HMA for elderly patients with previously untreated AML | Track 6 | Activity and tolerability of liposomal cytarabine/daunorubicin in patients with secondary AML |
| Track 3 | Management of venetoclax-associated TLS and myelosuppression | Track 7 | Case: A 47-year-old man with relapsed/refractory AML and an IDH2 mutation receives enasidenib on a clinical trial |
| Track 4 | Use of venetoclax/decitabine as salvage therapy for younger patients with relapsed/refractory AML | Track 8 | Incidence of IDH1/2 mutations in AML; integration of enasidenib and ivosidenib into clinical practice |

Interview with Dr Cortes (continued)

- Track 9** **Case:** A 65-year-old man with previously untreated AML and a FLT3-ITD mutation experiences a complete remission with midostaurin and chemotherapy
- Track 10** Similarities and differences among approved and investigational FLT3 inhibitors
- Track 11** Activity and tolerability of FLT3 inhibitors alone or in combination with HMAs
- Track 12** Choosing between gilteritinib and quizartinib
- Track 13** Voluntary market withdrawal of the antibody-drug conjugate gemtuzumab ozogamicin and recent FDA reapproval for AML
- Track 14** Clinical use of gemtuzumab for patients with low- to intermediate-risk AML and no adverse cytogenetics
- Track 15** Activity and unique side-effect profile of the investigational hedgehog inhibitor glasdegib in AML
- Track 16** Treatment selection for younger and older patients with ALL
- Track 17** Activity and side effects of asparaginase preparations for ALL
- Track 18** Responses and tolerability with the antibody-drug conjugate inotuzumab ozogamicin in patients with ALL
- Track 19** FDA-approved indications for blinatumomab in ALL and management of immune-related side effects
- Track 20** Effectiveness of CAR T-cell therapies for ALL

Video Program

View the corresponding video interviews with (from left) Drs Pollyea and Cortes by Dr Love at www.ResearchToPractice.com/AcuteLeukemiasUpdate118/Video



Have Questions or Cases You Would Like Us to Pose to the Faculty?



Submit them to us via Facebook or Twitter and we will do our best to get them answered for you

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QUESTIONS (PLEASE CIRCLE ANSWER):

- An analysis of real-world outcomes for elderly patients with AML in the United States demonstrated that it is common for these patients not to receive any specific anticancer treatment.
 - True
 - False
- A single-arm Phase I study evaluating venetoclax in combination with an HMA for elderly patients with previously untreated AML demonstrated _____.
 - Response rates of 70% to 80%
 - Durable responses
 - Substantial toxicity
 - All of the above
 - Both a and b
 - Both a and c
- Which of the following strategies is typically employed to help mitigate venetoclax-associated TLS?
 - Dose escalation during the initial days of venetoclax treatment
 - Frequent monitoring and hydration
 - Administration of prophylactic allopurinol
 - All of the above
 - Both a and b
 - Both b and c
- Blinatumomab is currently FDA approved for adults and children in which of the following subpopulations of patients with ALL?
 - Minimal residual disease-positive
 - Relapsed/refractory B-cell precursor
 - Treatment-naïve B-cell precursor
 - All of the above
 - Both a and b
- _____ is an investigational tyrosine kinase inhibitor that targets both FLT3-ITD mutations and the DA35 point mutation.
 - Gilteritinib
 - Quizartinib
 - Both a and b
- Which of the following statements is true regarding IDH mutations in AML?
 - The incidence of IDH1 mutations is much higher than the incidence of IDH2 mutations
 - The overall response rate with IDH inhibitors is about 40% for patients with IDH mutations
 - Both enasidenib and ivosidenib are active in patients with IDH1 mutations and in those with IDH2 mutations
- Which of the following categories reflects the mechanism of action of blinatumomab?
 - Anti-PD-1/PD-L1 antibody
 - Bispecific T-cell engager
 - CAR T-cell therapy
 - IDH1/2 antibody
- Results of a Phase III study evaluating a liposomal encapsulation of cytarabine and daunorubicin (CPX-351) versus the conventional cytarabine/daunorubicin chemotherapy (7 + 3 regimen) demonstrated a statistically significant improvement in overall survival with CPX-351 for older patients with _____.
 - Primary AML
 - Secondary AML
 - AML with an NPM1 mutation
 - Both a and b
 - All of the above
- The mechanism of action of inotuzumab ozogamicin involves _____.
 - Binding to FLT3
 - Binding to CD22
 - Inhibiting IDH2
- The cytokine release syndrome and neurotoxicity associated with blinatumomab and CAR T-cell therapy in patients with ALL can typically be managed with corticosteroids.
 - True
 - False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Acute Leukemias Update — Volume 2, Issue 1

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Safety and preliminary efficacy of venetoclax in combination with an HMA for elderly patients with previously untreated AML	4 3 2 1	4 3 2 1
Management of venetoclax-associated TLS and myelosuppression in patients with AML	4 3 2 1	4 3 2 1
Similarities and differences among approved and investigational FLT3 inhibitors for AML	4 3 2 1	4 3 2 1
Activity of the FDA-approved IDH1/2 inhibitors enasidenib and ivosidenib for patients with AML; management of differentiation syndrome and other side effects	4 3 2 1	4 3 2 1
Activity and tolerability of liposomal cytarabine/daunorubicin in patients with secondary AML	4 3 2 1	4 3 2 1
Effectiveness and durability of responses with CAR T-cell therapy in ALL; identification and management of cytokine release syndrome and other common side effects	4 3 2 1	4 3 2 1

Practice Setting:

- Academic center/medical school Community cancer center/hospital Group practice
 Solo practice Government (eg, VA) Other (please specify).....

Approximately how many new patients with the following do you see per year?

ALL..... AML..... Acute promyelocytic leukemia

Was the activity evidence based, fair, balanced and free from commercial bias?

- Yes No If no, please explain:

Please identify how you will change your practice as a result of completing this activity (select all that apply).

- This activity validated my current practice
 Create/revise protocols, policies and/or procedures
 Change the management and/or treatment of my patients
 Other (please explain):

If you intend to implement any changes in your practice, please provide 1 or more examples:

.....

.....

The content of this activity matched my current (or potential) scope of practice.

- Yes No If no, please explain:

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- Appraise current data on recent therapeutic advances and changing practice standards, including FDA approvals, in acute forms of leukemia, and integrate this information into clinical care. 4 3 2 1 N/M N/A
- Recognize the clinical and prognostic significance of specific cytogenetic and molecular abnormalities, and use this information in treatment decision-making for patients with acute forms of leukemia. 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

As a result of this activity, I will be able to:

- Consider age, performance status and disease-related factors in the identification of patients with acute lymphoblastic leukemia who are appropriate for targeted agents or chemotherapy. 4 3 2 1 N/M N/A
- Counsel patients regarding the incidence and manifestation of side effects and toxicities associated with newly approved and investigational agents and regimens in the treatment of acute forms of leukemia. 4 3 2 1 N/M N/A
- Identify the proposed mechanisms of action of and recall new data with investigational agents demonstrating promising activity in acute forms of leukemia, and refer appropriate patients for participation in trials evaluating these approaches. 4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

Would you recommend this activity to a colleague?

Yes No

If no, please explain:

PART 2 — Please tell us about the faculty and editor for this educational activity

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Faculty					Knowledge of subject matter					Effectiveness as an educator
Daniel Pollyea, MD, MS	4	3	2	1		4	3	2	1	
Jorge E Cortes, MD	4	3	2	1		4	3	2	1	
Editor					Knowledge of subject matter					Effectiveness as an educator
Neil Love, MD	4	3	2	1		4	3	2	1	

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Acute Leukemias[™]

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