



**Five-Day Decitabine Therapy  
for Elderly Patients with Acute  
Myeloid Leukemia (AML)**

## CME INFORMATION

### OVERVIEW OF ACTIVITY

Acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS) account for approximately 20 percent of all hematologic cancer and related hemopathies diagnosed on an annual basis. Emerging and continuing clinical research has resulted in an increased understanding of the heterogeneous nature of these diseases and in the availability of novel treatment strategies and options. In order to offer optimal patient care — including the option of clinical trial participation — the practicing medical oncologist must be well informed of the rapidly evolving data sets in AML and MDS. To bridge the gap between research and patient care, this CME activity will deliver a serial review of recent key presentations and publications and expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for AML and MDS.

### LEARNING OBJECTIVE

- Recognize the efficacy and safety of an alternative five-day dosing regimen of decitabine for the treatment of elderly patients with newly diagnosed AML.

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**FACULTY** — The following faculty (and their spouses/partners) reported no real or apparent conflicts of interest:

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

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Inside this issue: Four interesting AML nuggets:

1. **A Phase II study** evaluating clofarabine in 112 older patients (median age 71) with AML and one or more adverse prognostic factors. Treatment was “well tolerated” and resulted in 38% CRs.
2. **A Phase II study** of the hypomethylating agent decitabine in 55 older patients (median age 74) with AML. Morphologic CR was observed in 24%; febrile neutropenia was observed in 24%.
3. **A literature review** suggesting that assays for NPM1mut and FLT3 ITDneg could be the new ER and HER2 of AML. (Ok, maybe that is an overstatement, but these are highly prognostic and predictive.)
4. **A retrospective analysis** demonstrating roughly similar results with allogeneic hematopoietic stem cell transplant in patients with AML over and under age 65.

#### **Editor’s comment: Who should treat patients with AML?**

Mike Schwartz, a Memorial-trained medical oncologist practicing in Miami Beach, is one of several dozen “master clinicians” across the country who have assisted us with our CME programs. Mike’s most recent contribution was helping us plan an upcoming **Satellite Symposium** that we will host in New Orleans on Friday night, December 4, preceding the ASH annual meeting.

Dr Schwartz will join four other community-based physicians as they present challenging cases of AML, MDS, CML, and myeloma from their practices to our all-star faculty. In addition to discussing these carefully selected patients, we will also reveal the results of our recent **national Patterns of Care survey** of US-based oncologists, specifically focusing on the management of the cases being presented at the meeting.

One interesting survey question that we will discuss live is “Do you treat some or most patients with AML or do you generally refer them to a tertiary center?” To my mild surprise, more than two thirds of the survey respondents generally manage these patients themselves, and that includes Mike, who will present a 59-year-old woman recently diagnosed with AML.

Our prior surveys have documented that oncologists in practice see about as many cases of breast cancer a year as breast cancer investigators, but AML is a complicated disease that occurs at less than one tenth the frequency.

Of course there is more than science required in these intense situations, as evidenced by Mike's patient, an Asian woman, who asked if she could take traditional therapeutic herbs during chemo (Mike said "No," as did 79 percent of the oncologists surveyed).

Certainly physicians who offer patients a local means to receive treatment for a very scary disease must do their best to keep up with the gradual but definite progress in AML. In New Orleans, we'll see what our faculty has to say about Mike's patient and whether they think she, like many others, can be effectively managed in the community. From my standpoint, this woman is fortunate to be receiving care from one of the many, many extraordinary clinicians working outside of academic medicine.

Next up on 5-Minute Journal Club: The final four papers highlighted in our series along with results from our Patterns of Care study documenting oncologists' management of MDS.

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## **Five-Day Decitabine Therapy for Elderly Patients with Acute Myeloid Leukemia (AML)**

**Presentation discussed in this issue:**

Cashen AF et al. **Preliminary results of a multicenter phase II trial of 5-day decitabine as front-line therapy for elderly patients with acute myeloid leukemia (AML).** *Blood* 2008;112:560. **Abstract**

**Slides from a presentation at ASH 2008 and transcribed comments from recent interviews with David P Steensma, MD (12/18/08) and Gail J Roboz, MD (10/6/09) below**

### **Preliminary Results of a Multicenter Phase II Trial of 5-Day Decitabine as Front-Line Therapy for Elderly Patients with Acute Myeloid Leukemia (AML)**

**Cashen AF et al.**

*Blood* 2008;112:Abstract 560.

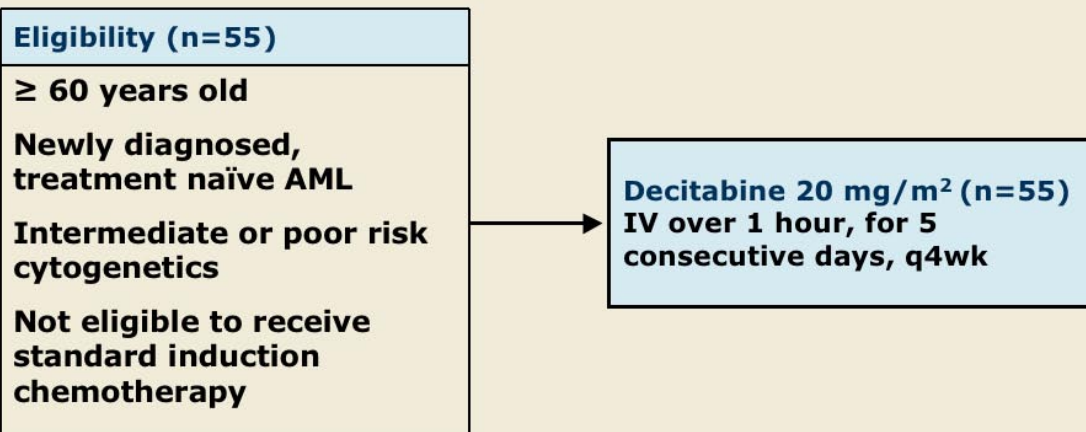
# Introduction

- Most patients with acute myelogenous leukemia (AML) are over 60 years of age.
- Treatment options for this patient subgroup are limited due to patient-related comorbidities and to high-risk disease features, such as complex cytogenetics and preceding myelodysplastic syndrome (MDS).
- Decitabine is used to treat patients with all French-American-British (FAB) subtypes of MDS and IPSS intermediate-1, intermediate-2 and high risk groups.
- Decitabine is a lower intensity therapy that may be better tolerated in this challenging, older patient population with AML.
- **Current study objectives (n=55):**
  - Establish the morphologic complete response rate (CR) in patients  $\geq 60$  years old with newly diagnosed, untreated AML who were treated with an alternative 5-day dosing regimen of decitabine.

Source: Cashen AF et al. *Blood* 2008;112:Abstract 560.

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## Phase II, Multicenter, Open-Label Trial of an Alternative 5-Day Decitabine Regimen in Elderly Patients with AML



Source: Cashen AF et al. *Blood* 2008;112:Abstract 560.

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## Patient Characteristics and Decitabine Treatment Courses

Patient Characteristics (n=55)	
Median age, n, (range)	74 years (61-87)
ECOG Performance Score	
0	47%
1	35%
2	18%
Cytogenetic risk	
Intermediate	53%
Poor	42%
Median number of decitabine cycles administered	3
Patients receiving $\geq 3$ cycles of decitabine	64%

Source: Cashen AF et al. *Blood* 2008;112:Abstract 560.

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## Overall and Complete Response Rates in Elderly Patients Treated with 5-Day Decitabine Regimen

	CR	CRi	ORR
Overall, intent-to-treat (n=55)	24%	2%	26%
<b>AML Diagnosis</b>			
De novo (n=31)	23%	0%	23%
Transformation from MDS (n=19)	21%	5%	26%
Secondary to prior therapy (n=4)	50%	0%	50%
Other (n=1)	0%	0%	0%
<b>Cytogenetic Risk</b>			
Poor (n=23)	22%	0%	22%
Intermediate (n=29)	21%	3%	24%

CRi = incomplete CR, ORR = overall response rate.

Source: Cashen AF et al. *Blood* 2008;112:Abstract 560.

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## Adverse Events and Deaths

Adverse Event <sup>a</sup> /Deaths <sup>b</sup>	
Febrile neutropenia	24%
Fatigue	24%
Pneumonia	11%
Sepsis	9%
Dyspnea	9%
Bacteremia	7%
Deaths (n)	3
30-day mortality rate	7%

<sup>a</sup>Myelosuppression was also reported. <sup>b</sup>Deaths due to sepsis.

Source: Cashen AF et al. *Blood* 2008;112:Abstract 560.

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## Summary and Conclusions

- The preliminary results suggest that 5-day decitabine demonstrates efficacy in elderly patients with newly diagnosed AML.
  - Responses were the same in intermediate and poor cytogenetic risk groups.
- The alternative 5-day dosing regimen of decitabine was well tolerated in this elderly patient population.
  - The reported adverse events were as expected and manageable.
  - The mortality rate compared favorably to the rate seen in this patient population when treated with standard induction therapy (7% vs ~20% [*CA Cancer J Clin* 2002;52:363]).
- The study results support the investigation of the 5-day dosing regimen of decitabine therapy in elderly patients with AML in an ongoing Phase III trial (DACO-16, NCT00260832).

Source: Cashen AF et al. *Blood* 2008;112:Abstract 560.

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**DAVID P STEENSMA, MD:** Decitabine is another agent that is trying to enter the elderly AML clinical scenario. This paper examined five-day decitabine as front-line therapy for patients who are “unfit or unsuitable” for induction therapy. The study had 55 patients over age 60 with newly diagnosed AML. About half of the patients had de novo disease. The study demonstrated an overall response rate of 26 percent and the median time to the best response was about three months.

**GAIL J ROBOZ, MD:** This paper is important because decitabine has been thought of as a drug for the treatment of myelodysplastic syndromes (MDS). However, the data describing the use of this drug in acute myelogenous leukemia (AML) appear to be even more promising. The use of decitabine is moving forward in the cooperative group setting as a possible front-line strategy for older patients with AML. The community should be aware of these data and not think of decitabine as a drug for the treatment of MDS only.

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