

The logo features a white stopwatch icon with the number '5' inside the circular face. To the right of the icon, the word 'Minute' is written in a large, bold, white sans-serif font, and 'Journal Club' is written below it in a smaller, white sans-serif font.

5 Minute Journal Club

Key ASH Presentations

Issue 8, 2011

Single-Agent Lenalidomide as Initial Induction and Postremission Therapy for Older Patients with Del(5q) Acute Myeloid Leukemia (AML)

CME INFORMATION

OVERVIEW OF ACTIVITY

The annual American Society of Hematology (ASH) meeting is unmatched in its importance with regard to advancements in hematologic cancer and related disorders. It is targeted by many members of the clinical research community as the optimal forum in which to unveil new clinical data. This creates an environment each year in which published results from a plethora of ongoing clinical trials lead to the emergence of many new therapeutic agents and changes in the indications for existing treatments across virtually all malignant and benign hematologic disorders. As online access to posters and plenary presentations is not currently available, a need exists for additional resources to distill the information presented at the ASH annual meeting for those clinicians unable to attend but desiring to remain up to date on the new data released there. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets from the latest ASH meeting, including 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 hematologic cancer.

LEARNING OBJECTIVE

- Recall the activity and tolerability of single-agent lenalidomide in older patients with del(5q) AML not eligible for intensive chemotherapy.

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[Click here for key papers on AML, MDS and APL](#)

In recent years, the use of hypomethylating agents — specifically decitabine and even more commonly azacitidine (AZA) — has for the first time allowed oncologists to help patients with myelodysplastic syndromes live longer and enjoy a better quality of life. However, as with many systemic agents in oncologic practice, these advances have brought with them controversy. Dr William Blum reviewed this topic in a spectacular ASH discussion, and in his accompanying education book write-up, he colorfully describes this recent chapter of the MDS story with a number of well-known quotes by, of all people, Hall of Fame Yankee baseball player Yogi Berra.

What made this review so worthwhile is that beyond finding a way to make the information entertaining, Dr Blum also made it eminently practical. He speculated that the survival advantage seen with AZA and not with decitabine may have more to do with the amount of drug exposure (median number of cycles delivered was over twice as many in the key trial of AZA) than inherent differences in the two drugs. For patients with high-risk disease, for whom the goal is extending survival, he suggested the same not-always-practical AZA schedule as the pivotal trial (days 1 to 7 every four weeks), but for patients with lower-risk disease being treated for transfusion dependence, he considers the days 1 to 5 every four weeks approach reasonable. He believes that a minimum of four to six cycles should be administered if the patient is tolerating treatment, as responses in some individuals can occur very slowly. Again mimicking the trial approach, treatment until progression is optimal.

When it comes to the less-often utilized decitabine, Dr Blum quoted Yogi: “It’s like déjà vu all over again.” He prefers the days 1 to 5 schedule à la the ADOPT trial and noted that at least three to four cycles should be administered before “giving up.”

While this lively presentation was definitely one of my ASH highlights, the conference is, of course, as much a forum to unveil information as it is to review what we already know. For this reason we profile several new data sets on MDS, AML and one of the world’s more fascinating diseases, APL.

1. Three key papers in MDS

Guillermo Garcia-Manero presented a [fascinating study](#) evaluating *oral* AZA — a strategy that perhaps opens up a whole new way to derive more benefit from this agent by delivering lower levels of drug but for more prolonged periods of time. In this study, treatment was administered for up to 21 days of a 28-day cycle, and although only a Phase I effort, data on overall response (67 percent) and tolerability were impressive. Hopefully this pioneering effort will soon be followed by Phase II and III data.

In another interesting [presentation](#), Cleveland Clinic MDS maven Mikkael Sekeres presented data from a US-based MDS registry study (AVIDA) demonstrating similar efficacy and tolerability findings for AZA in secondary MDS to those reported for primary disease. Finally, a [report](#) of 19 patients receiving AZA as a bridge to potentially curative allogeneic stem cell transplant demonstrated favorable safety and efficacy outcomes, supporting this active approach while a donor is sought.

2. Lenalidomide in del(5q) AML

This IMiD® has an established and important role in del(5q) low-risk MDS, and therefore evaluation in del(5q) AML was logical. Unfortunately, results from a [SWOG study](#) of lenalidomide alone in older patients with AML not eligible for transplant were disappointing in terms of response (five of 37 patients). In another [study](#), in which lenalidomide was combined with intensive induction chemotherapy, response rates were reasonable (60 percent) but disease-free survival was short, and investigators want to see further research with this agent in AML before considering it outside of a clinical trial.

3. The shifting winds of APL

A [European study](#) evaluating arsenic trioxide (ATO) as consolidation after induction with chemotherapy/all-trans retinoic acid (ATRA) did not have enough events at this point to define long-term outcome. However, the MD Anderson group believes this question may now be outdated in view of their just-presented [ASH paper](#) demonstrating a 98 percent complete response rate with a nonchemo regimen (ATRA/ATO) with higher-risk patients (WBC > 10 × 10⁹/L) also receiving gemtuzumab. Dr Garcia-Manero (he seems to be everywhere in these diseases) believes that one dose of idarubicin can be administered instead of the now-unavailable gemtuzumab, but most other investigators seem to want more data before making this major conceptual leap essentially abandoning chemo as induction.

In many ways the papers presented here support the notion that “the future ain’t what it used to be” and suggest that things will get better as long as dedicated investigators

like Drs Blum, Garcia-Manero and Sekeres and their colleagues continue to push the field forward and live another Yogi motto, "It ain't over 'til it's over."

Speaking of over, this concludes our ASH edition of this series. Stay tuned for an upcoming four-part GI cancer activity developed from our recent case-based educational symposium at the GI Cancers Symposium in San Francisco.

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Single-Agent Lenalidomide as Initial Induction and Postremission Therapy for Older Patients with Del(5q) Acute Myeloid Leukemia (AML)

Presentation discussed in this issue

Sekeres MA et al. **A phase II study of lenalidomide for previously untreated deletion (del) 5q acute myeloid leukemia (AML) patients age 60 or older who are not candidates for remission induction chemotherapy (Southwest Oncology Group study S0605).** *Proc ASH 2010*; **Abstract 332**.

Slides from a presentation at ASH 2010 and transcribed comments from a recent interview with B Douglas Smith, MD (1/4/11)

A Phase II Study of Lenalidomide for Previously Untreated Deletion (del) 5q Acute Myeloid Leukemia (AML) Patients Age 60 or Older Who Are Not Candidates for Remission Induction Chemotherapy (Southwest Oncology Group Study S0605)

Sekeres MA et al.

Proc ASH 2010; Abstract 332.

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Background

- Older patients (≥ 60 years) with AML have a poor prognosis.
 - Majority of these patients never receive chemotherapy
 - Many have antecedent myelodysplastic syndromes (MDS)
 - 20-30% harbor chromosome 5 abnormalities
- Phase II studies have shown that lenalidomide results in hematologic responses in patients with MDS and the del(5q) cytogenetic abnormality.
 - 67% hematologic response in lower-risk MDS (*Proc ASH* 2006;Abstract 251)
 - 27% hematologic response in higher-risk MDS (*Blood* 2009;113:3947)

Sekeres MA et al. *Proc ASH* 2010;Abstract 332.

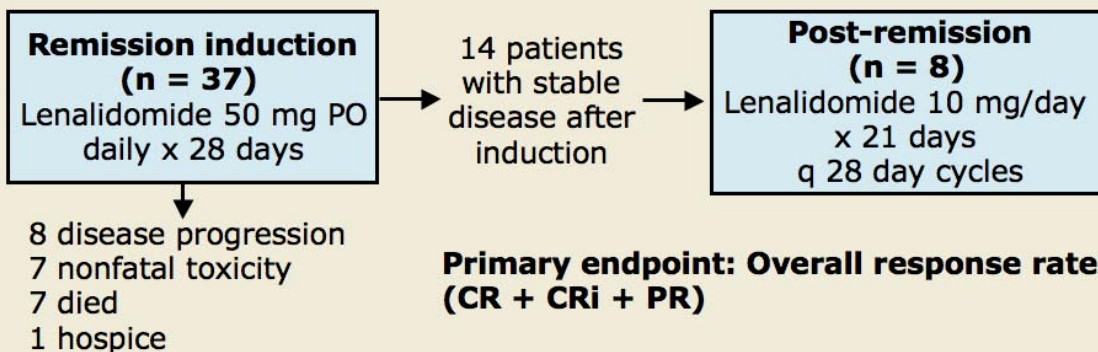
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SWOG-S0605: A Phase II Study of Lenalidomide for Newly Diagnosed Del(5q) AML

Eligibility

Newly diagnosed AML; ≥ 60 years; not eligible for intensive induction therapy

Chromosome 5 or 5q interstitial deletion either alone or with additional abnormality of complex karyotype (≥ 3 abnormalities)



Sekeres MA et al. *Proc ASH* 2010;Abstract 332.

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Efficacy Outcomes

	N = 37
Overall Response Rate CR/CRi/PR	5/37 (14%) 2/2/1
Time to relapse (median)	5 months
Survival (median)	15 months

Sekeres MA et al. *Proc ASH 2010*;Abstract 332.

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Baseline Characteristics of All Study Patients versus Responding Patients

Characteristic	All study patients (n = 37)	Responding patients (n = 5)
Median age	74 yrs	68 yrs
Female/male	21/16	2/3
Prior MDS diagnosis	19 (51%)	3 (60%)
Cytogenetic abnormalities		
Isolated del(5q) - FISH	2 (7%)	—
Isolated del(5q) - MC	5 (17%)	2 (40%)
Complex	23 (77%)	3 (60%)

MC = metaphase cytogenetics

Sekeres MA et al. *Proc ASH 2010*;Abstract 332.

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Select Adverse Events

Grade \geq 3 adverse event	Lenalidomide (N = 37)
Fatigue	30%
Febrile neutropenia	41%
Lung infections	14%
Muscle weakness, whole body	8%

Sekeres MA et al. *Proc ASH* 2010;Abstract 332.

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Author Conclusions

- Lenalidomide as a single agent has modest activity and expected toxicity in older patients with del(5q) AML.
 - Current study demonstrates about one half the rate of response previously shown with single-agent lenalidomide in a similar population (*Blood* 2011;117:1828).
- Higher doses used in induction therapy may overcome cytogenetic abnormalities beyond del(5q).

Sekeres MA et al. *Proc ASH* 2010;Abstract 332.

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Investigator comment on single-agent lenalidomide for older patients with (del)5q AML

This study shows that single-agent lenalidomide has only modest activity in older patients with (del)5q AML. I believe this study was well done and showed expected toxicities and some activity. This is a small group of patients, with a small proportion achieving remissions. Maybe this drug should be combined with either cytotoxic or other targeted therapies in the future. By itself, it is clearly not very effective.

I would currently caution about putting this into practice right away and don't believe that there are enough data to indicate that it works that well. The best responses they saw, or the most significant ones, are mostly stable disease.

Interview with B Douglas Smith, MD, January 4, 2011

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