



## **Patterns of Care Survey for Myelodysplastic Syndromes (MDS)**

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## 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

- Evaluate management issues for patients with MDS for whom relative agreement and heterogeneity exist in patterns of care, and make treatment decisions considering this information.

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## IN THIS ISSUE:

**Two reports** of combinations of biologics in MDS: First, a Phase I study of lenalidomide with 5-azacitidine. The encouraging response rate of 72 percent (39 percent CRs) and favorable tolerability profile have now resulted in the launch of a Phase II study evaluating this combination. The second paper we profile is another 5-azacitidine combination — this time with the histone deacetylase (HDAC) inhibitor valproic acid (VPA) and the differentiating agent ATRA in patients over age 70 with high-risk AML/MDS. A 29 percent response rate is reported, and further research will evaluate this interesting trifecta.

**Another paper** focuses on 23 patients with high- or intermediate-risk MDS or AML who received maintenance treatment with 5-azacitidine after experiencing a CR with induction daunorubicin/cytarabine. Treatment was well tolerated, and the median CR duration was 13.5 months. The probability of reaching CR was negatively correlated with hypermethylation of the *E-cadherin (CDH)* promoter.

We also pulled **two papers on the use of deferasirox** in patients with MDS requiring transfusions. Treatment was demonstrated to be effective in removing iron, although the correlation of the use of iron chelation with clinical endpoints such as reduced incidence of cardiac or hepatic dysfunction remains to be documented.

Finally, an interesting **case report** of two patients with AML and isolated trisomy 13 who both experienced sustained morphologic and cytogenetic remission after treatment with lenalidomide, in a manner similar to responses observed with the same agent in MDS and chromosome 5q deletion. While this condition is rare, the authors are hopeful that understanding the unique biology of this observation will further unravel the mysteries of myeloid leukemogenesis.

## EDITOR'S NOTE: ROUNDS WITH THE INVESTIGATORS

One of the techniques we frequently employ in creating a diverse array of enduring and live education activities is inviting community-based medical oncologists to present actual cases from their practices to clinical investigators with an expertise in a specific tumor type — our so-called *Meet The Professors* programs. The objective of this approach — as with a lot of our work — is to explore the vast subtleties of applying clinical research data to individuals with cancer.

**This Friday night** in New Orleans, prior to the ASH Annual Meeting, we will once again host an event utilizing this type of “oncology improv” format. In addition to myeloma

and CML, we will also delve into MDS and AML, the focus of this special four-part email/web series.

As with all of these case-based adventures, I met by phone with each oncologist to better understand the issues they would most like to see discussed and to select actual patients from their practices to present to the faculty. To prepare for the “show,” we also randomly recruited 100 US-based oncologists to take our most recent [Patterns of Care](#) survey, which included a number of queries directly related to the cases being discussed Friday night.

While many of the most pressing issues relate to MDS, I heard about a number of very challenging cases of AML, as discussed in our [last email program](#). Dr Bob Moss from Fountain Valley, California told me about an 81-year-old man who ten years previously had declined medical care for asymptomatic pancytopenia. The patient returned to Dr Moss a few months ago with full-blown AML. He finds the management of elderly patients with this disease “trickier than younger patients” and is curious how investigators approach octo- and nonagenarians.

In contrast, Dr Margaret Deutsch of Raleigh, North Carolina told me about a 45-year-old woman who recently attended her son’s wedding during a second remission after conventional treatment for AML. The next day the patient developed fever and chills and was found to have Proteus sepsis and circulating blasts. Dr Deutsch asks in desperation if there are any new options for such a patient, and if there is a role for stem cell transplant in this population?

The most common questions about patients with MDS surround the use of hypomethylating agents, and as usual, the survey yielded interesting data but also generated more questions. For example, while we predictably demonstrated that physicians were more likely to begin “hypomethylation” with 5-azacitidine as opposed to decitabine because of the available survival data, we did not ask how often physicians utilize the other agent on disease progression. On a recent audio program, Dr Allen Yang commented that he has observed useful responses to a second demethylator — a somewhat anecdotal finding at this point, but it reminded me of similar observations with the VEGF TKIs in kidney cancer.

For MDS, Ken Hoffman, who practices in Teaneck, New Jersey, told me about a 69-year-old woman he treated for breast cancer as a first-year oncology fellow 20 years ago. At the time, the patient received six cycles of adjuvant CMFVP without complication on a CALGB protocol, and for all intents and purposes was cured. Unfortunately, two decades later, she presented to her gynecologist with fatigue, and workup revealed anemia, which proved to be from MDS.

Somehow fate sent the patient back to Ken, who isn’t sure if his prior chemo caused the MDS or if it was just bad luck. Either way, after several months of frequent transfusions, 5-azacitidine was started, and the patient is now transfusion independent and doing well. Dr Hoffman’s main question for investigators is whether it’s reasonable

to skip the weekends with this agent (as discussed in our [last issue](#)), and just give treatment on days one through five. Ken — a former hospice director and true patient champion — feels strongly that the non-FDA-approved weekday schedule “makes the patient’s life a whole lot easier.”

Bill Harwin of Fort Myers, Florida has another patient with MDS doing well on 5-azacitidine but questions how long treatment needs to be continued. This 68-year-old woman also has mild Alzheimer’s disease, and she became transfusion independent after four treatment cycles yet remains on therapy after 11 courses. Dr Harwin questions whether treatment needs to be indefinite or until progression as in the survival study reported in *Lancet Oncology*. His patient is on cycle 11, compared to a mean of 12 in the study. According to Bill, even if he stretches out the treatment interval to every five or six weeks, “Patients get sick of it after a while.”

Bob Moss is treating a 93-year-old man who had received 28 units of packed red cells from another oncologist for a presumed diagnosis of MDS, but the prior treating oncologists did not perform a bone marrow exam because of the patient’s age. Bob did the procedure and found MDS with a chromosome 5q deletion. After two weeks of lenalidomide 10 milligrams daily, the man’s platelets dropped from 109,000 to 13,000 and his WBC count dropped from 7,100 to an ANC less than 200. Our Patterns of Care survey shows that 74 percent of physicians would do what Bob did, which was to hold treatment until the counts recovered and then restart lenalidomide at five milligrams daily. A year later, the patient is still on treatment, doing well and transfusion independent — another victory for quality of life.

This email marks the end of our four-part snapshot on AML/MDS. However, at ASH and well into the foreseeable future we will continue to vigorously pursue this increasingly interesting topic in order to provide you with the most current data and perspectives on these very challenging diseases.

Neil Love, MD  
Research To Practice  
Miami, Florida

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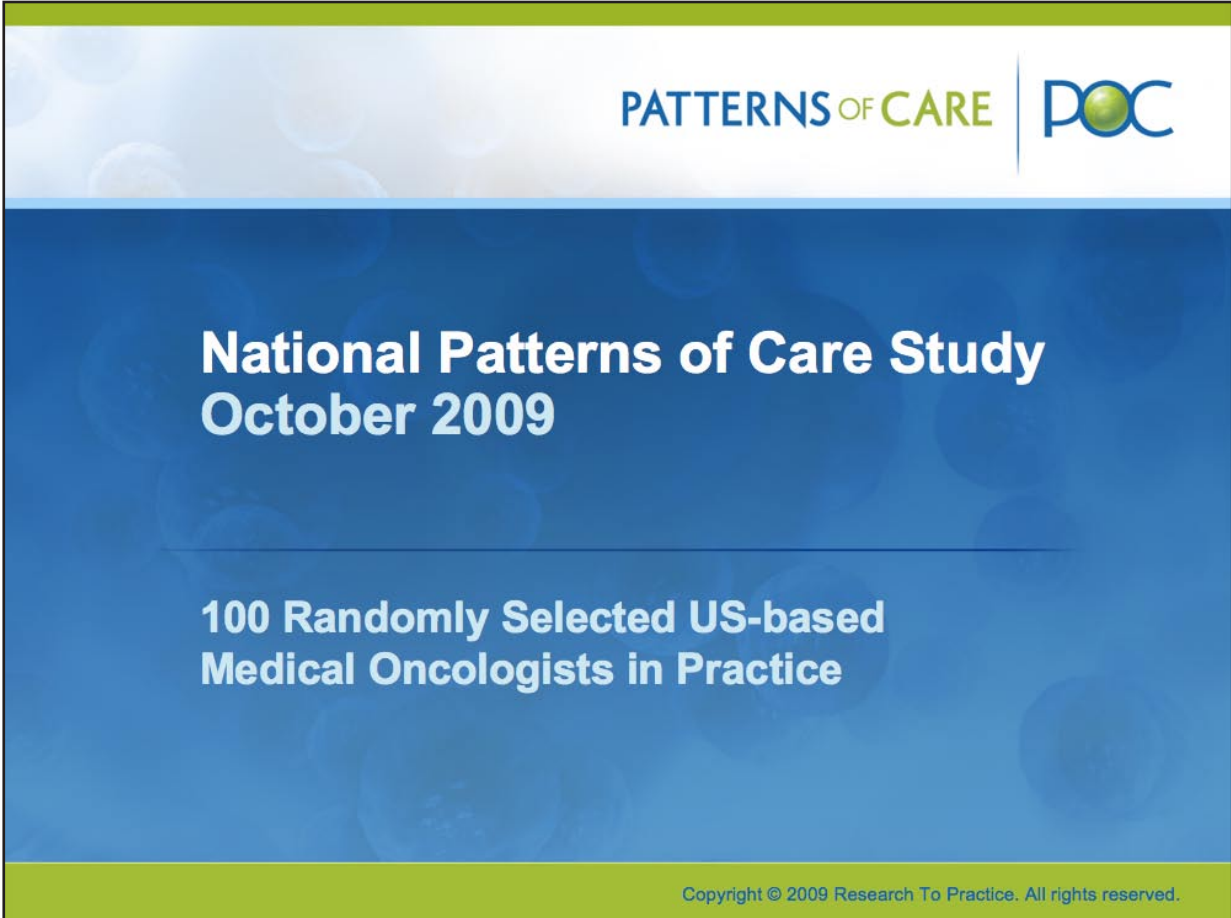
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# **Patterns of Care Survey for Myelodysplastic Syndromes (MDS)**

## **Presentation discussed in this issue:**

Research To Practice Patterns of Care Study, October 2009.

## **Slides from a national Patterns of Care study on MDS**



The slide features a white header with the text "PATTERNS OF CARE" in blue and green, followed by a vertical line and the acronym "POC" in blue with a green circle. The main body is a dark blue rectangle with white text. At the bottom is a green footer with small white text.

**PATTERNS OF CARE | POC**

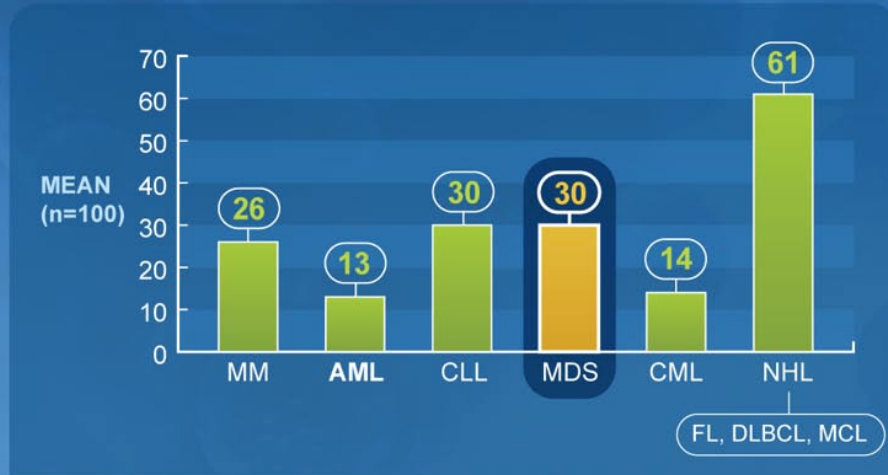
**National Patterns of Care Study  
October 2009**

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**100 Randomly Selected US-based  
Medical Oncologists in Practice**

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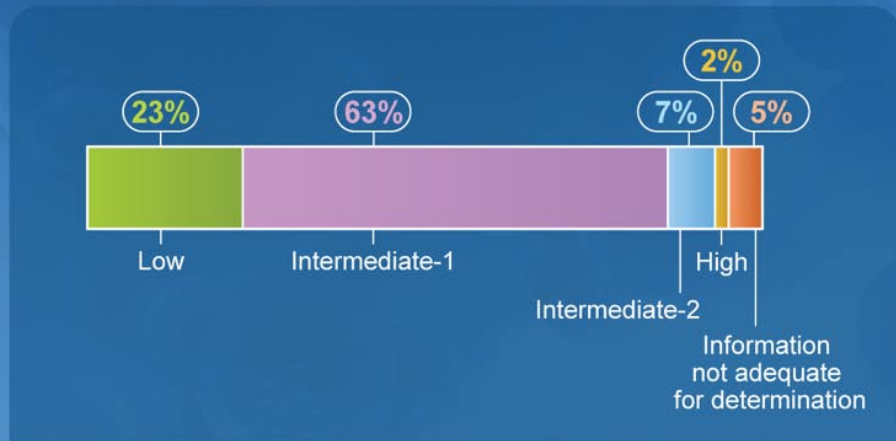
**In the past year, how many patients have you seen with the following hematologic cancers?**



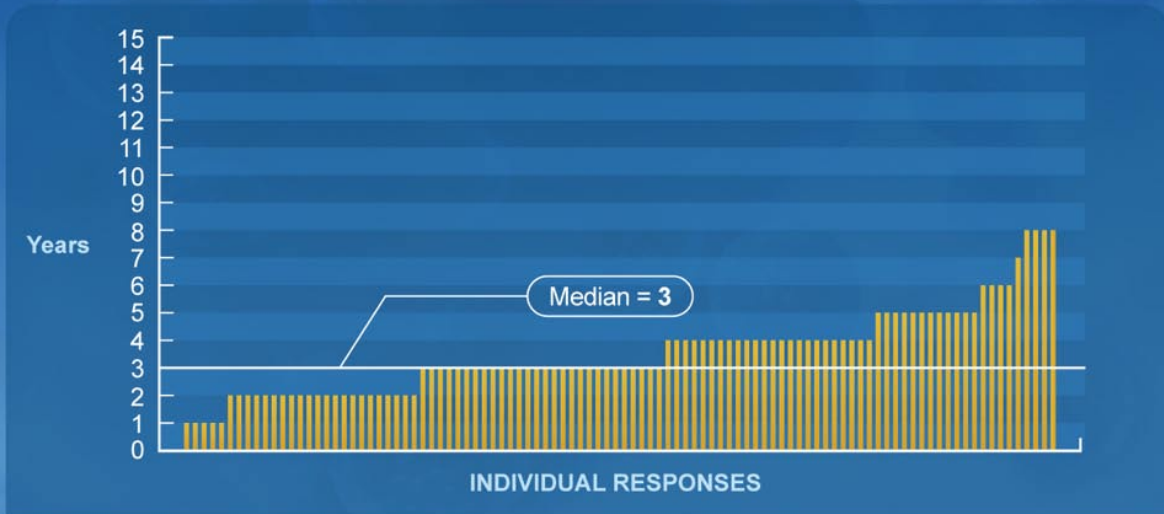
### CASE 1

- A 78-year-old man
- WBC  $2.5 \times 10^3/\text{mm}^3$ , Hgb 8.8 g/dL, Hct 25.7%, platelets  $87,000/\mu\text{L}$
- Bone marrow biopsy: MDS, no excess blasts
- Normal cytogenetics and FISH

## What is this patient's IPSS classification?

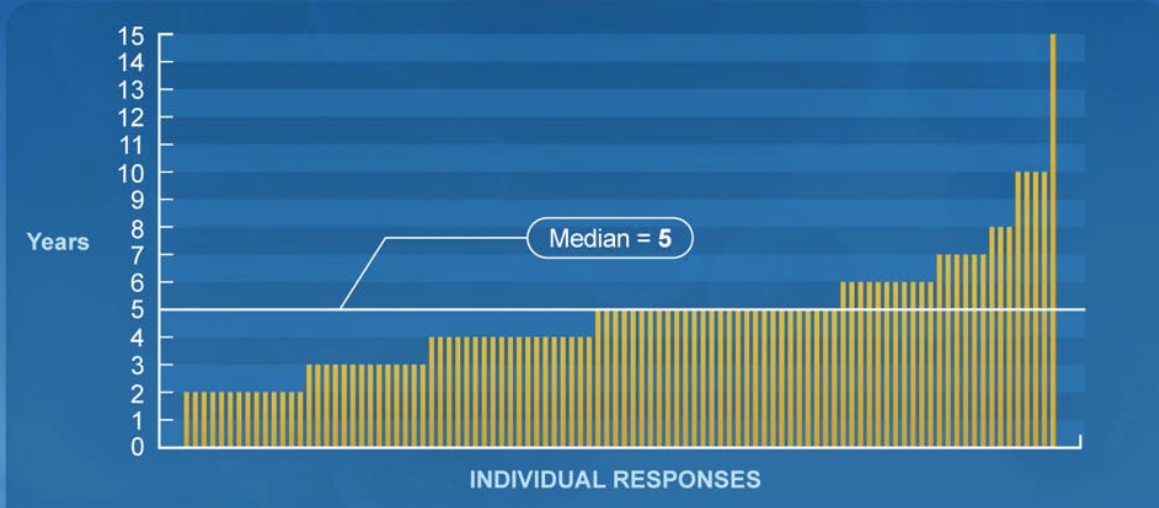


## What is this man's estimated survival with no active treatment? (supportive care only)





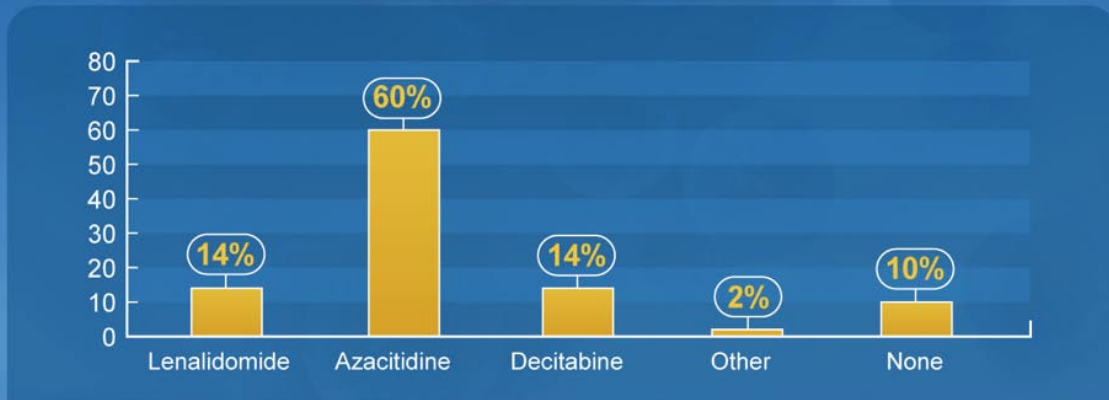
## What is this man's estimated survival with conventional systemic therapy?



## CASE 1 continued

- Patient chose observation
- Platelet count ↓ 50,000/ $\mu$ L
- Became RBC transfusion dependent
- Received darbepoetin, no response, platelet count ↓ 30,000/ $\mu$ L

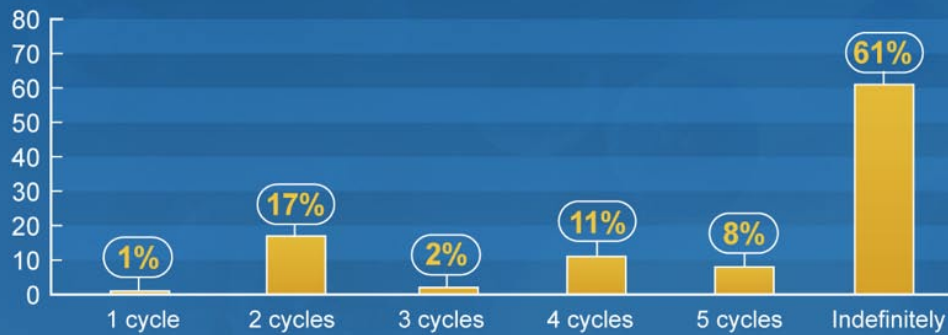
Which treatment would you recommend at this time?



### CASE 1 (continued)

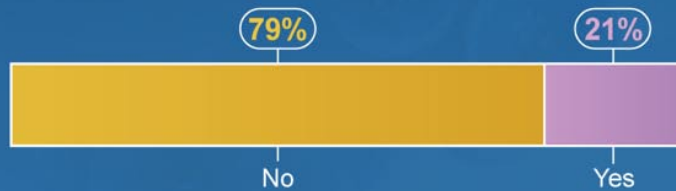
- Administered azacitidine 75 mg/m<sup>2</sup>/d SQ x 5 days q4wk
- Transfusion independent after 4 cycles
- Hgb 9.5 g/dL, platelet count 50,000/μL

## How much longer would you recommend that the azacitidine be continued?



- Administered azacitidine 75 mg/m<sup>2</sup>/d SQ x 5 days q4wk
- Transfusion independent after 4 cycles
- Hgb 9.5 g/dL, platelet count 50,000/μL

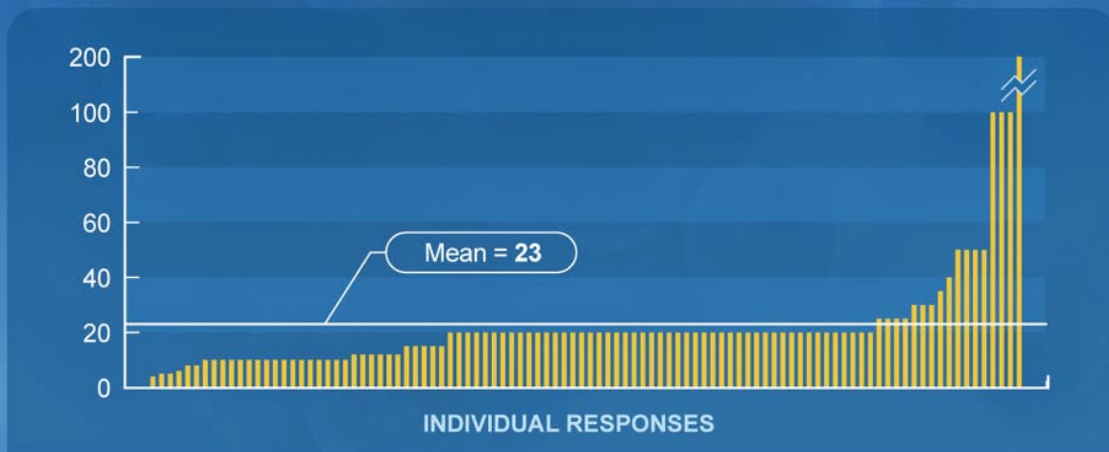
## At this time, would you increase the dosing interval?



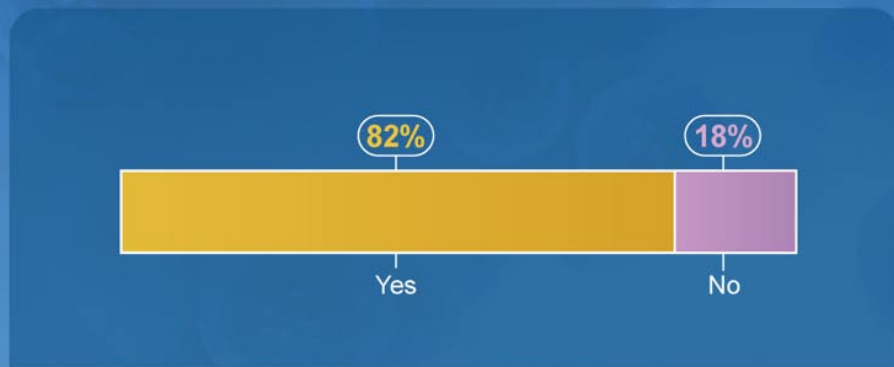
## CASE 2

- A 93-year-old man treated for MDS
- Received 28 units of packed RBC
- Hgb 8.0 g/dL, WBC normal, platelet count 109,000/ $\mu$ L
- Bone marrow biopsy: Hypercellularity, increased iron
- Chromosomes: del(5)(q15q33)

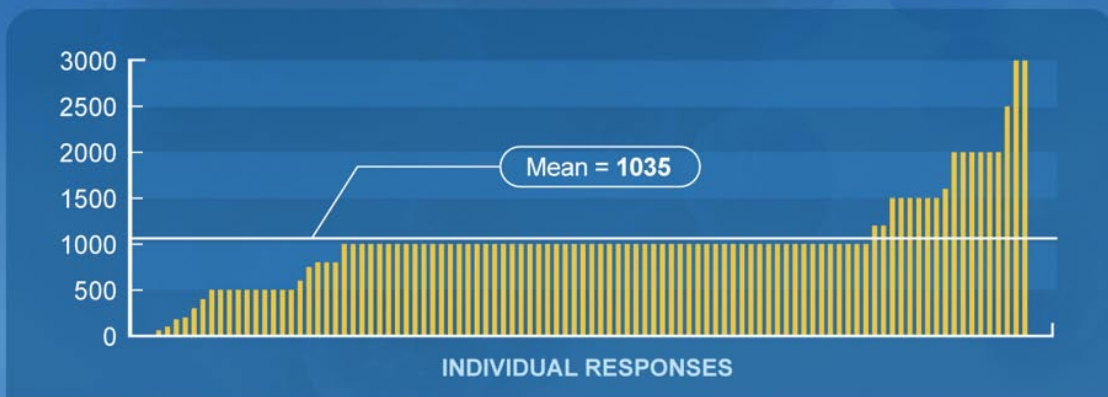
**After how many units of packed RBCs do you  
become concerned about iron overload?**  
\_\_\_\_\_ units



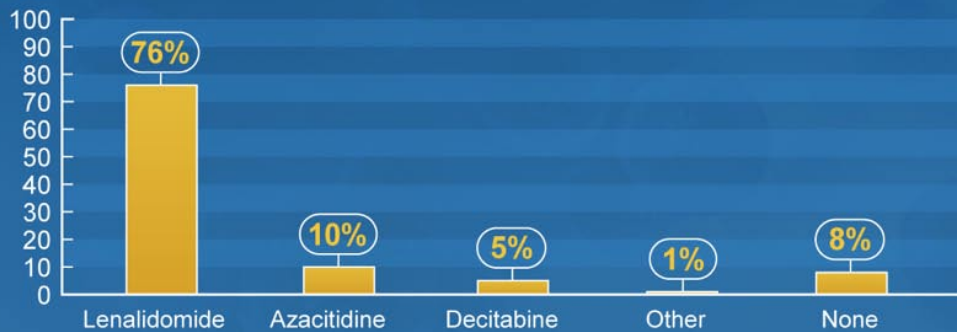
## Do you routinely check erythropoietin levels in patients diagnosed with MDS?



## At what ferritin level do you routinely start iron chelation therapy? \_\_\_\_\_ µg/dL



Which treatment would you recommend for this patient at this time?

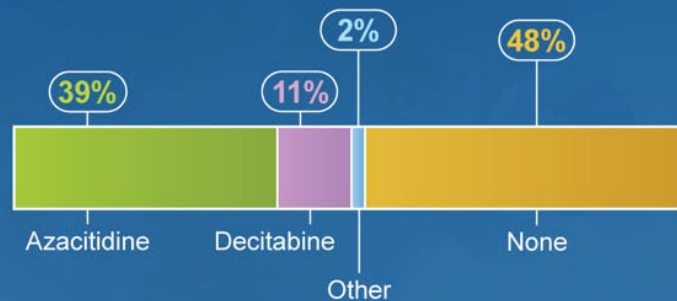


- Patient receiving lenalidomide 10 mg daily
- After 2 wks platelets ↓13,000/μL, ANC less than 200/mm<sup>3</sup>

Which treatment strategy would you likely recommend?

Continue lenalidomide at a reduced dose of 5 mg daily	10%
Hold lenalidomide until platelets > 50,000/μL and ANC > 1,000/mm <sup>3</sup> , then resume lenalidomide at 10 mg daily	10%
Hold lenalidomide until platelets > 50,000/μL and ANC > 1,000/mm <sup>3</sup> , then resume lenalidomide at 5 mg daily	74%
Discontinue lenalidomide	6%

## Which treatment would you recommend if this 93-year-old patient experienced intolerance or progressive disease on or after lenalidomide?



**EDITOR'S COMMENT:** Our most recent Patterns of Care survey of 100 US-based medical oncologists in community practice revealed few surprises. In our last email program, we reviewed data related to **management of AML**, and in this issue we review questions on MDS.

I was fascinated by the divergence of perspectives on this complex disease. For example, for a 78-year-old man with intermediate IPSS MDS, 60 percent of oncologists would recommend 5-azacitidine, 14 percent chose decitabine, and 14 percent chose lenalidomide, but it could be that as in other types of cancer, a rational future goal might be to give patients a series of agents sequentially.

Duration of therapy may be another key issue to explore in other studies, but the survey found that in contrast to the landmark clinical trial demonstrating a survival advantage in which 5-azacitidine was continued indefinitely or until disease progression, 39 percent of our respondents generally planned on nine or fewer cycles of treatment.

One consistent observation in our CME activities is that there is a direct correlation between the frequency of specific types of cancer and the interest oncologists have in learning about new clinical research and investigator opinion. From that perspective our survey shows that MDS seems to be about as common in oncology practice as CLL and multiple myeloma, so we hope the pace of clinical research on this disease will continue to accelerate, and we will have additional important options and issues to evaluate in future surveys.