APTITUDE HEALTH®

CASES

INSIGHTS INTO ACUTE MYELOID LEUKEMIA (AML)

April 15, 2021

Central United Sates Region

HOW TO NAVIGATE THIS REPORT

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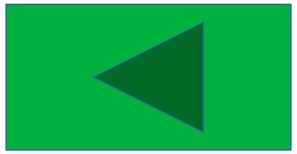
Click to move to topic of interest or ARS supporting data



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REPORT OBJECTIVES:

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STUDY OBJECTIVES
> To gain perspectives on community oncology treatment practices in first-line treatment of AML, management of relapsed/refractory AML, and promising strategies in AML
> To gain insight into the influence of recent data and approvals on community treatment practices

REPORT SNAPSHOT: SESSION OVERVIEW

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A moderated roundtable discussion was held with community oncologists from across the Central region of the United States in a virtual setting on **April 15, 2021**

Disease state and data presentations were led by **Dr Gabriel N. Mannis** from Stanford Cancer Center and discussions moderated by **Dr Elias Jabbour** from MD Anderson Cancer Center, in conjunction with content developed by the Aptitude Health clinical team

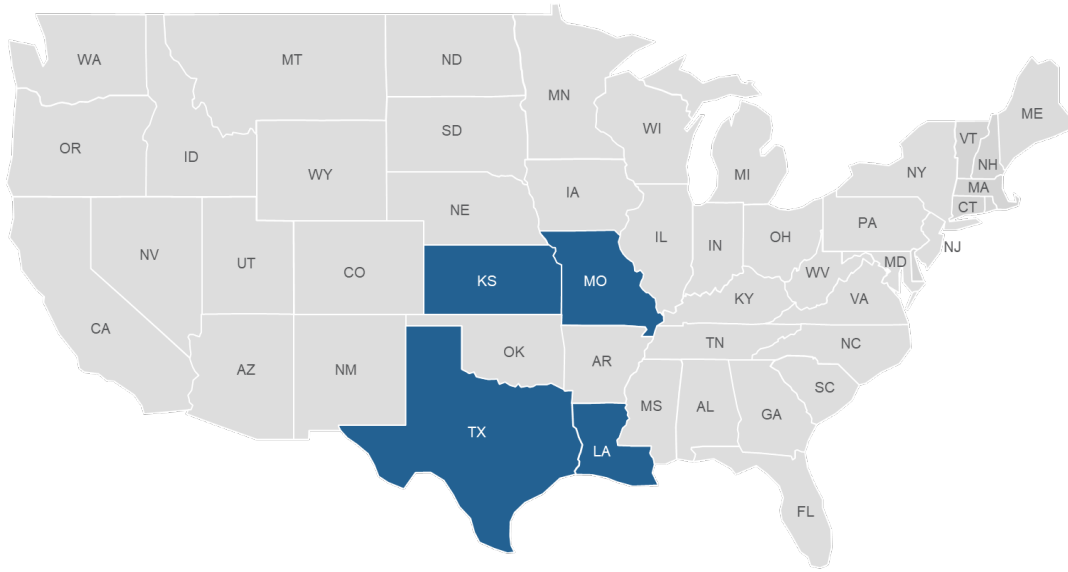
Insights on the **treatment and management of AML patients in the community setting** were obtained

Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

REPORT SNAPSHOT: ATTENDEE OVERVIEW

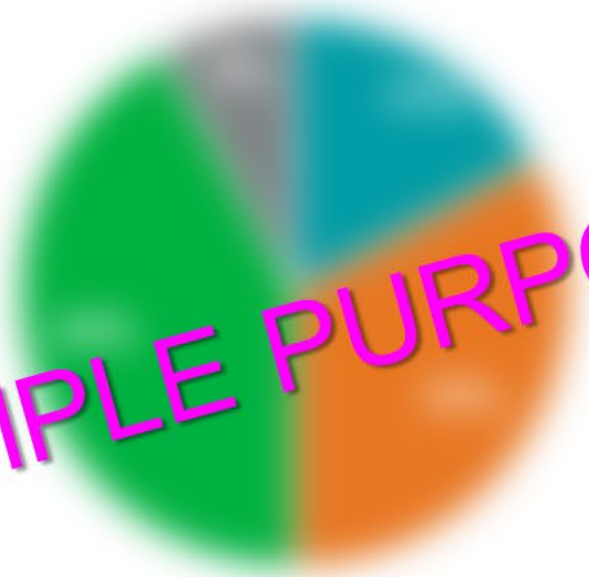
- The group of advisors comprised 10 community oncologists from across the Central United States
  - Attendees of the roundtable represented community oncologists from Kansas, Louisiana, Missouri, and Texas

INSTITUTION	CITY	STATE
The Center for Cancer & Blood Disorders	Fort Worth	TX
Cancer Center of Kansas	Wichita	KS
Texas Oncology	Dallas	TX
Texas Oncology	Tyler	TX
Texas Oncology	Wichita Falls	TX
Ochsner Medical Center	New Orleans	LA
Saint Louis University	Saint Louis	MO
Oncology Consultants	Houston	TX



REPORT SNAPSHOT: ATTENDEE DEMOGRAPHICS (1/2)

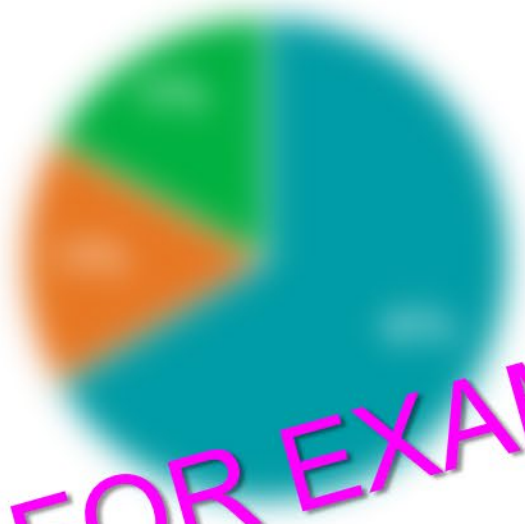
What percentage of your AML patients fall into the poor-risk category? (N = 9)



ATTENDEE DEMOGRAPHICS (2/2)

What percentage of your AML patients are 75 years or older? (N = 10)

What percentage of your AML patients are under 75 years old, but have comorbidities that prevent use of intensive chemotherapy? (N = 10)



AGENDA

Time (CT)	Topic
6.00 PM – 6.15 PM (15 min)	Introduction
6.15 PM – 7.25 PM (70 min)	First-Line Treatment of AML
7.25 PM – 7.35 PM (10 min)	Break
7.35 PM – 8.45 PM (70 min)	Management of Relapsed/Refractory AML and Promising Strategies in AML
8.45 PM – 9.00 PM (15 min)	Key Takeaways and Meeting Evaluation

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Key Insights and Discussion Summary

KEY INSIGHTS

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How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 3 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

KEY INSIGHTS

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DISCUSSION: FIRST-LINE TREATMENT OF AML (1/2)

First-Line Treatment of AML – INSIGHTS AND DATA

"I look at the patient and the age, the comorbidities, and also the psychosocial situation, whether they're able to come to the clinic for regular

- Treatment success in frontline DLBCL

- Data needed to switch from SOC in frontline

issues, so we haven't used it."

DISCUSSION: FIRST-LINE TREATMENT OF AML (2/2)

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First-Line Treatment of AML – INSIGHTS AND DATA

“[In induction treatment] when I use [antifungal therapy] posaconazole, I reduce the dose of venetoclax to 200. I used to give the treatment for

DISCUSSION: MANAGEMENT OF RELAPSE/REFRACTORY AML

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Management of Relapsed/Refractory AML – INSIGHTS AND DATA

"I think most people do not enjoy taking care of patients with relapsed/refractory AML. It is a hard thing to treat [. . .]. Outcomes for

- Treatment success in frontline (3+3/7)

- Data needed to switch from 3/7/C in frontline

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Advisor Key Takeaways

ADVISOR KEY TAKEAWAYS (1/3)

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ADVISOR		ADVISOR	
1	> I have a better understanding of sequencing therapies > I really wasn't that familiar with polatuzumab and tafasitamab but now I have a better understanding of these drugs and have a better idea of when to use them in my practice	5	> I can use less venetoclax and have good efficacy: I'm > For relapsed/refractory patients it's nice to have different options besides R-CD. and auto or going to CAR-T
2	> I have a better understanding of some of my relapse options > I'm particularly interested in the tafasitamab and hope that tafa and Rev would be tolerated for a second-line option for my very elderly patients > There's a lot more enthusiasm for targeted therapy and for things like polatuzumab that may offer lesser side effects	6	> I'm hoping that some of these second-line agents will get added onto frontline and hopefully improve the cure rate
3	> It was great to hear about innovations and what's coming down the pipeline for relapsed/refractory	7	> Very interesting to learn about all these relapsed/refractory treatments, specifically the bispecific antibodies > A lot of options coming up in the future. The only issue will be to learn how to sequence these drugs
4	> There's a lot of good options for second line than just CAR-T and transplant with decent side effect profile and good response rates > Sequencing is an issue	8	> Still R-CHOP is the standard

ADVISOR KEY TAKEAWAYS (2/3)

CASES

ADVISOR		ADVISOR	
1	> Obtaining mutation testing upfront and at relapse is > I have a better understanding of sequencing therapies > I really wasn't that familiar with ixazomib and selinexor but now I have a better understanding of these drugs and have a better idea of when to use them in my practice	5	> One learning point is that the venetoclax dosing can > For relapsed/refractory patients it's nice to have different options besides R-CD and auto or going to CAR-T
2	> I have a better understanding of some of my relapse options > I'm particularly interested in the selinexor and hope that tafa and Rev would be tolerated for a second-line option for my very elderly patients > There's a lot more enthusiasm for targeted therapy and for things like proteasomals that may offer lesser side effects	6	> I'm hoping that some of these second-line agents will get added onto frontline and hopefully improve the cure rate
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ADVISOR KEY TAKEAWAYS (3/3)

ADVISOR		ADVISOR	
1	> I have a better understanding of sequencing therapies > I really wasn't that familiar with polatuzumab and tafasitamab but now I have a better understanding of these drugs and have a better idea of when to use them in my practice	5	> My takeaway from hearing all the comments: for > For relapsed/refractory patients it's nice to have different options besides R-CD. and auto or going to CAR-T
2	> I have a better understanding of some of my relapse options > I'm particularly interested in the tafasitamab and hope that tafa and Rev would be tolerated for a second-line option for my very elderly patients > There's a lot more enthusiasm for targeted therapy and for things like polatuzumab that may offer lesser side effects	6	> I'm hoping that some of these second-line agents will get added onto frontline and hopefully improve the cure rate
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ARS Data

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First-Line Treatment of AML

ARS RESULTS

AGE AND GENOMIC AND MUTATIONAL ANALYSIS ARE THE MOST USED METHODS TO RISK-STRATIFY NEWLY DIAGNOSED AML PATIENTS

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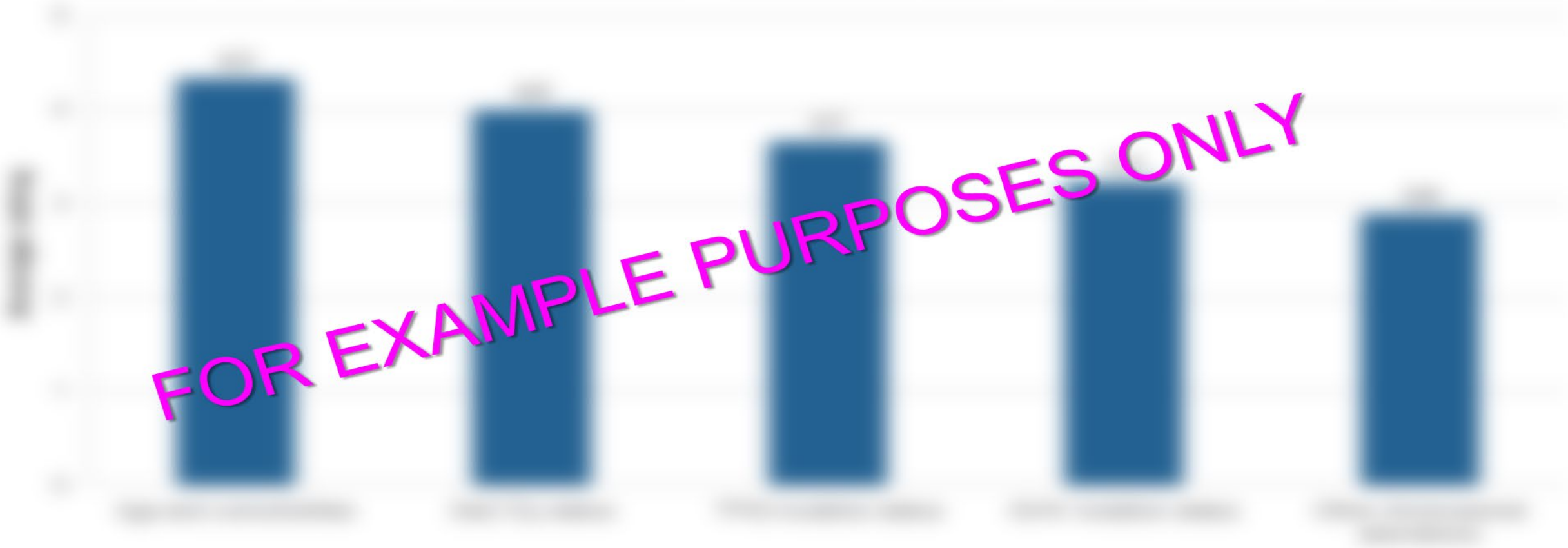
If you risk-stratify your newly diagnosed AML patients, what method do you use?
(Select all that apply) (n = 9*)



*One advisor did not respond.

FLT3, *CEBPA*, AND *IDH1/2* ARE THE MOST TESTED MOLECULAR MARKERS, FOLLOWED BY *TP53* AND *NPM1*

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In addition to cytogenetics, which of the following molecular markers are you routinely testing for in your newly diagnosed AML patients? (Select all that apply) (n = 9*)

*One advisor did not respond.

MOLECULAR/GENOMIC TESTING IS MAINLY PERFORMED OUTSIDE LOCAL HOSPITALS

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When it comes to molecular/genomic testing: (n = 9*)

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*One advisor did not respond.

THE TURNAROUND TIME TO GET FINAL TESTING RESULTS IS LONGER THAN 1 WEEK

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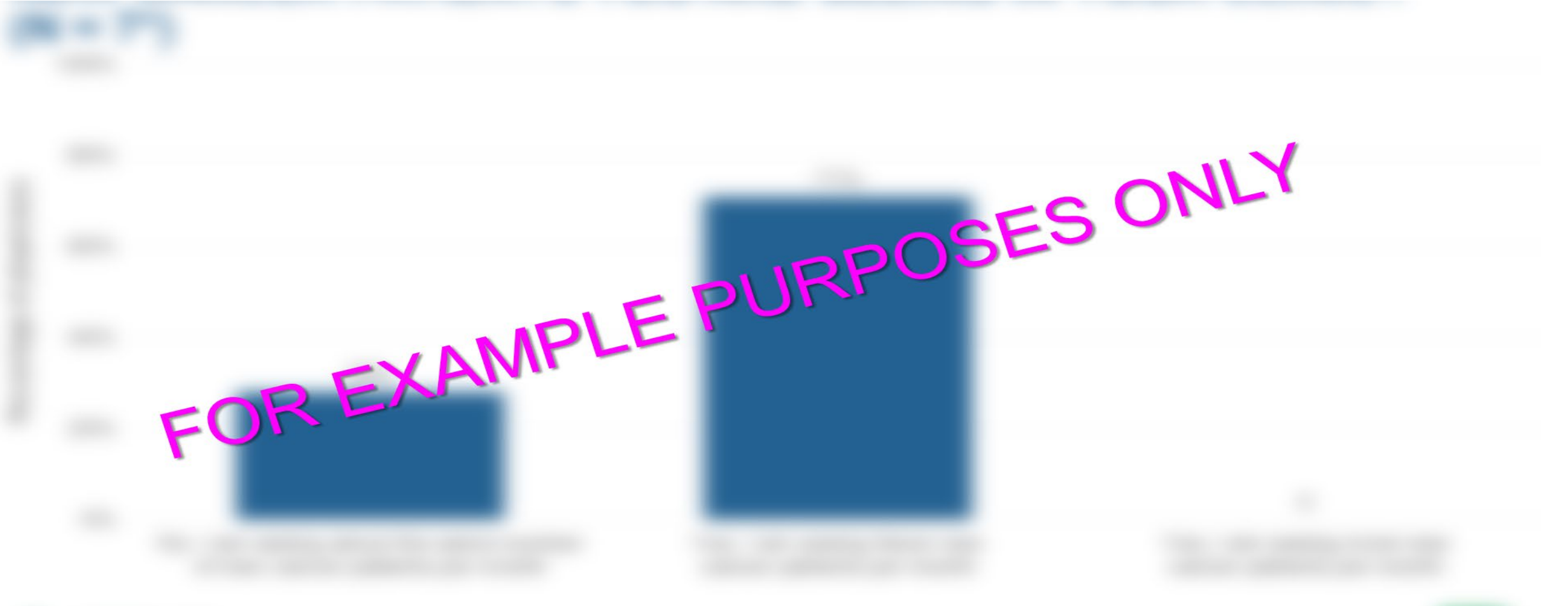
When it comes to molecular/genomic testing, the turnaround time to get the final results is: (n = 10)



MOST ADVISORS SOMETIMES START AML FRONTLINE THERAPY BEFORE THE GENOMIC/MUTATIONAL TEST RESULTS ARE AVAILABLE

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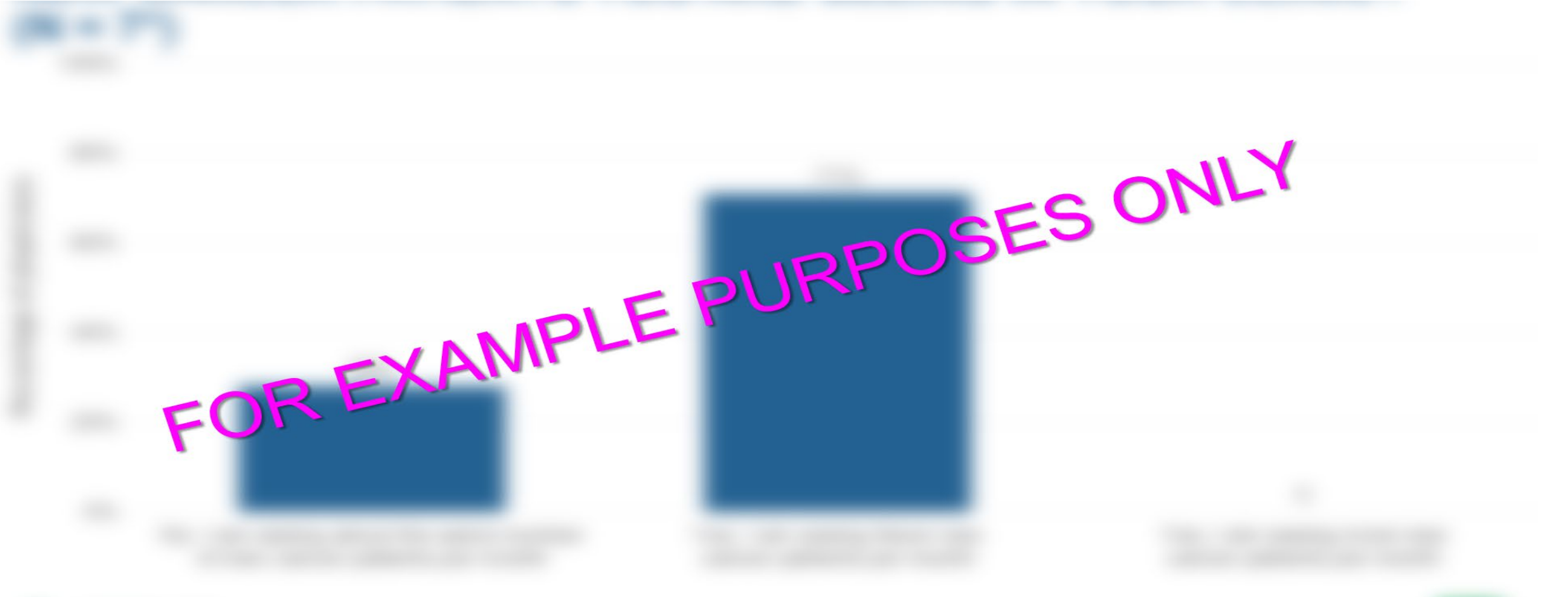
In general, the following statement describes me best: (n = 10)



MOST ADVISORS USE STANDARD 7+3 AS THE INDUCTION REGIMEN FOR A YOUNG PS 0 PATIENT WITH INTERMEDIATE-RISK AML (CD33 POSITIVE AND WITHOUT *FLT3* MUTATION)

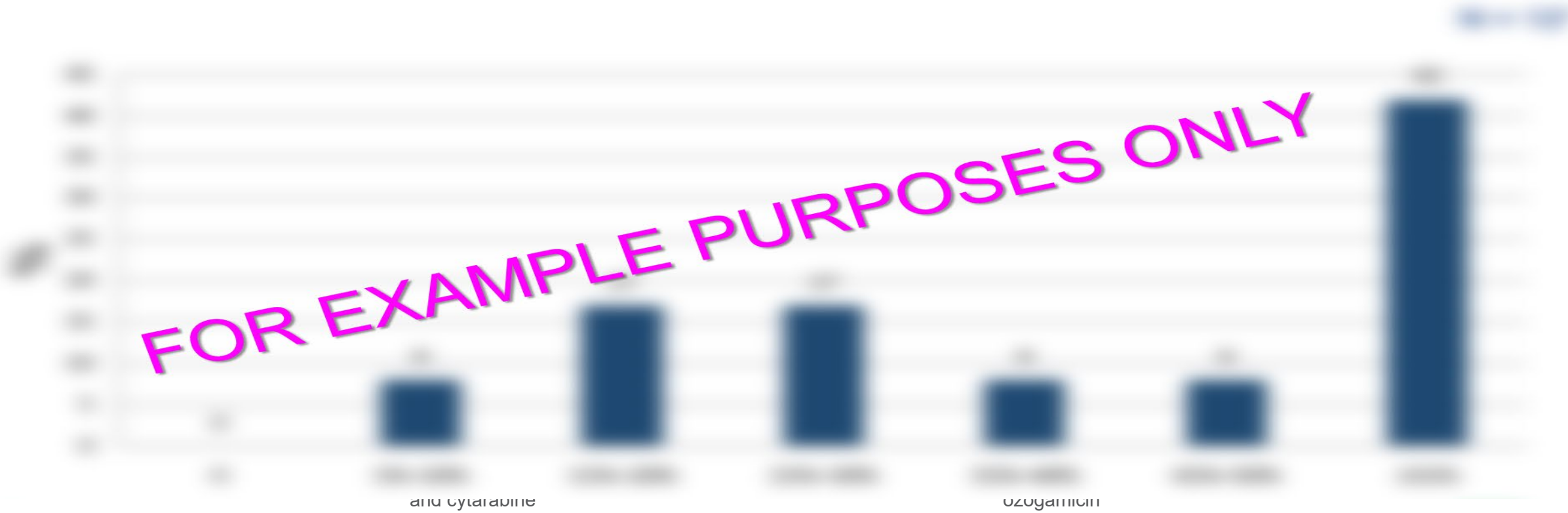
CASES

What induction regimen do you routinely recommend for a 50-year-old PS 0 patient with intermediate-risk AML (CD33 positive and without *FLT3* mutation)?

NEARLY HALF OF ADVISORS USE LIPOSOMAL CYTARABINE-DAUNORUBICIN AS THE INDUCTION REGIMEN FOR A YOUNG PS 2 PATIENT WITH CARDIOVASCULAR COMORBIDITIES AND INTERMEDIATE-RISK AML (CD33 POSITIVE AND WITHOUT *FLT3* MUTATION)

CASES

What induction regimen would you recommend for a 50-year-old PS 2 patient who has a history of cardiovascular disease, including a previous heart attack, with intermediate-risk AML (CD33 positive and without *FLT3* mutation)? (n = 9*)



*One advisor did not respond.

FOR AN ELDERLY PS 1 PATIENT WITH INTERMEDIATE-RISK AML (CD33 POSITIVE AND WITHOUT *FLT3* MUTATION), MOST ADVISORS USE VENETOCLAX (± HMA OR LDAC) AS INDUCTION REGIMEN

CASES

What induction regimen do you routinely recommend for a 77-year-old PS 1 patient with intermediate-risk AML (CD33 positive and without *FLT3* mutation)? (n = 9*)

*One advisor did not respond.

THE INDUCTION REGIMEN ROUTINELY RECOMMENDED BY MOST ADVISORS FOR AN ELDERLY PS 1 PATIENT WITH THERAPY-RELATED AML FOLLOWING TREATMENT FOR MANTLE CELL LYMPHOMA AND UNKNOWN GENOMIC PROFILING IS VENETOCLAX (± HMA OR LDAC)

CASES

What induction regimen do you routinely recommend for a 70-year-old PS 1 patient with therapy-related AML following treatment for mantle cell lymphoma (including autologous stem cell transplant)? Genomic profiling is unknown (n = 9*)

*One advisor did not respond.

FOR AN ELDERLY PS 2 PATIENT WITH INTERMEDIATE-RISK AML AND *IDH1* MUTATION, IVOSIDENIB + HMA IS THE INDUCTION REGIMEN RECOMMENDED BY NEARLY HALF OF ADVISORS, FOLLOWED BY VENETOCLAX (± HMA OR LDAC)

CASES

What induction regimen do you recommend for a 70-year-old PS 2 patient with intermediate-risk AML and *IDH1* mutation revealed by NGS? (n = 9*)

*One advisor did not respond.

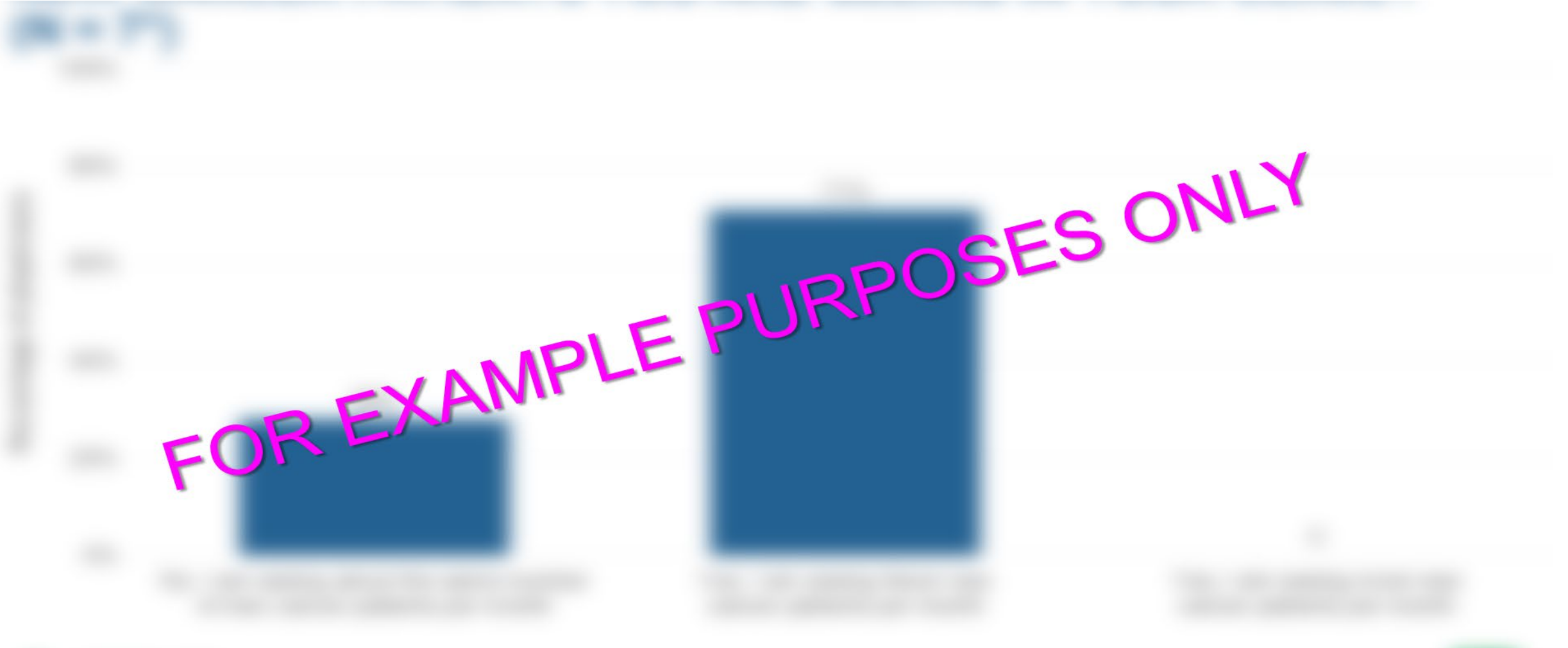
THE ADVISORS' MOST-USED DOSING SCHEDULE FOR VENETOCLAX IS DAILY DOSE RAMP-UP

Which of the following dosing schedules do you use for venetoclax in AML? (n = 9*)

*One advisor did not respond.

MOST ADVISORS MODIFY VENETOCLAX DOSING ON THE BASIS OF PROPHYLACTIC ANTIFUNGALS USE

Do you modify your dosing of venetoclax on the basis of prophylactic antifungals use? (n = 8*)



*Two advisors did not respond.

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ARS Data – Management of Relapsed/Refractory AML

BIOMARKER TESTING IS ROUTINELY REPEATED BY THE MAJORITY OF ADVISORS AT DISEASE RELAPSE

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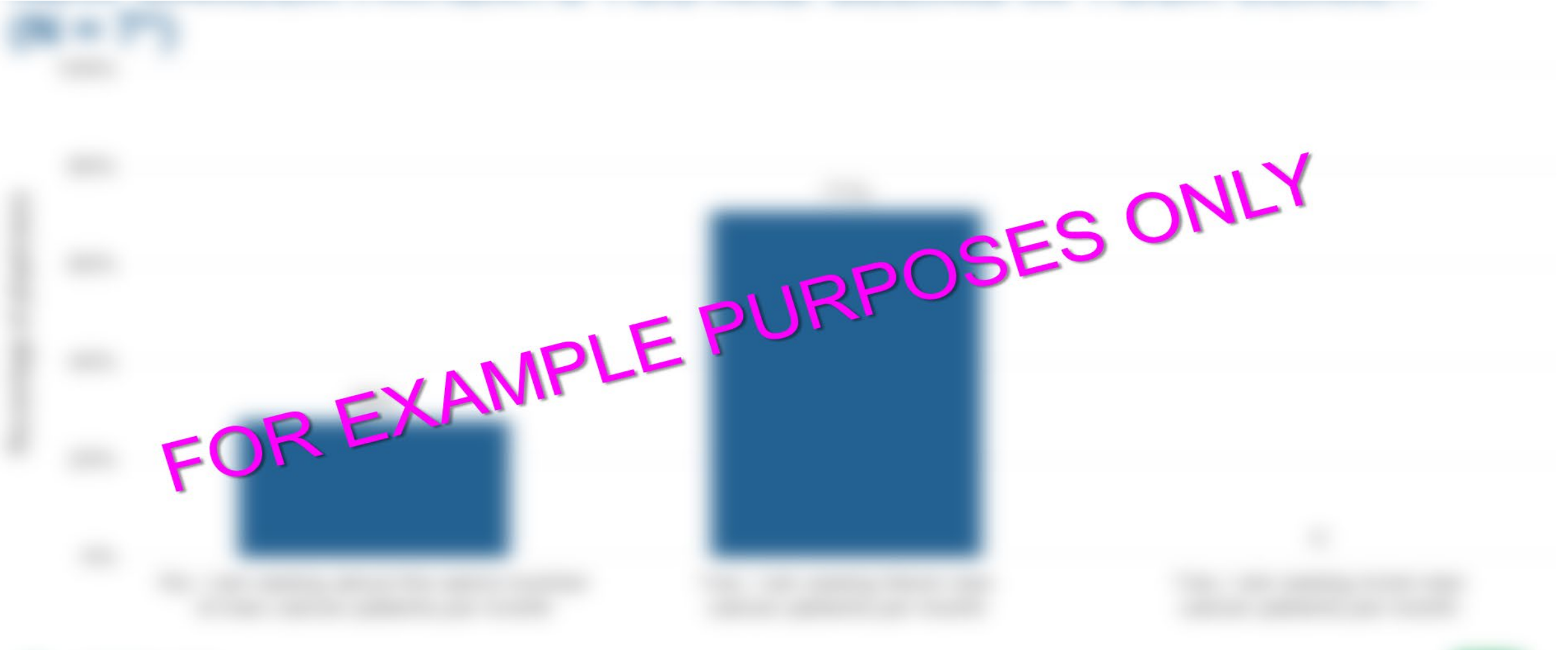
Do you routinely repeat biomarker testing in your AML patients at the time of relapse? (n = 8*)



*Two advisors did not respond.

IDH1/2 AND *FLT3* ARE CONSIDERED THE MOST IMPORTANT MUTATIONS TO BE TESTED FOR AT DISEASE RELAPSE FOR THERAPEUTIC DECISION MAKING

CASES

Which of the following mutations are most important to be checked in all patients with relapsed AML for therapeutic decision making? (n = 9*)

*One advisor did not respond.

FOR THE MAJORITY OF ADVISORS, REPEATING 7+3 OR BMT EVALUATION AND POSSIBLE REINDUCTION ARE THE PREFERRED TREATMENT APPROACH FOR THE DESCRIBED YOUNG PATIENT WITH INVERSION 16, PS 0, AND COMORBIDITIES AT DISEASE RELAPSE

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*One advisor did not respond.

MOST ADVISORS WOULD CONTINUE TREATING THE DESCRIBED PATIENT WITH INDUCTION LIPOSOMAL CYTARABINE-DAUNORUBICIN WHEN THEY SHOW REDUCTION IN DISEASE UPON DAY 14 BONE MARROW

CASES

*One advisor did not respond.

HALF OF THE ADVISORS WOULD TREAT THE DESCRIBED ELDERLY PATIENT WITH ENASIDENIB AT DISEASE RELAPSE

CASES

*Two advisors did not respond.