



Insights Into Management and Treatment Options for Acute Myeloid Leukemia (AML)

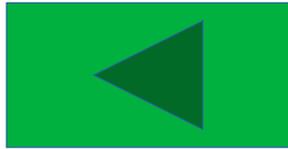
July 20, 2021

Speaker and Chair: Elias Jabbour, MD
MD Anderson Cancer Center

How to Navigate This Report



Click to move to topic of interest or ARS supporting data



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MEETING OBJECTIVES

Gain advisors' perspectives on existing and emerging treatments for newly diagnosed and relapsed/refractory AML

Report Snapshot: Session Overview



A moderated roundtable discussion was held with community oncologists from 7 locations throughout the United States, in a virtual setting on **July 20, 2021**

Disease state and data presentations were led by **Elias Jabbour, MD**, from MD Anderson Cancer Center in conjunction with content developed by the Aptitude Health clinical team

Insights were obtained on physicians' preferred therapy choices; targeted therapies including *FLT3*-, *IDH1/2*-, and *BCL2*-targeting agents, Hedgehog pathway inhibitors; and maintenance therapies

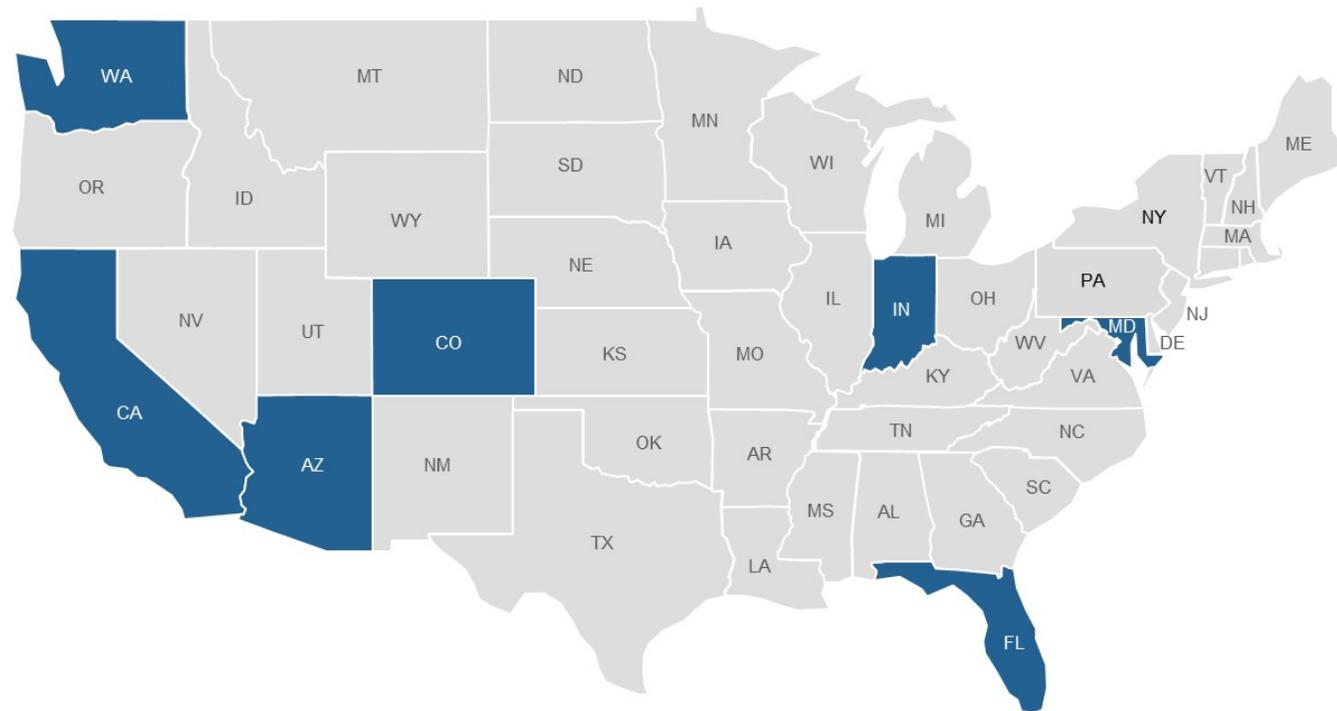
Data collection was accomplished through audience response system (ARS) questions and in-depth moderated discussion

Report Snapshot: Attendee Overview



> The group of advisors was composed of 10 community oncologists from 7 states across the US

INSTITUTION	CITY	STATE
Sutter Alta Bates Summit Medical Center	Berkeley	CA
Community Hospital St. Catherine Hospital	Munster East Chicago	IN
Virginia Mason Medical Center	Mercer Island	WA
Broward Health Coral Springs	Tamarac	FL
Chesapeake Oncology Hematology Associates	Annapolis	MD
Mid Florida Cancer Centers	Orange City	FL
David Walsh Center	Sterling	CO
Cancer Treatments Centers of America	Phoenix	AZ
Northern Hematology Oncology	Thornton	CO
Pacific Shores Medical Group	Long Beach	CA



Report Snapshot: Agenda



Time (CT)	Topic
6.00 PM – 6.15 PM (15 min)	Introduction and ARS Questions <ul style="list-style-type: none">• Program overview• ARS questions
6.15 PM – 7.25 PM (70 min)	First-Line Treatment of AML <ul style="list-style-type: none">• Overview of current data• Reaction and discussion
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 <ul style="list-style-type: none">• Overview of current data• ARS questions• Reaction and discussion
8.45 PM – 9.00 PM (15 min)	Key Takeaways and Meeting Evaluation



Topline Takeaways and Strategic Recommendations

Meeting Objectives Were Achieved: Topline Takeaways



OBJECTIVE

PROCESS

INSIGHTS

> Learn community

Through ARS questions and

> Most of these advisors treat their older, frail, and unfit AML patients.

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[Blurred text under Insights column]



Key Insights and Discussion Summary

Key Insights: Management and Treatment Options for AML



REPORT OBJECTIVES

- > Learn community oncologists' treatment paradigms for frontline/newly diagnosed AML
- > Understand advisors' current approaches to treating relapsed/refractory AML
- > Understand community oncologists' decision-making in their choice of therapy on the basis of patient type/prior therapy

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

MRD is routinely assessed at complete response (CR) by either multiplex PCR, MRD or multiplex flow. Interventions are used to treat MRD+ patients in the frontline by about half of the advisors (50%).

- MRD is assessed at CR by half of advisors (50%). The other advisors assess MRD at CR and 2 months from induction, and every 3 months thereafter (20%). Only a few assess CR/CR2 versus MRD positivity.
 - The time interval approach is performed either by the pathologists in the management 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 multiplex PCR (20%), and MRD (20%). The multiplex flow is used by 20% of advisors.
 - Although MRD 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 continued, followed by consolidation.
 - However, at least 3 advisors are using interventions to induce MRD negativity after induction in patients or after consolidation in patients. The remaining advisors would refer their patients to management departments.

Key Insights: Management and Treatment Options for AML



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 - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
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 - Although MRD 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 continued, followed by consolidation.
 - However, at least 2 advisors are using intravenous to induce MRD negativity after induction in patients in either consolidation or relapse. The remaining advisors would refer their patients to management departments.

Key Insights: Management and Treatment Options for AML



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 - The bone marrow biopsy is performed either by the pathologist in the management center, or by the advisor themselves, depending on the hospital.
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Advisors may or may not admit patients to local hospitals for induction with venetoclax, but noted that venetoclax is not always readily available at these centers

- > In these circumstances, it is common to have the venetoclax prescription filled as an outpatient and tell the patient, a member of their family, or other caregiver to bring this medication to the hospital
 - One advisor noted that their facility does keep 2–3 days of venetoclax on hand as startup medication until a regular venetoclax supply can be obtained at a local pharmacy
- > Some advisors do release their AML patients from the hospital following initial venetoclax treatment if they are medically stable, and will continue these patients on venetoclax on an outpatient basis

Key Insights: Management and Treatment Options for AML



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 - The more routine approach is performed either by the pathologists in the management centers, or by the advisors themselves, depending on the hospital.
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Several advisors said they prefer to remain strict in reaching the entire 28 days of venetoclax dosing while addressing treatment-related adverse events (AEs) such as myelosuppression as they arise

Other advisors are more flexible in their initial treatment cycle (and subsequent) with venetoclax, noting it is not uncommon for them to interrupt or dose-reduce venetoclax to mitigate AEs and wait for BM to recover

> Several advisors also noted they commonly use growth factors to address myelosuppression, but that pegfilgrastim (Neulasta®) can be difficult to obtain at community practices, due to financial coverage or high copays

After the initial cycle with venetoclax, advisors employ varying dosing strategies ranging from 7 to 14 days, to keep patients on this therapy while also ensuring AEs are manageable

> A few advisors said they also adjust their dosing strategy for azacitidine to facilitate managing AEs

Several advisors noted their good experience with venetoclax, with some patients able to stay on this regimen for long periods of time (up to ~1.5–2 years)

> Most physicians noted they have observed minimal numbers of patients with infections while on this regimen

Key Insights: Management and Treatment Options for AML



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INSIGHTS FROM DISCUSSION

“We have some venetoclax in the hospital, and we [get] patient prescriptions within 2 or 3 days . . . and we bring it from the clinic to the hospital the next day when I round.”

1. Treatment success in frontline AML

Dr. [Name] discussed the importance of having venetoclax in the hospital. He noted that having it in the hospital allows for a more streamlined process for patients, as they can get their prescriptions within 2 or 3 days. He also mentioned that they bring the medication from the clinic to the hospital the next day when they round. This ensures that the medication is available when needed, which is crucial for patient care.

2. Data needed to support front-line AML

Dr. [Name] discussed the importance of having data to support front-line AML. He mentioned that they need to know if the medication is working and if it is safe. He also mentioned that they need to know if the medication is cost-effective. He noted that they have been looking at various data points, including efficacy, safety, and quality of life. He also mentioned that they have been looking at the impact of the medication on the patient's overall health and well-being. He noted that they have been looking at the impact of the medication on the patient's ability to work and live their lives. He also mentioned that they have been looking at the impact of the medication on the patient's quality of life. He noted that they have been looking at the impact of the medication on the patient's overall health and well-being.

INSIGHTS FROM DISCUSSION

"We hold treatment, wait for the counts to recover. I don't give [venetoclax] continuous."

"I usually when they become neutropenic, I end up stopping the venetoclax, watching, and usually doing

the usual things that you do when they're neutropenic. There's no reason to believe that it's better. It's not like you're doing anything better. It's just like you're watching.

I would not give any significant long-term benefit. I think when you're neutropenic, I would not use a treatment option that's going to be 100% or 90%, and I would not start the disease that way at 1 year. I think it's important that there is significant benefit with the treatment, and usually going from something like that.

That's all, a lot of things have been done, nothing is better than 100% and 90%. It's usually better with less 100% and 90% for the patient.

I would not give any significant long-term benefit. I think when you're neutropenic, I would not use a treatment option that's going to be 100% or 90%, and I would not start the disease that way at 1 year. I think it's important that there is significant benefit with the treatment, and usually going from something like that.

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Advisor Key Takeaways

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ADVISOR	ADVISOR
<ul style="list-style-type: none"> > Will consider using some FLAG regimens in their AML • Have a better understanding of sequencing therapies • Have a better understanding of how to use FLAG • Have a better understanding of when to use FLAG 	<ul style="list-style-type: none"> > Eager to see new data with targeted therapies (FLT3i, IDH1/2, etc.) • Have a better understanding of when to use FLAG
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Advisor Key Takeaways



ADVISOR

> Views the newer therapies currently under

- There is a better understanding of sequencing therapies
- There is a better understanding of the combination and sequencing of these drugs and how a better idea of when to use them is being gained

- There is a better understanding of some of the newer agents
- It is particularly interesting in the combination and how the data and how much can be expected for a second-line agent for my own clinical practice
- There is a lot more evidence for targeted therapy and to change the combination that may offer some side effects

- It was good to hear about innovations and what's coming down the pipeline for immunotherapy

- There is a lot of good options for second-line that just look like first-line management with decent side effect profile and good response rates
- Sequencing is an issue

ADVISOR

> Use antifungal medications in newly diagnosed AML patients (when using venetoclax)

- The combination of these agents is not to have different options besides FICZ and with or going to GMR1

- It is hoping that some of these immunotherapy agents will get added into frontline and hopefully improve the outcomes

- It is interesting to learn about all these immunotherapy treatments, especially the targeted antibodies
- It is a lot of options coming up in the future. The only issue will be to learn how to sequence these drugs

- Not to forget to be updated



Audience Response System (ARS) Data

Advisors Have a Variety of Risk-Stratifying Considerations for Their AML Patients, Relying Slightly More on Comorbidities and Genomic Factors

FOR EXAMPLE PURPOSES ONLY

Nearly Half of the Advisors (43%) Said Poor-Risk Patients Comprise Approximately One-Fifth of Their Total AML Patients

What percentage of your AML patients fall into the poor-risk category? (N = 7*)

FOR EXAMPLE PURPOSES ONLY

For the Largest Proportion of the Advisors (58% = 29% + 29%), AML Patients at Least 75 Years Old Make Up Approximately One-Third to One-Half of Their Total AML Patient Population

FOR EXAMPLE PURPOSES ONLY

*Three advisors did not respond.

These Advisors Have Significant Proportions of AML Patients Who Are Younger but Cannot Tolerate Intensive Chemotherapy Because of Comorbidities

FOR EXAMPLE PURPOSES ONLY

The Advisors Routinely Test for Expected AML-Associated Molecular Markers/Mutations

FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.



All the Advisors Send Their Molecular and Genetic Testing Panels to an External Lab



FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.

The Largest Proportion of the Advisors (80%) Receive Their Molecular and Genetic Test Results Within the Second Week After Sending Specimens for Testing

FOR EXAMPLE PURPOSES ONLY

The Great Majority of Advisors (88%) Sometimes Begin Treatment for Their Newly Diagnosed AML Patients Before Receiving Molecular and Genetic Test Results

FOR EXAMPLE PURPOSES ONLY

*Two advisors did not respond.

Most of the Advisors (56%) Chose Standard 7+3 Chemotherapy + a CD33-Targeting Agent for a Younger, Fit AML Patient Who Is CD33 Positive

FOR EXAMPLE PURPOSES ONLY

For a Younger CD33-Positive Patient Who Cannot Accept Intensive Chemotherapy Due to Comorbidities, Over Half of the Advisors (56%) Chose Venetoclax (\pm HMA or LDAC) for Induction

FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.

For an Older CD33-Positive Patient With Good Performance Status and No *FLT3* Mutation, the Majority of the Advisors Chose Venetoclax (\pm HMA or LDAC) for Induction

FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.



For an Intermediate-Risk Older Patient With Poorer PS and *IDH1* Mutation, Advisors Were Split on Whether to Choose Venetoclax (\pm HMA or LDAC) or Single-Agent *IDH1*-Targeting Agent

FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.



More Than Three-Fourths of Advisors (78%) Use the Prescribed Daily Dose Ramp-up When Initiating Therapy With Venetoclax

CASES

FOR EXAMPLE PURPOSES ONLY

All Advisors Who Use Prophylactic Antifungal Medications With Venetoclax Modify the Venetoclax Dose When These Agents Are Used Concomitantly

FOR EXAMPLE PURPOSES ONLY

*Two advisors did not respond.

All Advisors Retest for Biomarkers on Relapse; Nearly All (88%) Do a Full-Panel Repeat

FOR EXAMPLE PURPOSES ONLY

The Majority of Advisors (75%) Selected *FLT3* and *IDH1/2* as the Most Important Mutations to Test for on Relapse

FOR EXAMPLE PURPOSES ONLY

The Largest Proportion of Advisors (43%) Would Refer a Relapsed Patient, Following Induction Chemotherapy and HiDAC Consolidation, for Bone Marrow Transplant Evaluation and Possible Reinduction

FOR EXAMPLE PURPOSES ONLY

Percentage

*Three advisors did not respond.



For a Patient Who Showed Significant Blasts After Anthracycline-Based Induction, Half of the Advisors Would Next Treat With FLAG-IDA

FOR EXAMPLE PURPOSES ONLY

Percentage

*Two advisors did not respond.

For an Older AML Patient Who Relapsed at 12 Months but Acquired an *IDH2* Mutation, the Largest Proportion of Advisors (50%) Would Treat This Patient With Single-Agent *IDH2* Inhibitor

FOR EXAMPLE PURPOSES ONLY

*Two advisors did not respond.

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