Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/clinical-insights-into-higher-risk-mds-treatment-goals-and-strategies/17850/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Clinical Insights into Higher-Risk MDS: Treatment Goals and Strategies

Announcer:
You're listening to Project Oncology on ReachMD, and this medical industry feature, titled "*Clinical Insights into Higher-Risk MDS: Treatment Goals and Strategies*", is developed and sponsored by AbbVie. This activity is intended for United States healthcare professionals only. The US Medical Affairs department of AbbVie Inc. is the sole author and copyright owner of this presentation and has paid ReachMD to host this presentation. AbbVie is solely responsible for all written and oral content within this presentation. The following speakers have received compensation from the US Medical Affairs department of AbbVie Inc. to prepare and present the following information and are speaking on behalf of AbbVie.

Here's your host, Dr. Gates Colbert.

Dr. Colbert:
This is ReachMD, and I'm Dr. Gates Colbert.

Today we're diving into myelodysplastic syndromes, or MDS which about 13,400 cases are diagnosed each year in the United States.[1] These clonal myeloid stem cell neoplasms involve bone marrow failure leading to cytopenias. Around 30 percent of MDS patients will develop acute myeloid leukemia, or AML, and sadly, most patients will die from complications from the disease.[1–4] MDS can be stratified as lower-risk or higher-risk, with higher-risk MDS having a very poor prognosis with a median overall survival of about 1.5 years.[5–8] Today, we'll explore how to best manage higher-risk MDS patients through proper diagnosis, risk assessment, and treatment selection. Joining me today to help us understand these challenges and address unmet needs, are Drs. Uma Borate and James Dugan. Dr. Borate is an Associate Professor and the Director of Acute Leukemia Clinical Research at The James: Ohio State University Comprehensive Cancer Center, in Columbus.

Dr. Borate, welcome to the program.

Dr. Borate:
Thank you for having me.

Dr. Colbert:
And also with us is Dr. James Dugan, a hematologist and the physician lead for the Transplant and Cellular Therapy department at Novant Health Care Institute in Winston-Salem, North Carolina. Dr. Dugan, thank you for joining us today.

Dr. Dugan:
Thank you. It's great to be here.

Announcer: Chapter 1: MDS Diagnosis, Risk Assessment, and Treatment Goals for HR-MDS

Dr. Colbert:
Let's start off with you, Dr. Borate. How is MDS diagnosed, and what are the best practices for diagnosing MDS?

Dr. Borate:
So, the MDS diagnosis journey begins after routine lab work which typically shows low blood counts, like anemia, thrombocytopenia, or neutropenia.[9] These persistent, unexplained cytopenias are essential for an MDS diagnosis. And once we rule out other causes through additional testing, we then proceed with a bone marrow aspirate and biopsy to confirm the diagnosis of MDS.[7,10] Now a definitive

diagnosis of MDS typically includes clinical, morphological, and genetic factors. In addition to the persistent cytopenias without any other cause, the diagnosis also needs at least one of the following, such as dysplasia in at least 10 percent in one or more of the three major bone marrow cell lines, a blast count between five to 19 percent, or an MDS-defining genetic abnormality.[10,11] From the biopsy, we check the percentage of blasts, the cell morphology, and the bone marrow structure. And then, in addition cytogenetic and molecular testing helps us identify genetic abnormalities that are linked to the prognosis. This information is all really important to calculate a prognostic score, which will then in turn guide the treatment plan for the patient based on the identified risk category.[2,7–9]

Dr. Colbert:
Now turning to you, Dr. Dugan, can you tell us more about risk assessment for MDS? What's the role of prognostication scores for MDS in guiding treatment decisions and how have they evolved?

Dr. Dugan:
Yeah, I'd be happy to. Because MDS is a heterogeneous disease with different factors affecting AML transformation and survival, we need to be able to accurately assess a patient's risk in order to provide them with the most appropriate treatment regimens. In clinical practice, we use standardized risk-assessment tools to stratify patients based on a prognostic score.[2,7,10] Risk assessment for MDS patients is important because the treatment goals will differ greatly based on this risk.[1] Lower-risk MDS presents more indolently, so we often focus on symptom management and reducing complications. But, as mentioned earlier, higher-risk MDS behaves more aggressively with a high mortality rate and a median overall survival of only one and a half years with current treatment options. So our goals here are to prolong survival and improve or maintain quality of life.[12] The Revised International Prognostic Scoring System, or IPSS-R, is a widely used tool for risk assessment. It assesses cytopenia severity, blast percentage, and cytogenetic abnormalities to calculate a risk score. However, it doesn't account for somatic mutations that add additional risk.[7] To address this, the International Working Group for Prognosis in MDS developed a Molecular International Prognostic Scoring System, or IPSS-M. This newer system includes marrow blast percentages, cytopenias, IPSS-R cytogenetic categories, and genetic information from 16 main effect genes and 15 residual genes, offering superior accuracy compared to IPSS-R.[8] There are free tools online to help clinicians conveniently calculate IPSS-R and IPSS-M scores for patients with MDS.

Dr. Colbert:
And building on these tools, starting with you Dr. Borate, what practical challenges have you encountered with assessing risk?

Dr. Borate:
There's always challenges with MDS risk assessment because the field is constantly changing as we learn new information. So it's important to stay current and use the right risk assessment tool because it impacts not only how you generate a prognostic score, but also how you explain the diagnosis and prognosis to your patients. That said, staying current and accessing testing can definitely be a challenge for all of us.

Dr. Colbert:
Now, how about you Dr. Dugan, what are practical challenges you've seen in your experience?

Dr. Dugan:
Yeah, so in my experience IPSS-M may re-stratify some patients from intermediate to high risk based on molecular mutation information, and that can change the decision whether to move to transplant. It could be a challenge in some community centers if they can't get this information right away. We also have had insurance say that they aren't going to accept our assessment of high risk based on IPSS-M for patients to undergo transplant and that they were only taking IPSS-R. We've appealed those things and eventually they've changed course, but this is something that we've seen a few times.

Dr. Colbert:
Staying with stratifying risk with the IPSS-M tool, sometimes mutation results for all 31 genes are unavailable, what practical challenges does this pose, Dr. Dugan?

Dr. Dugan:
So not being able to get those 31 genes is tricky for treating MDS appropriately, even without considering transplant. For example, RUNX1 and U2AF1 mutations are associated with poor prognosis and AML transformation.[13,14] As you know, you continue to treat these patients, even though the patient is more likely to not have a response. Having the knowledge is important to be able to filter it into the conversation and help guide patient expectations. How about you Dr. Borate?

Dr. Borate:
Absolutely, I agree with you Dr. Dugan. On a related note, given these challenges, I'd like to mention that we have results from a large

real-world evidence study called VALIDATE, integrating a publicly available dataset with data from 14 specialized MDS treatment centers and looking at the performance of the IPSS-M even with some missing molecular mutation data.[15] To me, an important finding from the study is that you don't have to have every gene mutation resulted to get the benefit. If you have data from a few key mutations, such as TP53, the IPSS-M results from that will still give you meaningful information.

Dr. Colbert:
So, Dr. Borate, can you tell us more about the treatment goals for both lower-risk and higher-risk MDS?

Dr. Borate:
Sure. For lower-risk MDS, the treatment goals are reducing symptoms, decreasing or hopefully eliminating the need for transfusions, and minimizing complications from cytopenias. Our goal is to manage the disease for symptom control while obviously maintaining a good quality of life for the patient.[12]

With higher-risk MDS, we must urgently treat patients to prolong their survival. We aim to do this by improving their cytopenias, achieving remission when possible, and preventing or delaying AML progression. Let's also keep in mind that extending survival should go hand in hand with enhancing their quality of life.[5,12]

Announcer: Chapter 2: Treatment Algorithm of HR-MDS

Dr. Colbert:
Let's dive further into treatment for higher-risk MDS. Dr. Dugan, could you explain the standard treatment approach for these patients?

Dr. Dugan:
Sure. The only potential cure for higher-risk MDS is an allogeneic stem cell transplant. It's vital to promptly screen all patients for eligibility to offer curative therapy to those who are candidates.[5,16] For the many patients who aren't eligible for a transplant, the standard treatment includes hypomethylating agents, or HMAs, which help prolong survival and reduce the risk of AML transformation.[5,16] Supportive care also plays a role in managing cytopenias and infectious complications in higher-risk MDS, often with transfusions for anemia and thrombocytopenia, and anti-infective prophylaxis to reduce infection risk from neutropenia.[17–19]

Dr. Colbert:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Gates Colbert, and today I'm speaking with Dr. Uma Borate and Dr. James Dugan about treatment approaches for MDS.

So with the information that Dr. Dugan just discussed in mind, Dr. Borate, what are some of the considerations and challenges for stem cell transplant in higher-risk MDS patients?

Dr. Borate:
So as Dr. Dugan noted, stem cell transplant is the *only* potentially curative treatment for higher-risk MDS. So while not every MDS patient is able to undergo this intensive regimen, it's critical that all candidate patients at least be evaluated for eligibility to potentially benefit from this therapy.[5,16]

For eligible patients, current pre-transplant bridging therapy options aren't ideal due to the trade-off between the clinical response and toxicity. We still need more effective and less toxic bridging therapies for potential stem cell transplant-eligible patients.

Dr. Colbert:
And this next question is for both of you, Dr. Borate first, what common challenges have you or your colleagues experienced once the right patient is identified to undergo transplant?

Dr. Borate:
So transplants are such a complex process, and there are so many factors that go beyond just the physical fitness or disease aspects of the patient. These include social support, financial burden, and other elements tied to social determinants of health—factors that are so often beyond our control.[20] So there continues to be significant challenges in ensuring that the right patients can undergo transplant. Dr. Dugan, what have you seen?

Dr. Dugan:
Dr. Borate, I completely agree. Sometimes it can just be personal preference or lack of education, some patients may not really understand why they would spend a month or longer in the hospital, and they're just not going to do that. So those reasons have nothing to do with their health but are more related to the social situations that come with each patient that makes the disease even more heterogeneous.[20] You talk about MDS itself, and then consider MDS in a person, and that makes it very complicated.

Dr. Colbert:
Now coming back to you, Dr. Dugan, what is the role of HMA monotherapy in treating higher-risk MDS patients who are ineligible for stem cell transplant?

Dr. Dugan:
Only a minority of patients are eligible for stem cell transplants due to age and comorbidities. For higher-risk MDS patients, HMA monotherapy has been the standard since the 2009 AZA-001 study, which showed a median overall survival of about 24 months.[5,21]

However, newer studies have struggled to replicate this result. Four contemporary randomized controlled trials that are published within the past few years reported an average overall survival of about 18 months for HMA monotherapy.[22–25] And a meta-analyses of multiple randomized controlled trials and observational studies has estimated the pooled complete remission rate was found to be between 14 and 16 percent, with a median duration of response of only about 10 months.[5] It can take about four to five cycles, and sometimes up to 10, to even see this response.[26]

And while HMA monotherapy remains a cornerstone of treatment for stem cell transplant-ineligible higher-risk MDS patients, it does have limitations.

- These include: The median duration of response to HMAs is typically no more than one year, and very few patients achieve long-lasting remissions.[5,27,28]
- The prognosis for patients who fail HMA therapy is generally poor, with median survival often less than six months.[27,28]
- While HMAs can be effective across various cytogenetic subgroups, responses are usually short-lived in patients with poor-risk cytogenetic abnormalities.[27,28]
- HMA therapy can cause significant hematologic toxicities, including neutropenia and thrombocytopenia, which require careful management and can impact quality of life.[26,29]

Announcer: Chapter 3: Cytopenia Management in HR-MDS

Dr. Colbert:
Dr. Borate, can you tell us more about the hematologic toxicities of HMA monotherapy in higher-risk MDS patients?

Dr. Borate:
Sure. Cytopenias are a major concern in higher-risk MDS, as most MDS patients die from complications related to cytopenias. While some patients may experience blood count recovery once the underlying disease is improved while on HMA therapies, HMAs can also be myelosuppressive and cause cytopenias.[26,29] Although the rate of cytopenias is highest during the first treatment cycles, many patients can continue to experience anemia and neutropenia and thrombocytopenia even up to cycle nine or ten.[29] For example, in the AZA-001 and CALGB 9221 studies, over three-quarters of patients had hematologic adverse events, like anemia, thrombocytopenia, and neutropenia.[26,29] So managing cytopenias is especially important for our patients on HMA monotherapy.

Dr. Colbert:
And how can we manage hematologic toxicity in higher-risk MDS patients on HMA monotherapy, Dr. Dugan?

Dr. Dugan:
Well, cytopenias can be managed by dose delays, dose reductions, or supportive care such as transfusions.[26] For example, in the AZA-001 and CALGB 9221 trials, roughly around 25 percent of hematologic adverse events were managed by dose delay, and about 10 percent by dose reductions.[26,29] And supportive care measures such as erythropoiesis-stimulating agents or ESAs may be useful to stimulate red blood cell production for some higher risk patients and may reduce their transfusion burden.[29,30] But in my experience, oftentimes ESAs won't work in this scenario because in higher risk patients, if the factories to produce red blood cells are already knocked down, pouring more gasoline in the tank won't make them produce more red blood cells. So these patients will still be subject to red blood cell and platelet transfusions while getting HMA therapy.

But whether due to the underlying disease or hematologic toxicity from HMA therapy, transfusions are commonly used to manage low blood cell counts in higher-risk MDS patients, with almost 90 percent of anemia cases and around 30 percent of thrombocytopenia cases managed this way.[29] However, frequent transfusions can lead to complications such as alloimmunization, be associated with even worse clinical outcomes, and reduced quality of life.[17–19] So achieving transfusion independence is an important clinical goal for both longer survival and improved quality of care for patients with high-risk MDS.

Dr. Colbert:
Dr. Borate, and how can neutropenia be managed in higher-risk MDS patients?

Dr. Borate:
Managing neutropenia in high-risk MDS patients is crucial for preventing infections. If your patient starts the journey already neutropenic and remains neutropenic until they achieve a response, the first step in infection prevention is to start prophylactic antimicrobials, such as antibiotics, antivirals, and antifungals.[30]

We aim to reserve the use of growth factors like G-CSF for patients with severe illness, febrile neutropenia, hospitalizations, or severe infections. It's important not to use them routinely in patients with asymptomatic neutropenia just to raise the ANC and start the next treatment cycle. This approach can sometimes complicate the situation, particularly in MDS patients who haven't been adequately treated. So if you give a growth factor and then perform a bone marrow biopsy, you could see circulating blasts, which can then lead to the uncertainty—are these due to the disease, or are they a result of the growth factor? So it's essential to use growth factors judiciously and not as a routine measure.[30]

Dr. Colbert:
So to both of you, what are practice challenges you or your colleagues have encountered using HMAs? And what are your best practices with HMAs to achieve optimal outcomes in High-risk-MDS?

Dr. Borate:
You have to give treatment in a timely manner and also be patient, vigilant, and thoughtful, keep in mind that cytopenias are expected, and give treatment breaks or adjust the dose as needed, as well as maximize supportive care. Dr. Dugan?

Dr. Dugan:
We have experienced both ways with HMAs. Some patients can do well on HMA alone where after a few cycles they're transfusion independent and doing better, and they can remain on a routine schedule for HMA. But in my experience, often, these patients will remain cytopenic. They require a lot of transfusion support with reduced quality of life because they spend a lot of time in clinic. So, unfortunately, HMAs are not a slam dunk.

Announcer: Chapter 4: Opportunities for Future Advancements in HR-MDS

Dr. Colbert:
And as we near the end of our program, Dr. Dugan, could you summarize the key challenges in treating higher-risk MDS and the potential for future advancements?

Dr. Dugan:
Sure. There are several significant treatment challenges for higher-risk MDS. First, most patients are ineligible for transplant. For these patients, we haven't had any new therapies in the first-line setting in nearly two decades, and we currently have limited effective therapy options beyond HMAs. Unfortunately, 30 to 40 percent of patients don't respond to or tolerate HMAs. For patients who do respond, the response may not be durable, and there are limited second-line therapy options for refractory or relapsed patients.[27] Despite these challenges, several novel mechanisms of action are currently being investigated in frontline treatment of higher-risk MDS. These include BCL-2 Inhibition, targeted therapy of RARα agonists, and IDH1/2 Inhibition.[31,32] As of now, we still need confirmation of the efficacy and safety of these pathways through ongoing clinical trials to understand whether they can improve outcomes for patients with higher-risk MDS. Dr. Borate, what are your thoughts here?

Dr. Borate:
So I think higher-risk MDS is a disease with poor prognosis, and it's important to properly diagnose, risk stratify, and offer patients appropriate treatments to improve outcomes.[2,8] Managing higher-risk MDS requires a comprehensive approach, including timely transplant evaluations, effective cytopenia management, understanding the role of transfusions, and staying informed about emerging therapies. And we really look forward to results from ongoing clinical trials that may add more options to HMA therapies for High-risk-MDS patients in the future.

Dr. Colbert:
And with that encouraging look to the future, I'd like to thank my guests, Dr. Uma Borate and Dr. James Dugan, for sharing their insights on treatment challenges and opportunities for improving higher-risk MDS care.

Dr. Borate, Dr. Dugan, it was great speaking with you today.

Dr. Borate:

Thank you for the great discussion.

Dr. Dugan:
Yes, thank you very much.

Announcer:
This medical industry feature was sponsored by AbbVie. If you missed any part of this discussion, visit *Project Oncology* on ReachMD.com. This is ReachMD. Be Part of the Knowledge.

References:

1. Zeidan AM, Shallis RM, Wang R, Davidoff A, Ma X. Epidemiology of myelodysplastic syndromes: Why characterizing the beast is a prerequisite to taming it. *Blood Rev*. 2019;34:1-15. doi:10.1016/j.blre.2018.09.001
2. Cazzola M. Myelodysplastic syndromes. *N Engl J Med*. 2020;383(14):1358-1374. doi:10.1056/NEJMra1904794
3. Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. *Blood*. 2022;140(11):1200-1228. doi:10.1182/blood.2022015850
4. Hoff FW, Madanat YF. Molecular drivers of Myelodysplastic Neoplasms (MDS)—Classification and prognostic relevance. *Cells*. 2023;12(4):627. doi:10.3390/cells12040627
5. Hasegawa K, Wei AH, Garcia-Manero G, et al. Azacitidine monotherapy in patients with treatment-naïve higher-risk myelodysplastic syndrome: A systematic literature review and meta-analysis. *Clin Lymphoma Myeloma Leuk*. 2023;23(2):127-137. doi:10.1016/j.clml.2022.11.002
6. Zeidan AM, Stahl M, Hu X, et al. Long-term survival of older patients with MDS treated with HMA therapy without subsequent stem cell transplantation. *Blood*. 2018;131(7):818-821. doi:10.1182/blood-2017-10-811729
7. Greenberg PL, Tuechler H, Schanz J, et al. Revised International Prognostic Scoring System for Myelodysplastic Syndromes. *Blood*. 2012;120(12):2454-2465. doi:10.1182/blood-2012-03-420489
8. Bernard E, Tuechler H, Greenberg PL, et al. Molecular International Prognostic Scoring System for Myelodysplastic Syndromes. *NEJM Evid*. 2022;1(7). doi:10.1056/EVIDoa2200008
9. Marques FK, Sabino A de P. Myelodysplastic neoplasms: An overview on diagnosis, risk-stratification, molecular pathogenesis, and treatment. *Biomed Pharmacother*. 2022;156:113905. doi:10.1016/j.biopha.2022.113905
10. Valent P, Horny HP, Bennett JM, et al. Definitions and standards in the diagnosis and treatment of the myelodysplastic syndromes: Consensus statements and report from a working conference. *Leuk Res*. 2007;31(6):727-736. doi:10.1016/j.leukres.2006.11.009
11. Greenberg PL SRAKA et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myelodysplastic Syndromes, V.3.2023. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for MDS 3.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed October 31, 2023. *To view the most recent and complete version of the guideline, go online to NCCN.org NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.*
12. Sekeres MA, Taylor J. Diagnosis and treatment of myelodysplastic syndromes. *JAMA*. 2022;328(9):872. doi:10.1001/jama.2022.14578
13. Kaisrlikova M, Vesela J, Kundrat D, et al. RUNX1 mutations contribute to the progression of MDS due to disruption of antitumor cellular defense: a study on patients with lower-risk MDS. *Leukemia*. 2022;36(7):1898-1906. doi:10.1038/s41375-022-01584-3
14. Li B, Zou D, Yang S, Ouyang G, Mu Q. Prognostic significance of *U2AF1* mutations in myelodysplastic syndromes: a meta-analysis. *Journal of International Medical Research*. 2020;48(3):030006051989101. doi:10.1177/0300060519891013
15. Kewan T, Bewersdorf JP, Blaha O, et al. Evaluation of the Molecular International Prognostic Scoring System (IPSS-M) in patients (Pts) with myelodysplastic syndromes/neoplasms (MDS) with missing molecular data. *Blood*. 2023;142(Supplement 1):4607-4607. doi:10.1182/blood-2023-187053
16. Kota V, Ogbonnaya A, Farrelly E, et al. Clinical impact of transformation to acute myeloid leukemia in patients with higher-risk myelodysplastic syndromes. *Future Oncol*. 2022;18(36):4017-4029. doi:10.2217/fon-2022-0334
17. Kaphan E, Laurin D, Lafeuillade B, Drillat P, Park S. Impact of transfusion on survival in patients with myelodysplastic syndromes: Current knowledge, new insights and transfusion clinical practice. *Blood Rev*. 2020;41:100649. doi:10.1016/j.blre.2019.100649
18. Kaka S, Jahangirnia A, Beauregard N, Davis A, Tinmouth A, Chin-Yee N. Red blood cell transfusion in myelodysplastic syndromes: A systematic review. *Transfus Med*. 2022;32(1):3-23. doi:10.1111/tme.12841
19. Braga Lemos M, Rodrigues SR, Schroeder T, Kulasekararaj AG, Matos JE, Tang D. Association between red blood cell transfusion dependence and burden in patients with myelodysplastic syndromes: A systematic literature review and meta-analysis. *Eur J Haematol*. 2021;107(1):3-23. doi:10.1111/ejh.13619

20. Miranda-Galvis M, Tjioe KC, Balas EA, Agrawal G, Cortes JE. Disparities in survival of hematologic malignancies in the context of social determinants of health: a systematic review. *Blood Adv*. 2023;7(21):6466-6491. doi:10.1182/bloodadvances.2023010690
21. Fenaux P, Mufti GJ, Hellstrom-Lindberg E, et al. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomised, open-label, phase III study. *Lancet Oncol*. 2009;10(3):223-232. doi:10.1016/S1470-2045(09)70003-8
22. Zeidan AM, Xiao Z, Sanz G, et al. Primary results of the Phase III STIMULUS-MDS2 study of sabatolimab + azacitidine vs placebo + azacitidine as frontline therapy for patients with higher-risk MDS or CMML-2. Abstract S180. 29th European Hematology Association Congress. June 13-16, 2024. Madrid, Spain.
23. Zeidan AM, Ando K, Rauzy O, et al. Sabatolimab plus hypomethylating agents in previously untreated patients with higher-risk myelodysplastic syndromes (STIMULUS-MDS1): a randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Haematol*. 2024;11(1):e38-e50. doi:10.1016/S2352-3026(23)00333-2
24. Sallman D, Garcia-Manero G, Daver N, et al. Magrolimab (Magro) + azacitidine (AZA) vs placebo (PBO) + AZA in patients (pts) with untreated higher-risk (HR) myelodysplastic syndromes (MDS): Phase 3 ENHANCE study final analysis. Abstract S181. 29th European Hematology Association Congress. June 13-16, 2024. Madrid, Spain.
25. Adès L, Girshova L, Doronin VA, et al. Pevonedistat plus azacitidine vs azacitidine alone in higher-risk MDS/chronic myelomonocytic leukemia or low-blast-percentage AML. *Blood Adv*. 2022;6(17):5132-5145. doi:10.1182/bloodadvances.2022007334
26. Götze K, Platzbecker U, Giagounidis A, et al. Azacitidine for treatment of patients with myelodysplastic syndromes (MDS): practical recommendations of the German MDS Study Group. *Ann Hematol*. 2010;89(9):841-850. doi:10.1007/s00277-010-1015-0
27. Platzbecker U. Treatment of MDS. *Blood*. 2019;133(10):1096-1107. doi:10.1182/blood-2018-10-844696
28. Platzbecker U, Kubasch AS, Homer-Bouthiette C, Prebet T. Current challenges and unmet medical needs in myelodysplastic syndromes. *Leukemia*. 2021;35(8):2182-2198. doi:10.1038/s41375-021-01265-7
29. Santini V, Fenaux P, Mufti GJ, et al. Management and supportive care measures for adverse events in patients with myelodysplastic syndromes treated with azacitidine*. *Eur J Haematol*. 2010;85(2):130-138. doi:10.1111/j.1600-0609.2010.01456.x
30. Fenaux P, Platzbecker U, Ades L. How we manage adults with myelodysplastic syndrome. *Br J Haematol*. 2020;189(6):1016-1027. doi:10.1111/bjh.16206
31. Cassanello G, Pasquale R, Barcellini W, Fattizzo B. Novel therapies for unmet clinical needs in myelodysplastic syndromes. *Cancers (Basel)*. 2022;14(19):4941. doi:10.3390/cancers14194941
32. de Botton S, Cluzeau T, Vigil C, et al. Targeting *RARA* overexpression with tamibarotene, a potent and selective RARα agonist, is a novel approach in AML. *Blood Adv*. 2023;7(9):1858-1870. doi:10.1182/bloodadvances.2022008806

ABBV-US-01703-MC Version 1.0 Approved 12/2024