



Insights Into the Management of Lower-Risk Myelodysplastic Syndromes (LR-MDS)

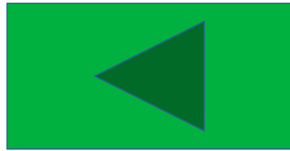
October 12, 2024

Chair: Danko Martincic, MD










How to Navigate This Report



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STUDY OBJECTIVE

Gain advisors' perspectives on current practices in the management of LR-MDS

REPORT OBJECTIVES

- > Discover advisors' experience with luspatercept in LR-MDS, including patient characteristics, management of cytopenias, and barriers to use
- > Gain advisors' perspectives on the updated efficacy and safety data from the phase III COMMANDS trial
- > Understand advisors' perceptions of the NCCN Guidelines and to what degree they influence treatment sequencing decisions in LR-MDS

Report Snapshot: Session Overview



A moderated roundtable discussion was held with 11 healthcare providers on **October 12, 2024**

Disease state and data presentations were chaired by **Danko Martincic, MD**, of Beacon Clinic, with content developed in conjunction with the Aptitude Health clinical team

Insights were obtained on physicians' current practices in the management of LR-MDS

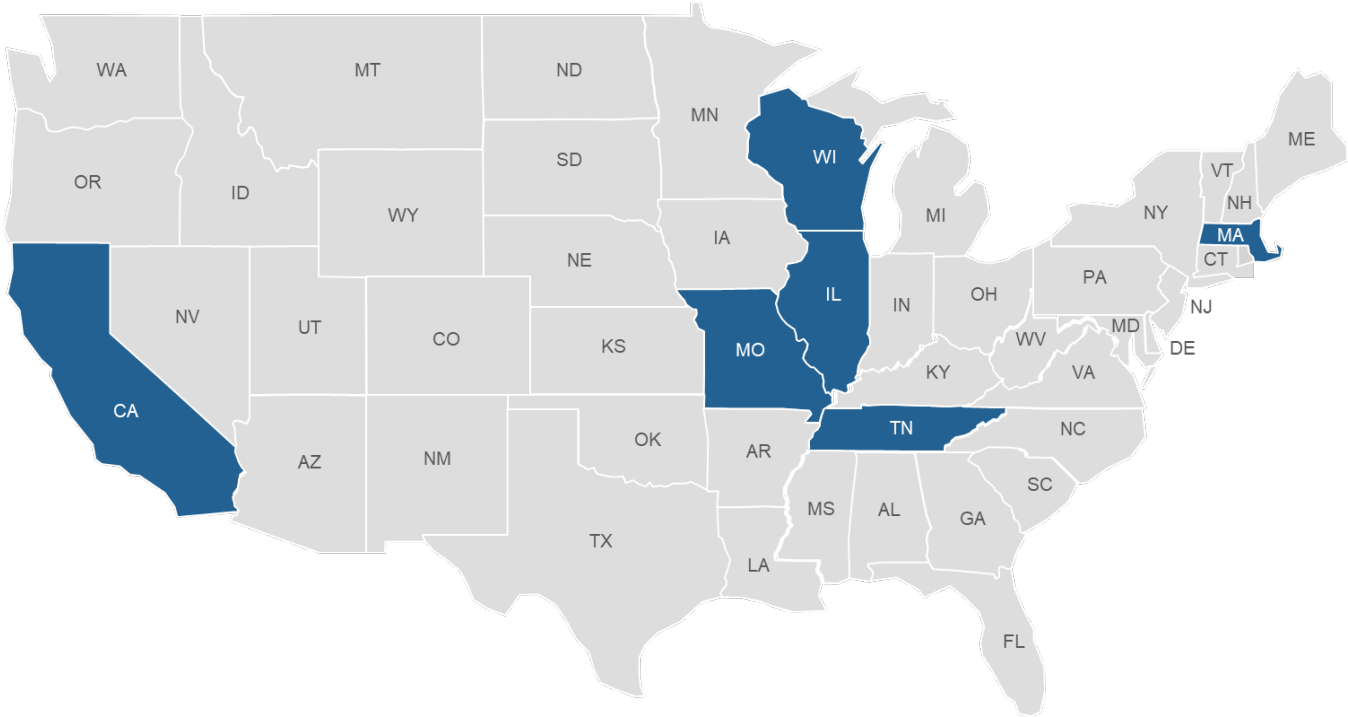
Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

Report Snapshot: Attendee Overview



> The group of advisors comprised 11 healthcare providers from across the United States

Institution	City	State
Washington University School of Medicine*	St Louis	MO
Loma Linda University Hospital	Loma Linda	CA
City of Hope National Cancer Center	Duarte	CA
Medical College of Wisconsin	Milwaukee	WI
University of Wisconsin	Madison	WI
University of California, San Francisco	San Francisco	CA
Robert H. Lurie Comprehensive Cancer Center of Northwestern University	Chicago	IL
University of Illinois – Chicago	Chicago	IL
Sarah Cannon Research Institute at TriStar Centennial	Nashville	TN
Tufts Medical Center	Boston	MA



*Two advisors from this institution attended.

Participant Demographics (1/2)

Approximately how many newly diagnosed patients with LR-MDS do you personally treat per year? (n = 10*)

What proportion of your newly diagnosed patients with LR-MDS do not have del(5q)? (N = 11)



*One physician did not respond.

Participant Demographics (2/2)

What percentage of your patients with non-del(5q) LR-MDS have you treated for symptomatic anemia in the past year? (n = 10*)



What percentage of your patients with non-del(5q) LR-MDS and symptomatic anemia required subsequent therapy in the past year? (n = 10*)



*One physician did not respond.

Report Snapshot: Agenda



Time (PT)	Topic
1.00 PM – 1.15 PM	Introduction <ul style="list-style-type: none">• Program overview• ARS questions
1.15 PM – 2.25 PM	First-Line Treatment Options in LR-MDS Without Del(5q) <ul style="list-style-type: none">• Overview of current data• Reaction and discussion
2.25 PM – 2.35 PM	Break
2.35 PM – 3.45 PM	Subsequent-Line Therapy in LR-MDS Without Del(5q) <ul style="list-style-type: none">• ARS questions• Overview of current data• Reaction and discussion
3.45 PM – 4.00 PM	Key Takeaways and Meeting Evaluation



Discussion Summary

INSIGHTS

"I typically use both scoring systems. I typically choose the higher of the 2."

1. Treatment success in females (N=20)

The overall survival rate was 100%. This is not statistically significant. It is a small dataset, so we need more data. I would also use a Kaplan-Meier plot to see if there is any difference in survival between the two groups. I would also use a log-rank test to see if there is a significant difference in survival between the two groups. I would also use a Cox proportional hazards model to see if there is a significant difference in survival between the two groups.

2. Data needed to confirm from NCI in females

What are all the things that have been done? Making a table that lists all the things that have been done. I would also use a Kaplan-Meier plot to see if there is any difference in survival between the two groups. I would also use a log-rank test to see if there is a significant difference in survival between the two groups. I would also use a Cox proportional hazards model to see if there is a significant difference in survival between the two groups.

INSIGHTS

"We know that patients with SF3B1 will do well with luspatercept."

1. Treatment success in frontline MDS

The overall survival data was very good. This is not necessarily because this is a curable disease, or an easy-to-treat disease. I think what luspatercept does is that it allows you to get a better response with less toxicity. I think the disease has a life of 3 years. I think as that life is dependent on there is significant toxicity with the treatment, and people going from something to something else.

2. Data needed to confirm from MDS in frontline

That's all a lot of things have been done, nothing is better than R-CHOP and Rituximab. It really helps with how R-CHOP performs for my patients. I think as a side effect, I would not be one of the first ones to move based on MDS or anything like that. I think something that's been done and we know that we'll do it.

If the toxicity was not very severe, I think a higher rate of MDS or better would be something that I would be looking at.

Overall survival data, that's good. But in this disease, with MDS, it's hard to come by. So you do have to use some surrogate of efficacy. So I think that's a bit of a trade-off. I think the overall survival data is that what's going to be driving the use of my agent. MDS is not sufficient.

INSIGHTS

“Some insurance companies mandate that you try ESAs first, and then if you can show failure with ESA, only then

1. Treatment success in females (5,000)

The overall success rate is very low. This is not necessarily because the drug is ineffective, but because of the way it is used. The drug is used in a way that is not optimal. The overall success rate is very low. This is not necessarily because the drug is ineffective, but because of the way it is used. The drug is used in a way that is not optimal.

2. Data needed to confirm that 50% is effective

That is all a lot of things have been done, nothing is better than 50% and that is the only way to see if the drug is effective. The overall success rate is very low. This is not necessarily because the drug is ineffective, but because of the way it is used. The drug is used in a way that is not optimal.



Advisor Key Takeaways

Advisor Key Takeaways



ADVISOR

> I learned more about imetelstat, the specialist

- There is a better understanding of sequencing therapy
- I really want to talk further with imetelstat and understand how we have a better understanding of these drugs and have a better idea of when to use them in my practice

- There is a better understanding of some of my other options
- I'm particularly interested in the combination and how that will work and how much we can expect to be a second line option for my own elderly patients
- There is a lot more information to suggest therapy and to change the combination that may offer some other options

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

- There is a lot of good options for second line that just look like you manage with second line other profile and good response rate
- Sequencing is an issue

ADVISOR

> The COMMANDS trial and first line versus ESA, and how to pick which one.

- The imetelstat/ESA combination, adding the need to have different options besides FOLFOX and what is going to look like

- The feeling that some of these combination agents will get added into practice and hopefully improve the look like

- This interesting to learn about all these imetelstat/ESA treatments, especially the specific antibodies
- A lot of options coming up in the future. The only issue will be to learn how to sequence these drugs

- Not focused on the standard

Advisor Key Takeaways*



ADVISOR

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> The most important thing is sequencing first-line treatments, what to choose, how to choose.

- Have a better understanding of sequencing therapies
- Really want to talk further with professional and understand how you - have a better understanding of these drugs and have a better idea of when to use them in the practice

- Have a better understanding of some of the newer agents
- It's particularly important in the subcutaneous and oral that will and then would be interested in a subcutaneous option for my own therapy options
- There's a lot more confidence in targeted therapy and to things the professional that may offer some side effects

- It was good to hear about innovations and clearly coming down the pipeline for immunotherapies

- There's a lot of great options for advanced line that you could try and manage with decent side effect profile and good response rates
- Sequencing is an issue

- The immunotherapies, getting the idea to have different options besides PD-1, and what is going to come next

- It's hoping that some of these immunotherapies agents will get added into frontline and hopefully improve the outcomes

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

- CAR T is still in the research



ARS Results

Most Advisors Test for All the Listed Biomarkers in Patients With Non-Del(5q) LR-MDS; Only 10% Do Not Perform Biomarker Testing in These Patients

FOR EXAMPLE PURPOSES ONLY

*One physician did not respond.



Level of Transfusion Dependence and RS Status Are the Most Influential Patient Factors in Advisors' Choice of First-Line Therapy for Symptomatic Anemia

FOR EXAMPLE PURPOSES ONLY

Transfusion Independence and Durability of Response Have the Greatest Influence on Advisors' Choice of First-Line Therapy for Symptomatic Anemia

FOR EXAMPLE PURPOSES ONLY

Inclusion in NCCN Guidelines Is Most Important to Advisors When Using New Therapeutic Options, Outside of Clinical Data



FOR EXAMPLE PURPOSES ONLY

Almost Three-Quarters of Advisors Used Luspatercept in 1–5 Patients With Non-Del(5q) LR-MDS and Anemia in the Past Year

CASES

FOR EXAMPLE PURPOSES ONLY



Most Advisors (82%) Did Not Use Imetelstat in Patients With Non-Del(5q) LR-MDS and Anemia in the Past Year



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For Most Advisors (90%), One-Fourth or Fewer of Their Patients Treated With Luspatercept Developed Cytopenias in the Past Year

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All Advisors Are Moderately to Extremely Comfortable Managing Luspatercept-Associated Cytopenias

On a scale of 1-5, where 1 = Not comfortable at all and 5 = Extremely comfortable, how

FOR EXAMPLE PURPOSES ONLY

Most Advisors Were Moderately Familiar With the COMMANDS Trial; None Were Extremely Familiar

On a scale of 1-5, where 1 = Not familiar at all and 5 = Extremely familiar, how familiar are

FOR EXAMPLE PURPOSES ONLY

Obtaining Prior Authorizations Is the Barrier Most Commonly Encountered by Advisors When Using Luspatercept; 36% of Advisors Encounter No Barriers

FOR EXAMPLE PURPOSES ONLY

> A 65-year-old man with newly diagnosed lower-risk MDS has recently become

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Most Advisors (64%) Recommended Luspatercept as Frontline Therapy for the Patient Described in This Case; 18% Recommended an ESA



FOR EXAMPLE PURPOSES ONLY



> A 65-year-old man with newly diagnosed lower-risk MDS has recently become

He has been treated with azacitidine and has achieved a partial response. He is currently on his second cycle of treatment and is feeling well. His hemoglobin is 10 g/dL, platelets are 150,000/mm³, and neutrophils are 1.5 x 10⁹/mm³. He has no evidence of extramedullary disease.

Over Half the Advisors (60%) Chose Luspatercept as Frontline Therapy for This Patient; 20% Recommended an ESA

What frontline therapy do you recommend for this patient? (n = 10*)

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Most Advisors (67%) Used Luspatercept in the 2L+ Setting in the Past Year in 1–5 Patients With Non-Del(5q) LR-MDS and Anemia; 22% Did Not Use Luspatercept in This Setting

FOR EXAMPLE PURPOSES ONLY

*Two physicians did not respond.

Nearly Three-Fourths of Advisors Had Not Used Imetelstat in the 2L+ Setting in the Past Year in Patients With Non-Del(5q) LR-MDS and Anemia

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Most Advisors (60%) Encounter No Barriers When Using Luspatercept in the Subsequent-Line Setting

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Prior Therapies Received and Response to Prior Therapy Most Significantly Influence Advisors' Choice of Subsequent Therapy

FOR EXAMPLE PURPOSES ONLY

Half the Advisors Were Moderately Familiar With the Results of the MEDALIST Trial; 20% Were Not Familiar at All

On a scale of 1-5, where 1 = Not familiar at all and 5 = Extremely familiar, how familiar are

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> A 62-year-old woman with newly diagnosed lower-risk MDS and transfusion-

Depressed, she had a history of chronic kidney disease, hypertension, and hyperlipidemia. She had been on dialysis for several years. Her medical history was significant for a recent diagnosis of lower-risk MDS and transfusion-dependent anemia. She had been on transfusions for several months. Her physical examination was unremarkable. Her laboratory studies showed a hemoglobin of 7.5 g/dL, hematocrit of 22.5%, and platelet count of 150,000/mm³. Her renal function was stable with a creatinine of 1.2 mg/dL. Her liver function tests were within normal limits. Her electrolytes were also within normal limits. Her complete blood count showed a hemoglobin of 7.5 g/dL, hematocrit of 22.5%, and platelet count of 150,000/mm³. Her peripheral smear showed no abnormality. Her bone marrow examination showed a hypercellular marrow with a normoblastic pattern. There was a marked increase in blasts, which were small to medium in size with scant cytoplasm and a high nucleus-to-cytoplasm ratio. The blasts were positive for myeloperoxidase and CD34, and negative for CD117 and CD22. The findings were consistent with lower-risk MDS. Her renal function was stable with a creatinine of 1.2 mg/dL. Her liver function tests were within normal limits. Her electrolytes were also within normal limits. Her complete blood count showed a hemoglobin of 7.5 g/dL, hematocrit of 22.5%, and platelet count of 150,000/mm³. Her peripheral smear showed no abnormality. Her bone marrow examination showed a hypercellular marrow with a normoblastic pattern. There was a marked increase in blasts, which were small to medium in size with scant cytoplasm and a high nucleus-to-cytoplasm ratio. The blasts were positive for myeloperoxidase and CD34, and negative for CD117 and CD22. The findings were consistent with lower-risk MDS.

Most Advisors (60%) Would Recommend Subsequent Therapy With Luspatercept for This Patient



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