Transcript Details
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Treating MDS: A Look at an Approved Treatment

Announcer:
Welcome to ReachMD. This is a medical industry feature sponsored by Taiho Oncology. This program is intended for healthcare professionals only.

Moderator:
In our last episode, we spoke with two oncologist nurses about their experience with myelodysplastic syndromes, also known as MDS. Today, we are joined by a hematologist/oncologist and oncology nurse team to discuss their experiences with one of the treatments for MDS.

We usually like to start Word of Mouth by having you tell listeners a little bit about yourselves, your practice, and the patients in your practice who have been diagnosed with MDS.

Dr Komrokji:
Hi, I am Rami Komrokji I'm a professor of medicine and section head for leukemia and MDS at Moffitt Cancer Center. I'm a hematologist that focuses on myelodysplastic syndromes. Most of the patients I see in my practice are diagnosed with MDS. We actually see one of the largest volumes of MDS patients countrywide, and I've participated and actively participating in several clinical trials in the area of myelodysplastic syndromes.

Natasha:
Hi, I'm a certified oncology nurse practitioner in the outpatient clinic in the malignant hematology department. I also work in the hospital a few days a year, but mainly I am in the outpatient setting and I've been there over eight years.

Moderator:
Is there a specific protocol you follow when diagnosing patients with MDS? Let's walk our listeners through your process.

Dr Komrokji:
So, as you know myelodysplastic syndrome is a neoplastic stem cell disease characterized by bone marrow failure with cytopenias. A simple workup for cytopenia is done and often requires a bone marrow aspirate and biopsy to make the diagnosis.

Once we make the diagnosis, obviously the pathologists give us the WHO classification. But really the most important step is the risk stratification. And the most used now is really the revised IPSS. It's a sum score based on the blasts, cytogenetics, and the cytopenias, where at the end we're going to try to decide are the patients in a higher risk group or a lower risk group, where we tailor the therapy accordingly.

Natasha:
IPSS-R stands for the Revised International Prognostic Scoring System, which looks at factors like percentage of blasts in the bone marrow, platelets, absolute neutrophil, hemoglobin, and cytogenetics. Once we look at these factors, we're able to determine whether or not a patient has MDS as well as identify the type, determine the level of risk– which can be low, intermediate, or high–and then discuss the best possible treatment regimen.

Natasha:
Unfortunately, most of our higher-risk MDS patients are not candidates for stem cell transplants, which is the only curative treatment. When that is not an option, we talk to them about hypomethylating agents, or HMAs. Some patients are able to get to their treatment center or office on their own, but others—especially since this tends to be diagnosed in patients who are older—can have trouble

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coordinating travel to their treatment appointments. Ever since I began using HMAs, they have only been available through an in-office infusion or subcutaneous injection, but we are finally seeing some advancements.

Moderator:
I know we're all excited to talk about some advancements, which we will do in just a moment. But first, I'd like you to paint a picture of the patients you treat for those listeners who might not be familiar. Can you tell us a bit about your MDS population?

Natasha:
Sure. Many of our patients have intermediate- or high-risk MDS and are between seventy and eighty years old. We see both male and female patients, though MDS tends to skew a bit higher towards men.

As I mentioned before, we have heard from some of our patients that traveling to and from the infusion centers or hospital for intravenous or subcutaneous treatment can be a challenge, especially if they aren't close and rely on a caretaker to coordinate. These infusions can last a while, and up to seven days straight. This can last months, or even years. It has been wonderful to tell them that there is an oral treatment that they can take in the comfort of their own home.

Moderator:
Let's talk about one of the developments in MDS treatment. INQOVI®–(decitabine and cedazuridine) tablets–is indicated for the treatment of adult patients with myelodysplastic syndromes, including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia, or CMML) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

Dr Komrokji:
We were excited about the approval after reading about the phase two and phase three studies, and we heard it had been approved, we knew we would be able to start prescribing it soon after. INQOVI is the first and only combination oral hypomethylating agent therapy that has been approved by the FDA for the treatment of MDS, including CMML. INQOVI is a fixed-dose combination of decitabine and cedazuridine.

Natasha:
And our patients, mostly those we mentioned earlier who have trouble with transportation, or challenges with the other administration methods, have been able to take their treatment at home.

Dr Komrokji:
INQOVI is an oral hypomethylating agent, so it's a pill that patients can take at home for 5 days in a row similar to the IV decitabine 5 days with the convenience of being able to take it at home.

Natasha:
What's more, we are still able to monitor them, and manage adverse events, as often as necessary with virtual visits and routine labs taken during in-person appointments. There is also a patient support program that helps us and may help patients and their caregivers with treatment and medication cost support.

Moderator:
That sounds amazing. Can you help our listeners understand how this treatment works?

Natasha:
Sure. INQOVI is one pill, taken orally once daily for five days out of a twenty-eight-day cycle. It is made up of thirty-five milligrams of decitabine, and one hundred milligrams of cedazuridine.

Dr Komrokji:
So, the drug is a combination of decitabine and cedazuridine which is a cytidine deaminase inhibitor that will stabilize the decitabine and allow the absorption, because decitabine is usually degraded by this enzyme. So, cedazuridine will prevent the breakdown of decitabine in the gut to allow the absorption and the exposure of decitabine.

Natasha:
I like to tell our patients that cedazuridine prevents the breakdown of decitabine in the gut to achieve exposure that is equivalent to IV decitabine.

Moderator:
And doctor, you mentioned earlier that you read about the phase three trial prior to the approval, leading to your anticipation of the

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treatment.

Dr Komrokji:
That's right. The phase three ASCERTAIN study was an elegantly designed study with a crossover trial design that assessed systemic decitabine exposure, demethylation, and safety between IV decitabine—which we just discussed—and oral INQOVI. The trial design included an interpatient comparison in the first two randomized treatment cycles, and then it assessed the long-term efficacy and safety of INQOVI as a single arm.

Moderator:
And when did you start using this treatment option in your practice?

Dr Komrokji:
As soon as we learned about it, we spoke to some of our eligible patients who were unable to or simply refused to have a port placement, as well as a few caregivers who expressed challenges in traveling to the infusion centers for the treatment options we had originally discussed. We discussed the possible benefits and risks with INQOVI, including the warnings on myelosuppression and need for follow up, as well as common other adverse events seen in clinical trials, and started to prescribe it to them once the approval occurred in 2020.

Moderator:
And what has been your experience with it so far?

Natasha:
So far, our patients are happy to have an option they can take in the comfort of their own homes.

Moderator:
And have you seen results?

Dr Komrokji:
We are seeing positive results, but it's a bit too early to tell. The phase three data were promising—meeting the primary endpoint of demonstrating equivalent systemic exposure to IV-administration decitabine and resulting in ninety-nine percent geometric mean ratio of oral to IV five-day decitabine area under the curve. That told me that INQOVI had nearly the same bioavailability as IV-decitabine, which I am familiar with because of my experience with that medication. It's important to note that as with all HMA medication, there are safety concerns. The safety results with INQOVI were similar to those seen with IV decitabine, and only five percent of patients taking INQOVI discontinued due to an adverse reaction. The incidence of adverse reactions seen in the phase 3 trial was slightly higher for INQOVI than for IV decitabine during the first cycle of treatment.

Natasha:
The most serious side effects that were seen in more than five percent of patients were febrile neutropenia at thirty percent, pneumonia at fourteen percent, and sepsis at thirteen percent. In our practice, we have been able to manage common adverse events that have been brought to our attention. As I mentioned before, there are resources and guides that provide tips to help patients manage adverse events. These are available at INQOVI.com for us, our patients, and their caregivers, and really help make the treatment experience manageable.

Moderator:
Well, I guess you can say that with INQOVI, there's no place like home. I'd like to thank you both for spending some time with us and sharing your experience with MDS treatment. Grab a seat and tune in for another episode of Word of Mouth. For more information, visit INQOVI.com, that's I-N-Q-O-V-I dot com. Please listen to the following Important Safety Information for INQOVI.

VOICEOVER OF ISI:

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS
Myelosuppression
Fatal and serious myelosuppression can occur with INQOVI. Based on laboratory values, new or worsening thrombocytopenia occurred in 82% of patients, with Grade 3 or 4 occurring in 76%. Neutropenia occurred in 73% of patients, with Grade 3 or 4 occurring in 71%. Anemia occurred in 71% of patients, with Grade 3 or 4 occurring in 55%. Febrile neutropenia occurred in 33% of patients, with Grade 3 or 4 occurring in 32%. Myelosuppression (thrombocytopenia, neutropenia, anemia, and febrile neutropenia) is the most frequent cause of INQOVI dose reduction or interruption, occurring in 36% of patients. Permanent discontinuation due to myelosuppression (febrile neutropenia) occurred in 1% of patients. Myelosuppression and worsening neutropenia may occur more frequently in the first or second

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treatment cycles and may not necessarily indicate progression of underlying MDS.

Fatal and serious infectious complications can occur with INQOVI. Pneumonia occurred in 21% of patients, with Grade 3 or 4 occurring in 15%. Sepsis occurred in 14% of patients, with Grade 3 or 4 occurring in 11%. Fatal pneumonia occurred in 1% of patients, fatal sepsis in 1%, and fatal septic shock in 1%.

Obtain complete blood cell counts prior to initiation of INQOVI, prior to each cycle, and as clinically indicated to monitor response and toxicity. Administer growth factors and anti-infective therapies for treatment or prophylaxis as appropriate. Delay the next cycle and resume at the same or reduced dose as recommended.

Embryo-Fetal Toxicity
INQOVI can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise patients to use effective contraception during treatment and for 6 months (females) or 3 months (males) after last dose.

ADVERSE REACTIONS
Serious adverse reactions in greater than 5% of patients included febrile neutropenia (30%), pneumonia (14%), and sepsis (13%). Fatal adverse reactions included sepsis (1%), septic shock (1%), pneumonia (1%), respiratory failure (1%), and one case each of cerebral hemorrhage and sudden death.

The most common adverse reactions (greater than or equal to 20%) were fatigue (55%), constipation (44%), hemorrhage (43%), myalgia (42%), mucositis (41%), arthralgia (40%), nausea (40%), dyspnea (38%), diarrhea (37%), rash (33%), dizziness (33%), febrile neutropenia (33%), edema (30%), headache (30%), cough (28%), decreased appetite (24%), upper respiratory tract infection (23%), pneumonia (21%), and transaminase increased (21%). The most common Grade 3 or 4 laboratory abnormalities (greater than or equal to 50%) were leukocytes decreased (81%), platelet count decreased (76%), neutrophil count decreased (71%), and hemoglobin decreased (55%).

USE IN SPECIFIC POPULATIONS
Lactation
Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with INQOVI and for 2 weeks after the last dose.

Renal Impairment
No dosage modification of INQOVI is recommended for patients with mild or moderate renal impairment (creatinine clearance of 30 to 89 milliliters per minute) based on Cockcroft-Gault). Due to the potential for increased adverse reactions, monitor patients with moderate renal impairment (creatinine clearance 30 to 59 milliliters per minute) frequently for adverse reactions. INQOVI has not been studied in patients with severe renal impairment (creatinine clearance 15 to 29 milliliters per minute) or end-stage renal disease (creatinine clearance less than 15 milliliters per minute).

Please see full Prescribing Information at INQOVI.com/PI.

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Announcer:
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