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Multiple Myeloma: Who to Screen & How

Announcer:
Welcome to ReachMD.

This medical industry feature, titled “Multiple Myeloma: Who to Screen & How” is sponsored by Quest Diagnostics. This program is intended for physicians.

Here’s your host, Dr. Yuri Fesko

Dr. Fesko:
Multiple myeloma can be a challenging disease to diagnose and treat, but current and emerging laboratory strategies can help us improve patient outcomes. This is ReachMD. I’m Dr. Yuri Fesko.

Joining me today to discuss laboratory testing for multiple myeloma and which patient populations should be screening, is Dr. Irene Ghobrial and Dr. Steven Kussick.

Dr. Ghobrial is an attending physician and a director of the Clinical Investigators Research Program at the Dana Farber Cancer Institute. She has recently been appointed as one of the Levine Family Chairs for Preventive Cancer Therapies, and she is a Professor of Medicine at the Harvard School of Medicine. Dr. Ghobrial, thanks for being here today.

Dr. Ghobrial:
Thank you for having me.

Dr. Fesko:
Dr. Kussick is the Medical Director, also the Director of Contract Research, the Director of Flow Cytometry at the PhenoPath Laboratories in Seattle. He is also an Affiliate Faculty at the University of Washington and is also the cochair of the Hematopathology Resource Committee at Quest Diagnostics.

Thanks for being here, Dr. Kussick.

Dr. Kussick:
My pleasure, thank you.

Dr. Fesko:
Before we dive into the role of laboratory testing, let’s take a high-level look at the screening for multiple myeloma. Dr. Ghobrial, why is screening so important for these patients?

Dr. Ghobrial:
Yeah, thank you so much. And it’s such an important and timely question because there were two large studies presented in the American Society of Hematology about screening.

And we know very well that cancer screening saves lives. I mean, we screen for breast cancer, for colon cancer, yet we don’t screen for simple blood cancer, and it’s a simple blood test. And you ask the question, “Why can’t we do that, and how can we make it happen?” And answer the question, “Can we identify it early? And by doing that, can we prevent end-organ damage? Can we prevent fractures, renal failure, anemia, and so on so that we can prevent multiple myeloma from happening?”

And the answer is yes, two studies have shown it. The iStop study in Iceland, where they screened 75,000 people, and indeed, they

showed that MGUS is about 4% of the population. But remember, most of the population, or all of the population, is white in Iceland.

And then, here in the United States, we worked with Quest Diagnostics and many others to screen a diverse population, high-risk population, who are either of African descent or African Americans, or people with a first-degree family member with blood cancer.

And indeed, we found in the first 7,000 people, a high number who do have indeed early monoclonal gammopathies. In fact, over the age of 50, we had 40% of people having a monoclonal gammopathy. About 14% of those were MGUS, which is the early precursor of multiple myeloma.

Dr. Fesko:
Dr Kussick, let's talk about a few specific laboratory tests for multiple myeloma, including tests that are best utilized at the time of the initial diagnosis, and then tests designed to look at measurable residual disease, or MRD, after the therapy's been initiated. What can you tell us about tests such as flow cytometry, FISH testing, gene expression profiling, and next generation sequencing?

Dr. Kussick:
Yeah, those are all commonly used tests in the laboratory once a patient is been identified, where there's concern for either MGUS or myeloma.

So, there are a variety of tests we can do on fresh material, such as a bone marrow aspirate, that a clinician would obtain.

Probably the first we thing we do is flow cytometry, which is a way we can look at the individual cells themselves in the bone marrow, and in particular, we're looking at the – at the malignant cell in multiple myeloma, which is a plasma cell. And by flow cytometry, we can specifically look at the plasma cells in a patient's bone marrow, decide if they're benign or malignant, and if they're malignant identify what particular markers of myeloma or a plasma cell neoplasm those cells have, that can enable us to look for them with a high degree of power after the patient's been treated. Flow cytometry also helps us identify certain markers on those cells, that may be targeted with specific drugs that are directed at those markers.

Another type of test we do on fresh material most commonly from bone marrow samples is called fluorescence in situ hybridization, or FISH. In contrast to flow cytometry, which looks at proteins expressed on the surface or inside of cells, FISH looks at nucleic acids, specifically DNA, in the nucleus of myeloma cells. And what we look for by FISH is specific abnormalities that have been associated with myeloma, and particular abnormalities that are associated with different types of prognoses. So, by doing FISH, we look at markers that could be associated with a favorable prognosis, and those that can be associated with an unfavorable prognosis. And depending on what that prognosis is the patient's oncologist will likely have different ideas about what the most appropriate therapy is.

Gene expression profiling is another type of test that can be done on fresh material. In this case, rather than looking at DNA, it looks at another type of nucleic acid called RNA, which is a marker also of how genes are expressed, and it's been known by a number of studies on large cohorts or groups of myeloma patients, that certain combinations of gene expression profiling results will indicate either favorable or unfavorable prognosis.

And finally, next generation sequencing, which is probably the most recent of all these technologies is a sensitive way to look for specific mutations in myeloma patients, in genes that may indicate different types of prognoses, either favorable or unfavorable. A particularly unfavorable prognostic gene is P53. And, also may look for mutations that are potentially targetable using either experimental or FDA-approved therapies to those mutations. One other thing about next generation sequencing, it actually can be used to identify a specific molecular signature that each myeloma patient should have, called an immunoglobulin gene rearrangement, that can be identified for therapy, and then searched for after therapy at a very sensitive level, even to the point of being able to identify one malignant cell, in either 100,000 or even a million benign bone marrow cells. So, those offer the prospect of very sensitive way to follow the disease after therapy.

Dr. Fesko:
With these tests in mind, Dr. Kussick, which patient population should be prioritized during screening for multiple myeloma?

Dr. Kussick:
Yes, and this relates directly to Dr. Ghobrial's PROMISE study, and other studies of early disease. We know that people with a first degree relative with any blood cancer, myeloma, leukemia, lymphoma, has a higher risk, higher likelihood of, developing myeloma particularly in patients over 50, so that's certainly a population that we should consider screening by serum protein electrophoresis, immunofixation, or even mass spectroscopy. And we also know that African Americans or people of African descent have a two to threefold higher risk of myeloma compared to other folks, and so those populations also should be considered for screening.

Dr. Fesko:
Dr. Ghobrial, let's look at the PROMISE trial. What can you tell us about this study, and how does it impact underserved communities?

Dr. Ghobrial:
Yeah, and it's been quite the journey when we started the PROMISE study. We started it a few years ago, with the help of Stand Up to Cancer, and in fact, with a strong collaboration with Quest Diagnostics. And the whole idea is, instead of having people come to us at Dana Farber and just screen a total population, we went specifically to ask the question, people at risk for multiple myeloma, nationwide, how can we screen them? And we started it as a direct-to-patient access, so you can actually sign up now on PromiseStudy.org, look it up, and see if you're eligible. And we specifically said let's screen people at risk who are either African American, because we know that they have two to three times higher chance of developing myeloma, or people who have a first-degree family member with a blood cancer, because they have a two times higher chance of developing myeloma. And having it direct-to-patient means you can be sitting, right now, anywhere in the United States, click on PromiseStudy.org, see if you're eligible, and we send you a kit. And you take that kit, go to Quest Diagnostic or any lab that's close to you, and get your blood results. And we will call you and tell you that you are positive or negative, and if you are positive, we make sure that we are part of that journey. We tell you what is the risk, potentially most of the people have a very small chance of developing myeloma, even less than 1% chance per year. We actually help you get care, locally or coming to see us, and we work through all of that, and we retest everyone every three years. So, part of it is early detection, finding it at the right time, and early interception if you need treatment before myeloma happens. And the hope is we cure myeloma before it even happens.

Dr. Fesko:
For those of you just joining us, this is ReachMD. I'm Dr. Yuri Fesko, and today, I'm speaking with Dr. Irene Ghobrial and Dr. Steven Kussick about the role of laboratory testing and the management of patients with multiple myeloma.

Okay, let's dive a little bit deeper into screening for multiple myeloma. Dr. Ghobrial, can you walk us through the diagnosis, prognosis, management of patients with monoclonal gammopathies?

Dr. Ghobrial:
Yeah, so it's a spectrum, when we diagnose someone with an early MGUS, monoclonal gammopathy of undetermined significance, we know that these people have a very small chance of developing myeloma, or other blood cancers like CLL or lymphoma or Waldenstrom's or amyloidosis, and we need to understand this better.

And part of it is really going through the journey with the patient, and understanding are they at that early event, and have a very small chance of progression? And that can be done from the blood tests. Or are they at later events, where we're looking at the imaging, at the bone marrow biopsy, and the other blood tests, to see if, indeed, they need treatment or they are getting close to treatment, something called smoldering multiple myeloma, where we're treating some of those patients early. And indeed, working with your doctor closely can help you understand, where are you at risk, and understanding all of your blood tests, your bone marrow biopsy and your imaging that CT scan or others can help you truly define where you are and whether you need treatment or not.

Dr. Fesko:
Before we close, I'd like to hear from each of you on how laboratory testing plays a role in the management and treatment of multiple myeloma. Dr. Ghobrial, can we start with you?

Dr. Ghobrial:
Yeah, I think it's so important now that we know that blood or liquid biopsies, as in many other cancers, are so important. And instead of doing bone marrow biopsies all the time, we have a great measurement here, with monoclonal protein, and in fact, even MRD disease that we're talking about now may also be done in the future in blood. So, we can actually use the blood to understand everything, from the circulating tumor cells, from the immune system, from the monoclonal protein that's circulating, and we can detect it and identify what is the type of myeloma, what is the stage of where it is in the disease progression, and how to treat it, and also what is the best response of the patient, MRD response, and how to prevent progression. And as we heard, there is next generation sequencing of the type and mutations that you have with multiple myeloma.

And with all of that, just a simple blood test can make a huge difference in understanding your disease and helping prevent also progression in the future.

Dr. Fesko:
Dr. Kussick, same question to you. How do you think these tests will impact the management and the treatment landscape of patients with multiple myeloma?

Dr. Kussick:
Yes, a great question, and obviously we're right in the kind of in the middle of an exponential increase in understanding of these diseases and how what we know can impact management and treatment.

We talked about prognosis both with FISH and mutational analysis as being obviously something that will impact thinking about treatment up front. The other thing that, that we can do in the laboratory is identify particular therapeutic targets in a patient's myeloma tumor cells up front at the time of initial diagnosis, that may be used to guide therapy antigens such as CD38 or CD319 where there are effective FDA-approved drugs already on the market that can be used. So, all these all the type of testing we do can not only indicate prognosis but can help really guide therapy in a way that will be maximally impactful for an individual patient.

Dr. Fesko:
With those expert insights in mind, I'd like to thank my guests today, for helping us get a better understanding of how laboratory testing helps patients with multiple myeloma. Dr. Ghobrial, Dr. Kussick, it was great speaking with you today.

Dr. Ghobrial:
Thank you.

Dr. Kussick:
Thank you. My pleasure.

Announcer:
This program was sponsored by Quest Diagnostics.

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