The Promise of Prevention. Multiple Myeloma and The Promise Study

Nearly all patients with multiple myeloma first develop one of its precursor conditions. People with these conditions do not have any symptoms, and they are told to watch and wait to see if they develop multiple myeloma. Currently, there are no treatments that prevent the progression of myeloma precursor conditions. To overcome this, researchers need to understand changes happening at the molecular level and identify potential targets for treatment. Dr. Irene Ghobrial of Dana Farber Cancer Institute is talking to us about the new PROMISE study, the biggest myeloma screening study ever run to help prevent myeloma before it begins and share how you can join the study and help in research.

Full Transcript:

Priya Menon: Good afternoon and welcome to another episode of Cure Talks. I'm Priya Menon and your host. And today the topic of our discussion is the largest ever myeloma screening study, the PROMISE study with the principal investigator of the study, Dr Irene Ghobrial from Dana Farber Cancer Institute. On the patient panel, to discuss the patient perspective, we have advocates, Dana Holmes, Tiffany Williams and Misty Callahan.So to begin with the discussion, we have with Dr Irene Ghobrial, Associate Professor at Dana Farber Cancer Institute leading the largest study on precursor myeloma conditions that will include 50,000 patients and family members. Dr Ghobiral, what is the PROMISE study and what the idea behind the study? Let's begin with that.

Dr Irene Ghobrial: Absolutely. Good afternoon Priya and thank you again everyone who's listening to this show. So the whole idea of the PROMISE study came from a very simple thing. When we go to see our primary care physicians and we get screened for cancers, whether it's breast cancer and we do mammography or colon cancer and you do colonoscopy, the idea is that if you look for cancer early and you find it by screening for it, potentially you can prevent it from going on to become a full blown disease and potentially curing you by early intervention or early interception. Yet if you think about it for all blood cancers, especially multiple myeloma, we don't do a very simple thing. We don't do a blood test to look for a protein in your blood that can detect myeloma and potentially by detecting it early, we can cure it. So this is the whole idea of the PROMISE study.

Can we screen for the first time in the US for multiple myeloma? And the question came by asking, can we screen for the people who are at risk for myeloma, meaning African Americans or first degree relatives of people who have myeloma? And I see that every day in my clinic when people tell me, how about my sister, my brother. I have three family members who have myeloma, could we look for this in the rest of them so that we are not surprised when we get myeloma. And it is true if you look for it and you can detect it by very simple protein test called Serum Protein Electrophoresis. And you find the early precursor conditions, namely MGUS, Monoclonal Gammopathy of Undetermined Significance or smoldering myeloma. You can find it early and potentially prevent it from going on to develop bad myeloma, which has organ function failure, meaning bone fractures, anemia, kidney failure, high calcium.

We can prevent all of this from happening. And that's another big problem for us in those precursor conditions. When we diagnose them early, the standard of care right now is we wait for people to have all of these problems and then we treat them and we want to change that. We want to diagnose people early and treat them early so that potentially we can cure myeloma and at least give a longer survival for people so that in the future we do not die from myeloma. So maybe I'll stop here and see what else you want to know about the PROMISE study.

Priya: Yes. So you did mention, Dr Ghobrial, the target population as African Americans and close families related and you have defined them as high risk, is that right?

Dr Irene Ghobrial: Yeah. So any person, Caucasian or African American, anyone who has a first degree relative with myeloma or Waldenstrom macroglobulinemia or MGUS is welcome to join the study or any African American, whether they have relatives or not is also welcome to join the study as long as their age is over 40 and the reason for that is they have a three times higher chance of developing myeloma. So believe it or not, myeloma is much more common in first degree relatives for an African American in general, much more than the rest of the population. And that's why we're targeting this.

The interesting thing is this is all online. It's very simple. You can be anywhere in the world as long as you are from the US or living in the US and you can click on PROMISEstudy.org and see if you're eligible. So it's all online, it's all available anywhere. And we will send the kits to wherever you live in Hawaii, in Alaska, anywhere you want. We will send you a kit to get tested. So it's very simple and easy. You do not have to go anywhere to get that test done.

Priya: Dr Ghobrial, so what I'm thinking is let's do the step by step, so for all the people who are listening today so if you say that I'm interested now that I know about the study and would like to participate in the throne, the study, what should be my first step.

Dr Irene Ghobrial: So the first step is going onto the website PROMISEstudy.org and checking if you are eligible, eligibility is there, it's simple. If you're age 40 or above, if you're African American or if you have a first degree relative with multiple myeloma or Waldenstrom or monoclonal protein.

Priya: Okay, so if I'm found eligible then what happens?

Dr Irene Ghobrial: You fill a small questionnaire, we will send you a kit that comes to you that has three blood tubes and we tell you there's instructions in it on how to go get tested in any place that has a phlebotomist. So QUEST diagnostics or your local lab or anything that's very easy and simple. And we have an amazing team here who are on the call all the time and then can help you answer any questions you have.

Priya: So if I may, what happens to my samples in the sense of what does it get tested for?

Dr Irene Ghobrial: Absolutely. So there are three tubes. One of them goes to Mayo Clinic where it's being tested for something called Serum Protein Electrophoresis and Serum Free Light Chain and Mass Spectrometry. These are very sensitive tests to see if you have a high protein, which means that you have an indicator that you have those cancer cells, the small number of cancer cells in your bone marrow because they all secrete that protein in the blood. The other tubes come to us here at Dana Farber so that we can keep them for research to try and understand better what causes this MGUS or this early abnormality in your protein, the precursors in everyone in the healthy population as we're looking at them.

Priya: So you've mentioned M Spike and Serum Free Light Chains. So is it sensitive enough to test MGUS which are probably too low for these tests to detect?

Dr Irene Ghobrial: That's a great question. So these are the standard tests that we currently use right now, but we're doing a third test called Mass Spectrometry. And this is a very sensitive test. It's three times more sensitive than the regular Serum Protein Electrophoresis and serum free light chain. And indeed we are doing that on all the samples. And if they are positive, we're letting everyone know about that extra sensitive test.

Priya: Okay. How often Dr Ghobrial should I be sending in my samples and for how long?

Dr Irene Ghobrial: Absolutely. So the first thing we want to know is are people positive – meaning they have

this early precursor condition or negative meaning they do not have it. We expect only 3000 of the 50,000 we will screen to be positive. So it's not a common thing. In fact, almost all of the people would not have this early precursor condition of myeloma. But the ones who have it and we detected early, we call them. And I can tell you that we've been calling every single patient and I was on the phone just last week with a few patients and we discuss it and then we refer them to a local hematologist or oncologist who can help follow up their blood samples and their protein level. And we will follow up with them.

And it usually depends on how high the protein is, how much risk they have for myeloma. Remember that in general, the risk is extremely low. It's only a 1% chance per year. And that's very important. Even if you screen you positive, it's very, very low chance to develop myeloma. But we want to follow you for life. And we usually check every six months to once a year to make sure we follow those patients and make sure that they never develop myeloma in the future.

Priya: Okay. That's great. So what you're saying is that in case I test positive for the precursors in your test I'll be informed of it probably you or someone would talk to me and refer me to a hematologist or help me like that, right?

Dr Irene Ghobrial: Correct. And we just make sure that we follow the protein level. We may need a bone marrow biopsy to see how much the patient has cancer cells in their bone marrow. But in general, we do not want you to be scared saying, Oh my God, I have myeloma. The most important thing is knowing that this is the precursor and the chances of developing myeloma is only 1% per year, meaning 99% chance I'll never develop myeloma.

Priya: Okay. So what happens if I am in the 99% and I do not have any of the precursors?

Dr Irene Ghobrial: So you have an MGUS, you have a precursor, but you do not develop active disease. And we keep checking every year. And I see many, many people every year we see them and their numbers are stable and we leave them alone. We just talk about life. But if your numbers increase and your chance of getting myeloma is very high, we will do something to prevent myeloma from happening. And we will treat you early to prevent fractures and kidney failure and anemia, which is what is myeloma as defined right now.

Priya: So is there any kind of compensation that is offered for the participants right now?

Dr Irene Ghobrial: So right now we do not compensate for it, but if you go to a QUEST diagnostics and you cannot get it there and you want to go to your local phlebotomist, then absolutely we will compensate for the phlebotomy draw there. But right now this is a free study for everyone to know about it as a research level. And again, this does not go to your insurance. This is a research level for you to know if you have a monoclonal protein or not.

Priya: Dr Ghobrial, when is the study complete, does it end after a certain period of time or how is it planned?

Dr Irene Ghobrial: Yeah, the accrual is for 50,000 individuals, but the follow up of the positive cohort, meaning the people who have protein levels is for indefinitely for as long as they are alive and they're following up for myeloma, the negative cohort meaning all of the other participants who tested negative, we will recheck them again if they are okay with it of course in three years time from the original time just in case if they develop that during the 3 years then we will follow up.

Priya: Okay, great. A great study design. Dr Ghobrial, can you tell us what you will be doing with the findings and how long do you think it will take to generate new insights or should I say what are you already seeing few months since the study has been launched?

Dr Irene Ghobrial: Absolutely. So the most important question we're asking here is, one, can we detect myeloma early by screening it two, can we define who would progress quickly to myeloma? And that's

important because we can find let's say 3000 people. Some of them will progress in three years, in four years to myeloma and some will never progress to myeloma. We want to be accurate in telling you today you have this much chance of developing myeloma.

So I said in general it's 1% per year. But what if you're one of those people who will progress to myeloma in two years and you're 40 years old. You want to know that you have a high risk of developing myeloma and you want to be followed very carefully and you want to be treated early to prevent it. There are other people who had progressed in five years and 10 years and want to know those numbers and be accurate in deciding who will progress in their lifetime or not.

So we do genomic studies, meaning we look at the DNA of the patient, we look at blood samples and we look at certain levels. We look at the immune micro-environment, meaning your own immune cells. Are they functioning to kill those bad cancer cells or not? Would they help you prevent myeloma? And then we try to resolve therapy specifically for you. We're not talking about chemotherapy, we're talking about vaccines and antibodies and immunotherapy that can prevent or cure myeloma in the future.

Priya: Awesome. Dr Ghobrial. I will now hand it over to the patient panel. We have Dana Holmes, Dana was diagnosed with smoldering multiple myeloma in 2012 and she's closely monitoring her myeloma, (unclear 13:37). Dana, all yours. Please ask your questions.

Dana Holmes: Yes. Thank you so much. Priya. Hi Dr Ghobrial. It's a pleasure to join you today. Just a quick little background on me – I was diagnosed in January of 2012 with smoldering myeloma, so I have a confirmed diagnosis of smoldering, so I'm not eligible for the PROMISE study. However, I am eligible for the PCrowd study, which I consider a very important study as well. I do routine labs every three months. So I've been submitting my lab work to the PCrowd researchers every three months for the past four years, just submitted my 16th sample. So it's so important to have that ongoing monitoring by your researchers to really see what's potentially changing should I ever progress. So that's a little information about my background with smoldering as well as that important study, the PCrowd. Now Dr Ghobrial concerning the PROMISE study in general, I do know that the 1% per year risk to progression would be applicable to someone who was determined to have low risk MGUS, is that a correct statement?

Dr Irene Ghobrial: Yeah, absolutely Dana. So thank you so much for bringing up PCrowd because I think that's a very important question. And I have a lot of people saying I'd love to be on PROMISE, but I already have MGUS or I already have smoldering myeloma. So we do have two sister trials. Both of them are exactly the same. Both of them are online. As you said, you've been submitting your samples. One is for people who are already diagnosed with MGUS and smoldering because your doctor incidentally found it and one is for us to screen for it, but the end results, because these are exactly the same when people have positive monoclonal protein and we send you a sample, we send you a tube to be tested every three to six months or every year depending on the level of protein you have and on the percentage of bone marrow cells.

So you're right. The 1% is in general for people who have MGUS, which is the stage is just before smoldering myeloma, but smoldering myeloma in general is much higher, 10% per year and in the first five years, you have a 50% chance of developing myeloma. There are people who have an even higher chance than that 50% chance in two years. But this all depends on many markers including the protein level, the percentage of plasma cells in the bone marrow, and we're now trying to define, especially with the PCrowd samples because of your health, we have defined new numbers of new genomic markers that can predict better for us who would progress much faster and who should call through their clinical trials or treatment options to present myeloma.

Dana: Yeah, it's an excellent study and it's such an easy, easy study to continue with. I get my little kit each quarter and it's filled with the vials, filled with all of the return mailing, packaging information and it is just so simple. Get the vials filled by my oncologists, phlebotomists. We packed them up, I put them in the case, I put them in a FedEx envelope and I walk them over right to the FedEx office or you can even call for a FedEx pickup. It's so easy and I'm grateful to be able to do something like that because it really does

empower me. It makes me feel that I'm doing something very proactive at this point as opposed to just sitting there scratching my head saying I have to watch and wait until this disease pops never made any sense to me. So I'm grateful for the inclusion in that study. Now Dr Ghobrial, if someone does test positive in the PROMISE study for a monoclonal precursor, how are you classifying their progression risk? What progression risk models, if any and the criteria are you using?

Dr Irene Ghobrial: Yeah, great question. So the first thing is we want to see their level of the monoclonal protein and most of the numbers, because we're finding it here by screening, not by incidental finding – very, very low. Most of the people are in the MGUS low risk MGUS setting by the old criteria, the regular Kyle criteria, which is the level of the protein, the type of protein. We do encourage some patients if their M Spike their monoclonal protein is elevated significantly above 0.5 0.6 we say, well maybe it's time to do a bone marrow biopsy. So in general we would love to have everyone get a bone marrow biopsy, but we're encouraging people who have a higher protein to go and get the bone marrow biopsy as soon as they can. And that would give you the number of plasma cells in the bone marrow. But it also gives you, are they having bad cytogenetics?

Do they have bad DNA changes that can predict for us who will develop myeloma in their lifetime? And I can tell you from the PCrowd study, we looked at about 300 people and ask the question if they have smoldering myeloma and they have certain genetic markers, will that make them progress much faster? And the answer is yes. Make alterations, MAP kinase mutation, certain mutations in your own chromosomes and in your own DNA can predict for us much more accurately than the clinical markers who would progress in their lifetime. So we are doing all of this on the samples that we get from the PROMISE study; we tested for next generation sequencing; we tested for single cell RNA sequencing. We're doing all of those fancy things to get better predictive markers of progression.

Dana: That is terrific. That is just so promising to coin a phrase. Now if a PROMISE participant is positive from monoclonal gammopathy, do they automatically cross over to the PCrowd study or would they need to apply to do that study or is that even necessary?

Dr Irene Ghobrial: Yeah, they don't need to because they are sister studies. So the PROMISE cohort that's positive will stay in the PROMISE cohort, but both studies are exactly the same. And actually we will be launching a new website for PCrowd that looks exactly like PROMISE and we have links to each other. So PCrowd stays alone, PROMISE stays alone. But the studies are very similar in both groups.

Dana: That's terrific. I have one last question and then we can pass it on to both Tiffany and Misty. I'm sure they're very anxious to speak to you as well. Dr Hoffmeister recently posted a link to an abstract in Blood journal, which presented data about familial risks. And this is obviously what the PROMISE study is all about. And the data supported that if you have a first degree relative with myeloma, it doubles your risk to develop this disease. So if we're saying that in general, there's only a 1% chance per year of actually progressing to myeloma, does that familial risks still remain low? Because when you hear that doubling, it's really kind of a scary term to hear, but is the risk still relatively low? I realize that the PROMISE study will reveal much more about this as the accrual goes on. But what are your early findings at this point?

Dr Irene Ghobrial: Yeah, great question. So the first thing that you said, which is absolutely true, is we're trying to understand germline meaning – So there are differences between what we're inheriting from our parents. Mom and dad give us DNA from each of them, 50-50 and one of them could make us at risk of developing myeloma. We don't know exactly all the risks, but we know that family members have a higher risk, meaning you probably inherit something from mom or dad that increases your risk, increases your susceptibility to develop MGUS or myeloma. The same goes true for African American.

There is something that we inherit potentially that increases our risk. Now once we have that risk MGUS in general or smoldering myeloma, we did not find differences of progression from that into overt Myeloma, like the different people who have familial factors or African Americans, but still we need more studies and larger cohorts to identify this. So there is a lot to be done in understanding who develops MGUS and when they

develop MGUS are they at a higher risk of developing myeloma in their lifetime.

Dana: Great. And just to confirm, the age group for inclusion in the PROMISE study was initially 45 to 75 but it now has changed to 40 years old to 75 and that would be for any African American and anyone with a first degree relative with a confirmed diagnosis of either myeloma or Waldenstrom's or a monoclonal precursor?

Dr Irene Ghobrial: Yes. Yes. This is correct. Absolutely.

Dana: Okay, excellent. Thank you so much Dr Ghobrial. Thank you Priya.

Priya: Thank you Dana. Thank you very much. I totally liked it when you said that you feel empowered being part of the PCrowd.

Dana: Oh without a doubt. Absolutely.

Priya: Yeah. Thank you for contributing to this. Thank you so much Dana. So the next advocate in the panel is Tiffany Williams. Tiffany was diagnosed with myeloma in 2013 and she just celebrated our fifth free year. So she's a core facilitator of the Charleston area Multiple Myeloma Networking Group and recently started a second support group in an area that is underserved. She is joining us from Charleston where I believe there is a hurricane issue going on and she's got her evacuation orders. Thank you so much for dialing in. Please ask your questions.

Tiffany Williams: Yeah, and thank you Dr Ghobrial for your work and this really important study. So, given the incidence of myeloma in African-Americans and the low rates of clinical trial participation, how does the PROMISE study compete compared to participation or in general too? How do the overall low rates compare to participation in the PROMISE study? And then also can you describe some effective tools that have been used to engage African Americans in this study?

Dr Irene Ghobrial: Yeah, absolutely. Thank you Tiffany for the call. And hopefully everything will be fine with you guys there. So thanks for taking the time now. So this is a very important point and actually we just recently had a meeting with the FDA and with many foundations asking the question, how can we encourage African-Americans and how can we empower African Americans to be part of myeloma therapy and improve myeloma therapy for them. And we've noticed and you probably are aware that there is low accrual for African Americans on clinical trials. There is worst survival for African Americans and that's because of care because of getting access to drugs because of so many things. Now this study does not include clinical trials, does not include therapy, but it includes empowering you to be aware that you have a monoclonal protein and giving you access to the best studies and the best research of understanding molecularly meaning biologically who would progress in their lifetime and getting potential access early to clinical trials and immunotherapy and vaccines that may not be as toxic as chemotherapy.

And given that we want to have at least 20% of this cohort African Americans and we're specifically asking for African Americans to be enrolled, we felt that this is a great opportunity for us to have everyone aware of it, to empower patients, to empower families of what is going on. And I can give you a story. It's a beautiful story. One of our participants, the very first African American who screened positive on the PROMISE study, we just called her a couple of weeks ago. Her sister was diagnosed with myeloma and she's undergoing stem cell transplants. She was just diagnosed with MGUS and she has, they have seven siblings. Her other sister was just positive also by mass spectrometry. And here's a wonderful family who are all willing to be part of this study, but to also know that this is important for them as a family to screen early to potentially prevent myeloma so that they do not have the same outcome as the sister who was diagnosed when she had symptoms and she had already problems.

And I think if we encourage everyone to tell their family members, their brothers and sisters, the church, the advocates, everyone around, Hey, this is something that will help the community in general. That's very important. Now for us to do that we've engaged many African American communities, we've talked to

advocates, we've talked to specific people who can tell us how to reach the community. We're talking to physicians who are African American. And that's very important because you want to reach the community by knowing exactly what are their needs and how can you engage with them and how can you keep that going on for generations to come, but also provide opportunity for access to good care and access to improving the therapeutic areas that we have for African Americans. So I think it's an amazing opportunity for us. I think that's where we are excited, especially about this part that we will help and hopefully we will help African Americans, but that we are giving African Americans an opportunity to help themselves and empower themselves to improve myeloma therapy for them.

Tiffany: I agree, I think it's so important to empower communities. And I think that's one of the, I guess my biggest driving forces as an advocate is to empower my community and communities like mine. And you really answered a lot of my second question, which was how can I and other myeloma community advocates promote and recruit, study participants in the community? And I do think, you answered a lot of that, but at the same time, I do think we learn from one another and to hear how you engage community advocates as well is important. And also in recognizing that no two community is alike, we just, we all have different needs and different areas of need. And so I think the bigger we expand the better. And so I would personally like to find ways to work with you to promote this in my community.

I do know that I didn't have very much background on this study myself prior to being invited to participate in this discussion. And so I would imagine there are many others who aren't aware of it. So I would like to do what I can to help increase that as well, it's very important work. And implementing a population science-based testing intervention that's also going to increase awareness and potentially impact screening guidelines for many generations. It is an innovative approach to advancing myeloma and cancer knowledge. And I'm curious how close you think we are to achieving the PROMISE study's aim of making myeloma a cancer that is preventable.

Dr Irene Ghobrial: Yeah. So Tiffany, first of all, thank you so much and it's exactly what we need is we need advocates. We need people who say, I am taking this and telling everyone I know about this and moving it forward to the next person and the next person. Because no one, not too many people know about this study and it's an amazing study that can make a huge difference. Now I'm a true believer that if we screen early and we have early interventions that are not toxic – vaccines, immunotherapy, we will potentially cure myeloma and prevents it from happening. And I joke but it's not the joke. Think about it like measles. We know about it because we have vaccines and we can prevent this from happening. I'm hoping in the future we will have a vaccine that cures myeloma or early interventions like breast cancer, we give people early on Tamoxifen so that you can prevent breast cancer from happening.

So I have a lot of excitement and hope and truly I'm a believer that we can prevent myeloma by early intervention. We are working so hard right now on all of the different types of intervention we can do. Whether they're simple things like and I'm giving you examples, metformin or things that we can change in our diet and exercise to present MGUS from going to myeloma into actual immunotherapy antibodies, vaccines. So that the middle part, the smoldering myeloma part do not go on to myeloma. So this is more of a true interception by immunotherapy. So there are lots of steps and all of those steps of intervention or interception will be there for everyone who participates on those trials, we will be having a two way communication for everyone.

We would not just have you get tested and that's it, we don't want to talk to you anymore. In fact, you are part of a community now, you will have your own advocates from us saying, here's the new updates, here's what we're doing new. Here are the new trials that are available for you. And we have them for everyone. And you're right. The other thing is when an African American or anyone goes and gets tested for protein level, well maybe they'll also say, well how about prostate cancer screening? How about your blood pressure check? How about diabetes? And in general, you improve screening and you improve health awareness for everything else. And that would make a huge difference for us because now we're infiltrating all of the communities to tell them about being helpful and taking care of themselves. And I think that would be an amazing thing that only people like you can help us move forward.

Priya: Thank you Tiffany and thank you Dr Ghobrial. Next we have Misty with us. Misty's mom was diagnosed with multiple myeloma in 2012 and she passed in 2013. Misty is part of MMRF's Young Professionals in Chicago and she has some questions for you. Yes, Misty over to you.

Misty Callahan: Thanks Priya, thank you so much Dr Ghobrial. I really do appreciate you taking the time to answer our questions. I also had read in depth of the PROMISE study, like the entrance age I guess was 45. Now I'm actually kind of happy to learn that 40 because I'm 41 and I definitely want to help and be like, just help research going forward with multiple myeloma. So I guess my question is what if somebody was like me and they're just like a year or two away from the entrance age for the PROMISE study, like say 38, 39 years old. Would they then able to ask for the PROMISE study once they reach that age or no?

Dr Irene Ghobrial: Yeah. Great question. And Misty, thank you so much and I'm sorry to hear about your mom. So we changed the age from 45 to 40 because we knew that so many people can also get diagnosed at an earlier age, especially the African American community. It's a much younger age and we didn't want to miss that opportunity. But as you know, myeloma as we get older, so if we are younger and younger, the chances of getting positive cases would be lower and lower. So if you're 39 and you're really worried, of course you can go get checked with your own physician. But the entrance criteria for this specific trial, it's 40. Of course if you are 40 minus one month we will do an exception or something like this. That's not an issue. Okay.

Misty: That's great news. I am 41, so I'm definitely looking forward to going to that website and signing up and seeing if that you guys will take me. I guess my second question is how will the PROMISE study help people like my mom now, she was diagnosed in late 2012 she was diagnosed late because she was asymptomatic for a very long time. She was only diagnosed after being admitted to the emergency room with severe bone pain. Found out, she had like a bone marrow biopsy, found out that she had bone lesions and it was a really aggressive form of multiple myeloma. So I guess my question is how will this study going forward, help people who were in my mom's position?

Dr Irene Ghobrial: Yeah, so it's a great question and the hope is that we never get to diagnose myeloma like this. Incidentally, we never wait for myeloma to present itself with bone pain and with fractures and with anaemia and with renal failure, the hope is that we get screened and find this early and present it from ever going to those two fractures, to anemia, to kidney failure. My hope is that we see that in our lifetime that we, that there will be no more cases of myeloma diagnosed this way because we shouldn't in our, the way we know now what we know of myeloma, we shouldn't be waiting for people to be found this way.

Misty: Yes, I absolutely agree completely. It's so funny to me, like I had never even heard of multiple myeloma prior to my mother's diagnosis. So I really appreciate everything that the doctors do on the multiple myeloma front. I guess my last question would be, concerning what my mother knew back in 2012, I remember she had asked her oncologist at that time, if I was susceptible or at risk for developing multiple myeloma, and she was told that my chances of developing it were very slim. And recent studies have come out saying, I'm like double as likely or triple as likely as just the average person to develop it because my mother came down with multiple myeloma. So I guess my question is what have doctors learned between 2012 to 2019 as far as both family members being at risk of developing multiple myeloma and how can people like myself with close family members use that information to keep an open dialogue with our own doctors and our personal care? Does that make sense?

Dr Irene Ghobrial: Yeah, absolutely. So in general, the risk of myeloma or MGUS is very, very small in the general population and it goes up with age. So at age 50, there's a 3% chance of having MGUS if we just look for the whole population. That was done in something in an area called the Onset County, which was all Caucasian people. So when we looked at the African American population, we found, Oh my God, that's not true. 3% is actually not the number. It's much higher. 6 to 8% and it happens at the younger age, 40 to 45 that the general public to numbers. When you look at first degree relatives, again, it's two times to three times higher than the 3% so you start getting into the 6% chance of getting it.

But this is where the numbers are. So you're right, 6% is a small number – of a hundred there are six that are positive. But what did we say? Because you had the first degree relative, should I be screened? This is what the PROMISE study will help us understand, with the screening numbers will they, how will we help make a difference in their lifetime and change survival and if the answer is yes, screening becomes part of the routine testing and we're hoping that that would happen, that people will go to their doctor and if they are at risk they get a blood test. It's simple, it's easy, cheap and they get to know if they had a monoclonal protein or not.

Misty: All right. Awesome. Well thank you so much. I look forward to signing up for the study. Thank you again, Dr Ghobrial and thank you Priya. Thank you.

Dr Irene Ghobrial: Thank you Misty. Actually I think the best thing you've said is I look forward to signing up for the study and I think it's so exciting for us to see that, that people want to be part of the study and I heard this again and again from all of you from Dana, Tiffany, Misty. It's so nice to hear that people want to be part of it.

Priya: Thank you Misty. Dr Ghobrial, we have questions coming up on our web page where people are listening to the talk live now, so I'll be reading those questions out and we can try to answer as many as we can. So the first one is what about first degree relatives who have other blood cancers? Would they be eligible or is it strictly for myeloma?

Dr Irene Ghobrial: So we're including anyone who has Waldenstrom macroglobulinemia myeloma, monoclonal protein, so MGUS or smoldering myeloma. For other blood cancers like CLL or leukemia as this is not included here because this is specifically for monoclonal protein, but it's a great question and in the future this can be expanded for the PCrowd, which is the other study for people who already have a precursor. It's open for all blood cancer precursor conditions. So if you have an MBL and early MDS, this is open for everyone.

Priya: The next one is can we accurately identify who the true high risk patients are and how?

Dr Irene Ghobrial: It's a great question. Currently there are clinical parameters that help us identify high risk smoldering myeloma or high risk MGUS. And these are the M-spike, the percentage of plasma cells, the light chain ratio. But these are not accurate enough. So what we are doing now is we're adding information, meaning mutations, copy number alterations, specific genetic markers like chromosomal abnormalities, 17p deletion, 4:14 translocation. All of these help us improve on it and then we're adding other markers, meaning your immune system is working well or not. So as we do the research and we define better biologically who will progress and who will not, we will add these tests into the current tests so that we can improve on it more.

Priya: Thank you Dr Ghobrial. We have another question. How do you know when a newly diagnosed myeloma patient had MGUS or smoldering at an earlier time in their life?

Dr Irene Ghobrial: It's a great question. So what we know now is every single patient who has myeloma today and was diagnosed today with myeloma, must have had MGUS or smoldering myeloma in their lifetime for years and years and did not know about it. And that's the sad part is if we knew about it because we screened, we would have found it before they got to be diagnosed.

Priya: Thank you. So there is another question or I should say a concerned person says, Please know that QUEST and I believe Labcorp too does not draw blood for any studies. I am a PCrowd study participant and I get my blood drawn at my doctor's office.

Dr Irene Ghobrial: Yeah that's perfectly fine. People can go to QUEST, they can go to their doctor's office there is no problem at all. And if people have specific questions for that, they can call us at any time.

Priya: Yes. We have one more question. Should I really treat early when I don't have any malignancy or will I cause more harm than good?

Dr Irene Ghobrial: It's a great question. We are not advocating for everyone to be treated. We are looking at specific markers. If the disease is going to progress very fast, meaning they're extremely high risk and they are likely going to develop myeloma in the next couple of years, then we offer options, specifically clinical trials to see if the patient is interested or willing to participate in a trial to prevent progression. However, many people do not progress in their lifetime and we just watch them carefully and we're looking for markers that predict if they will progress again and again.

So this is a continuous follow up and as long as you're following up, even if you don't get treated, just close follow up makes a difference. There was a study in Iceland where they said people who were followed up closely had a better survival than people who are lost to follow up. And then they showed up to the emergency room with myeloma because their fear of following up closely and your M-spike goes up higher and higher and higher. Your doctor would probably treat you early before you end up with kidney failure or fractures in your bones. So even just seeing your doctor without any treatment makes a difference in your survival.

Priya: Thank you Dr Ghobrial. We have, I think I covered almost all the questions that are posted on our page today. So to get back, Dr Ghobrial, I think you just mentioned the multiple myeloma study. I'm not very sure, but is the PROMISE study quite similar to what Iceland had launched, I believe Dr. Christensen was a PI at the time in 2016 called the iStop Multiple Myeloma.

Dr Irene Ghobrial: Yeah, great question. Yes, I thought it's something very similar in Iceland where they're screening the whole population for MGUS. Now the difference is that in Iceland they are very different than the American population. We are much more heterogeneous I think than the Icelandic group. And we have I think African-Americans here where they do not have an Iceland. So I think the genetics will be very different. But the two studies will complement each other. And that's very important that we can look at the data in the US and in Iceland and have a larger cohort that can make a difference to prevent myeloma in the future.

Priya: Thank you so much Dr Ghobrial, I think we can wrap it up now. So folks who are listening to this talk, if you are African American or family member of a myeloma patient between the ages of 40 to 75, it's time to join this important study which requires no travel. These two groups are involved in the study because they are more likely to develop into active myeloma. Joining the study is easy. You are mailed a kit that you take to a lab and the lab takes care of sending the samples to the researchers. So what can we learn from the study of 50,000 people who are likely to be at risk for early myeloma conditions and the family members, perhaps how to kill myeloma before it begins. So on that note, Dr Ghobrial thank you very much Dana, Tiffany and Misty. Thank you for your participation and your time. We thank the audience and the PROMISE study team at the Dana Farber Cancer Institute. The talk will be available on curetalks.com. Please visit our website for details on upcoming talks. Thank you, and have a great evening.