Understanding Myeloma Lab Tests and Results

Lets face it. Medical lab test results are difficult to understand. Specially if you are not a doctor or a nurse yourself. In this show we have oncology nurse, Anne McNeill breaking down myeloma lab test results helping us understand the nuances associated with the rare cancer.

Full Transcript:

Priya Menon – Hello, everyone, and welcome to the Cure Panel Talk Show. I am Priya Menon, Scientific Media Editor at the CureTalk, Cure Panel, joining you from India and I welcome all of you this evening to the first myeloma support group meeting of the year. This is the 45th episode of the Cure Panel Talk Show. Going forward, we have some very interesting shows on myeloma featuring eminent experts and interesting topics lined up for you this year. On Feb 26th at 5 p.m. eastern time, Cure Panel is featuring Dr. Vincent Rajkumar of Mayo Clinic. On 7th of March, we have Matt Goldman discussing fundraising on air. March 28th will see Dr. Robert Orlowski back on Cure Panel and in April, we will be featuring Dr. Rafael Fonseca. Please visit curepanel.carefeed.net for more information on our upcoming shows and you can always mail me, priya@trialx.com for any help. This is our live on-air support group meeting headed by myeloma survivor, author, advocate, Pat Killingsworth. Cure Panel's on-air myeloma support group meets every month on the Cure Panel Talk Show. The show is broadcast live on Blog Talk Radio. Today we have with us, myeloma survivors and advocates, Pat Killingsworth, Matt Goldman, Cynthia Chmielewski, and Dana Holmes. Welcome to the show, everyone.

Priya Menon – The guest on the show is oncology nurse, Anne McNeill. Anne McNeil is advanced practice nurse, Multiple Myeloma Division at John's Cancer Center at HUMC. Anne was with us in November and she helped us understand what lab tests and results mean for a myeloma patient. She is back with us this Feb. Anne, its wonderful to have you again. Thank you so much and welcome to the show.

Anne McNeill – Oh, thank you so much, Priya.

Priya Menon – I would like to inform all the people who are listening, our audience, that Anne's slides on the topic that we are discussing today can be accessed by going to the page curepanel.carefeed.net/event/rsvp/18. I repeat, the link is available on curepanel.carefeed.net/event/rsvp/18, 1-8. Before I hand over to Pat, I would also like to remind our listeners, we have quite a few today, that if you have a question for Anne or any one of our support group leaders, please press 1 on your keypad and we will be bringing you live on air to ask your question. Pat will now begin with the meeting. Pat, you are live on air.

Pat Killingsworth – Thank you, Priya, and thank you to all of our listeners and my fellow panelists, Matt, Cindy, Dana, great that you can join us tonight and especially you, Anne, I am so excited that you are back. That was too much to cover in an hour, it was impossible.

Anne McNeill – (Chuckles) I am happy to be… I am happy to return back.

Pat Killingsworth – Now, you do have this presentation, so I think we should start with that. That's great. That will be nice to bring us up to speed again before we ask some more specific questions.

Anne McNeill – Sure, sure. So, this presentation is a little overview of the immune system and trying to understand some of the laboratory values that we use in multiple myeloma. Of course, we all know how important the lab values are and I think that the patients and the caregivers really want to understand more fully, you know, what the doctors and the practitioners are looking at to assess disease status.

Anne McNeill – So, the first slide which should say the immune system, basically the first couple of slides should talk a little bit about the basics of the immune system and basically we have two parts to our immune system. We have a cellular immune system which is composed of our white blood cells predominantly and in the white blood cells we have granulocytes or neutrophils and then we have lymphocytes – two separate subsets of white cells that are very important in fighting infection and then we have what's called the humoral immune system and the humoral immune system is defined by antibody production. So, the cellular immune system is actually the cells that are involved in the immune system and the humoral immune system is the actual antibody production. Now, the antibody production is produced by cells and that cell is a B cell. The B cell is a very specialized lymphocyte and even more specialized is the plasma cell, which is responsible for direct antibody production.

Anne McNeill – So, if we go to the next slide, the B cell is shown here on the left hand side and the B cell works chiefly by secreting antibodies and I do want to point out that antibody and immunoglobulin are synonymous. They are two terms for the same exact thing and on this slide we see that the B cell matures into a plasma cell, so plasma cell is a very mature B cell and the responsibility of the plasma cell is to make the antibodies or immunoglobulins. That term is synonymous and the antibodies are very important part of our immune system. These are protective, soluble proteins that help us not to get the same kinds of infections more than once in our lifetime. That's just the reason why we don't get chicken pox twice in our life and certain other infections.

Anne McNeill – On the next slide shows the basic antibody structure and this is really important to understand the myeloma because we all know myeloma is a malignancy of the plasma cells, so its malignant plasma cells that make an antibody, so knowing about the antibody is crucial to understanding your disease. So, the basic structure of the antibody – it always appears as a Y, as the letter, the capital letter Y. In most of the literature or most of anything that you read about the immune system or myeloma, you will see the Y and that is the structure of the antibody and basically it has a heavy chain and a light chain and if you can't see the slide, the heavy chain is in green and the light chain is in yellow and I will go over what the heavy chains and light chains are composed of, but this is the antibody molecule and these heavy chains and light chains are actually attached. They are one molecule. They are attached by bonds.

Anne McNeill – So, on the next slide, we can see the different types of heavy chains and the different types of light chains and in our bodies, we make a lot of antibodies and there are five types of heavy chains and

two types of light chains. So, the types of heavy chains that we have are IgG, IgA, IgM, IgD as in dogs, and IgE and then we have two types of light chains. We have kappa and lambda. So, each antibody molecule in our body is a heavy chain and a light chain. So, you could have some IgG kappa and IgG lambda molecules floating around and have IgA kappa and IgA lambda and so on. You have all different types of antibodies normally present all throughout your body. This is normal. IgG is the most common one that we have in our body and IgA is the second most common.

Anne McNeill – So, if you go to the next slide, I am going to try to explain what happens in myeloma. So, we have these plasma cells and the plasma cell lives in the bone marrow. The normal home for the plasma cells is in the bone marrow. They don't normally come out of the bone marrow except in situations that are abnormal. So, they live in the bone marrow, that's where they like to stay, in the bone marrow and they secrete the antibodies and the antibodies do come out with the circulation. They come out with the blood and they can be spilled over into the urine and that's in a normal situation. What happens in myeloma is one of the plasma cells becomes malignant. It makes a clone of itself. So, it keeps accumulating into the marrow. It just kind of grows and grows and grows. It becomes a big, big clone and it accumulates in the bone marrow and the malignant plasma cells will still make an antibody. They do not lose their job. They still make an antibody, but the antibody, that has a special name, so all of you with myeloma know that this is called or you must be familiar with the M spike or the M protein or paraprotein or myeloma protein. It has a lot of different names, this antibody or immunoglobulin that the malignant plasma cells make. Okay? This antibody is not useful to the body. So, this antibody that the myeloma cells are making does not protect you against anything. Its just being made by the malignant plasma cells and it can be detected in the blood and/or the urine of most of our myeloma patients. A vast majority of them will have this antibody, that we can discuss, in their blood or in their urine sample.

Anne McNeill – So, laboratory testing for myeloma, why do we perform lab tests and there are many, many reasons why we perform lab tests. The first one, of course, is to help us diagnose the disease. Very frequently we are diagnosed, patients are diagnosed by a simple lab test. While that is giving us a clue that myeloma might be present, its a simple lab test. It could be a blood test, it could be a 24-hour urine sample, but very frequently…

Anne McNeill – …the first indication that we have that a patient might have myeloma is from the results of a lab test and then we want to determine how severe the disease is and to help us stage the patient's myeloma, we use lab tests. We also would like to see what's going on with the progress of the disease. We need to find out what's going on with the disease, so we do additional laboratory tests. We can also detect complications and I will talk more about this, especially bone complication, kidney complication. We can detect this by simple blood tests and then, of course, one of the most important reasons why we do lab testing is to monitor the effectiveness of treatments. So, all of you who have myeloma, who are on any kind of treatment, we need to make sure it is working before we keep giving you additional cycles of therapy and the way we do this is usually by doing a certain set of lab tests after the end of each cycle of treatment. So, that's one of the important reasons for doing lab test is to monitor the effectiveness of treatment.

Anne McNeill – So, if we go on to the next slide, for those of you who can view the slide, we will talk about the comprehensive metabolic panel or the chem screening or the… It has a bunch of different names, but basically its a chemistry analysis and this is a very common blood test. Its a group of tests used to determine how your kidneys and liver are functioning, your electrolyte status, determine your calcium level, your total protein level. So, three of them I want to go over are the total protein. So, the total protein in your body is very strictly regulated. When you have myeloma, the plasma cells, if you remember that I said the plasma cells will make this antibody that's secreted into your blood stream. This antibody is a protein. So, if you

have an excess of this antibody being secreted into your blood stream, your total protein will be elevated and that's frequently one of the first time that a patient may have a condition that is abnormal by having an elevated total protein.

Anne McNeill – We do look at the calcium level. The calcium level is very important because we all know that our bones, the major mineral in our bone is calcium. Myeloma has a very significant effect on the bone. If we destroy bones, we can leak calcium into our blood stream, so we can frequently determine how severe the disease is by measuring the calcium level. If it goes too high, now that's an emergency. The serum creatinine level is a very good measure of how your kidneys are functioning. So, if you want to determine how your kidneys are doing, how well they are filtering your blood, you will look at your serum creatinine level and that will determine your kidney function and again the organs that are most susceptible to damage in a multiple myeloma patient is the bones or the skeleton and the kidneys. So, we need to really protect your kidneys and your bones if you have myeloma and that's the reason why we look at these results on a chemistry panel.

Anne McNeill – And some of the other chemistry tests that are important in myeloma are the beta-2 microglobulin and the serum albumin level. So, the serum albumin level is part of the chemistry panel and the beta-2 microglobulin is actually a separate test that has to be ordered by your physician, and these two tests are very important in order to stage a patient's myeloma. Once we get the values of these two lab tests, the results can determine if you are stage 1, stage 2, or stage 3 and it gets kind of complicated as to why we check these two tests. We can just suffice to say that these two tests can indirectly determine how much disease you have and how active your disease is. So, that's why we use those tests. And the serum viscosity is a test that is important for certain patients. We all know what viscosity is. Its the thickness of anything and your blood can also be measured for viscosity. So, your blood has a normal viscosity. For patients with myeloma who have an excess, a very large excess of protein in their blood, these molecules are very, very big and it can make the blood more viscous or more thick. So, you can get a lot of situations where the blood is very viscous and it causes lot of symptoms based totally on the hyperviscosity state of the patient, so that's something that we sometimes measure.

Anne McNeill – The next slide talks about the CBC, the complete blood count, which is probably the most common blood test that's done on any patient in this country, the CBC, patients with myeloma, even that are not getting any active treatment and why is the CBC important? Because it measures a critical element in your marrow, which are your blood cells. Your bone marrow is the source of the manufacturing of your blood cells, but of course, all of your blood cells are released into the circulation and by doing a simple blood test and CBC, you can measure these numbers in your blood. So, the hemoglobin and hematocrit, this is very important in that this is a determination of how anemic you are. The hemoglobin is the molecule in the red blood cells that carries oxygen. So, if you are anemic, your hemoglobin is low and that's something that we need to know too. If you are a patient with myeloma or getting treated, we want to know how anemic you are.

Anne McNeill – The white blood cell count is very important. The white blood cell count and a subset of those white blood cells, which is the neutrophil count, is very, very important. The ANC is the absolute neutrophil count. These are very important because this evaluates infection risk. So, if you have a very low white count and especially a low neutrophil count, you are more prone to certain infections. So, its very important for us to look at these numbers and finally what's really important on your CBC is your platelet count. Your platelets are responsible for blood clotting. So, you will definitely know if your platelet count is very low because you will pump yourself or you will cut yourself and you will bleed for a longer period of time

and you will get a very big bruise. Those platelets are responsible for blood clotting and this is very important in patients who are on blood thinners. If you happen to be on aspirin or Coumadin or Lovenox or XARELTO, they will thin your blood for whatever reason. You want to make sure your platelet count is not that low because that just further increases your risk for bleeding. So, again, three things that we look at in your CBC are your hemoglobin, your white blood count or your ANC, and your platelet count.

Anne McNeill – And the next slide talks about some of the more specialized tests that we do when you have myeloma. The first of these and most of you may not have all of these tests done periodically, but maybe you only have one or two of these done to assess your disease status. So, depending on the physician or the group that you go to, in order to determine how your disease is, you might have quantitative immunoglobulin performed. So, what does this test mean? Well, this measures the amounts of the different immunoglobulins in your blood. So, particularly it measures IgG, IgA, and IgM. Most myeloma patients would be IgG or IgA. IgD and IgE are extremely rare and IgM myelomas are again very rare. Most patients who have IgM, what we call monoclonal gammopathies or these conditions where there is abnormal protein production of IgM, usually they have Waldenström's macroglobulinemia, which is a type of lymphoma. So, we are going to not talk about that. So, most myeloma patients have IgG or IgA. So, we have to measure these levels and that will help monitor the course of the disease. So, we are looking… If you are an IgG kappa, let's says that's your myeloma protein, we are going to focus on the IgG level as well as the kappa and we are going to see if these numbers go down after treatment, that means treatment is effective. Okay? So, it's also important to be aware of the levels of the normal or the non-myeloma immunoglobulins and by that I mean this test measures IgG, IgA, and IgM. So, if you are an IgG myeloma, you are going to focus on the IgG. You are going to say, "Wow, is it going up, is it going down, you know, is this treatment working, is my disease coming back?" You keep the focus on just that IgG, but it's really important to look at the levels of the IgA and IgM also because as treatment works and becomes more effective, not only will your myeloma protein go down, but your other immunoglobulin levels will start to recover. So, they kind of go to more normal level and that's a good sign. It means your immune system is recovering. So, its important to be aware of the levels of all of the immunoglobulins.

Anne McNeill – And one of the most important tests that we use in myeloma, unfortunately I can't go back on my slide, let's see…, is the protein electrophoresis. I apologize. I just had to go back to another slide, let's see…, just having a little… Protein electrophoresis, that's very, very important test or the SPEP, serum protein electrophoresis. This is a test which separates the protein in your blood or urine sample into several groups based on the size and the electrical charge of the protein in that fluid, in that body fluid. So, its a little bit complicated, but your blood sample or urine sample is put on a gel and after a certain amount of time the technician will come back to that gel after leaving it on the gel and exposing it to an electrical current and all the proteins in your blood or your urine will kind of migrate to different areas. In most patients with myeloma, large amounts of an abnormal immunoglobulin protein will appear as a large peak gamma region. The gamma region is where all the immunoglobulins migrate to and in most patients with myeloma, they will get the M spike in that area. If you have ever seen one of these graphs, its very, very characteristic of myeloma. So, actually I do have a picture of it in the next slide, but its very important. This measures the M spike. So, the protein electrophoresis is the test that will get you the measurement of your M spike. Okay? And that's a number. Okay. That quantification is a number. It's 2.0, 1.5, 3.2, 0.4. That's the measure of that abnormal antibody that's present in your blood or your urine. Usually its the blood right now we will talk about. Okay?

Anne McNeill – The immunofixation is done to identify the specific type of protein that is being produced by the malignant plasma cells. So, while the M spike tells us how much there is, it doesn't tell us what it is. It doesn't tell us if IgA lambda, IgG kappa. That test we need to do is the immunofixation to find out the type of protein that's being produced. Okay? The amount of the protein may vary throughout the course of the

disease. So, your M spike may vary. It might be the highest when you are diagnosed. It might go down, way down after treatment. Maybe you had a transplant and now its 0, you are in complete remission. So, your M spike can vary. If your disease has shown signs that its coming back, it might be creeping up a little bit. So, the M spike can vary, but the type will remain the same. So, if you are an IgA kappa, on your immunofixation you will see an IgA kappa myeloma during the course of your disease. That does not change. Okay?

Anne McNeill – And actually in the next slide, there is a little picture of a normal serum protein electrophoresis and if you don't have the slide, I apologize, but it just shows you how a normal graph looks. When the lab tests have a patient without myeloma, I just showed you these little bumps on how the serum protein electrophoresis looks and of course if you go to the next slide, we see a huge spike in the very far right hand side where the immunoglobulins migrate to and that spike is the M spike. That's the abnormal serum protein electrophoresis pattern that we typically see in patients with myeloma. Okay?

Anne McNeill – So, the next test that we can talk about a little bit is the serum free light chain assay or the free light assay and this is a little confusing. Some physicians and some institutions still do not use this routinely. It is a fairly new test. I think its only been around for about 10 years. It is becoming more common and in most myeloma centers, it is a standard of care to use this blood test to monitor patients. Its a very, very sensitive assay. What it does is, it measures the amount of free light chains in the blood. So, if you remember when I was talking about the antibody molecule, I said there were heavy chains and light chains. Okay? So, in normal instances, our plasma cells produce an excess amount of light chains compared to heavy chains. So, we do have a small amount of these light chains that will not become part of an immunoglobulin molecule.

So, remember I told you that they are like IgG kappa or IgA lambda, most of the antibodies… Well, we have some kappa and lambda floating around in our blood normally that's free, that does not become attached to any of these heavy chains. It just kind of floats around and its normal. These are called free light chains and they are present in our blood. So, its very normal to have a small amount of these light chains in everybody's blood. Okay? So, that's normal. However, in patients with myeloma, if you go to the next slide, they will produce increased amounts of either kappa or lambda light chains which can be measured in the blood. So, if they are an IgG kappa, we will frequently see an excess of kappa like, the serum kappa level will be higher in these patients and consequently, the ratio of kappa to lambda light chains is abnormal in those patients and its a very sensitive indicator for the disease. This test can be used to monitor progression and/or the effectiveness of treatments and let me just say one more thing about the serum free light chain assay. If you have a physician or a practice or an institution that does routinely use this test, very frequently we will see abnormalities in this test before we see any small rise in the M spike. This is a very sensitive test and we will see evidence that there is progression of disease based on this assay before there is an increase in the M spike or the IgG or IgA and before the patient gets sick. So, this is a very sensitive indicator of what is going on with the disease. Okay?

And the next two slides to talk about are the most definitive tests that we have to diagnose myeloma. So, most of the laboratory tests that I have discussed with you on this presentation provides indirect information about the amount of tumor present, indirect. So, what we are doing is we are measuring proteins that are secreted by the tumor into the blood and to the urine. We are very easily taking a blood sample from you or asking you to collect a urine sample. We are measuring the protein that is produced by the tumor cells. These tests do not provide the same information as looking up tumor itself. The myeloma cells are usually only found inside the bone marrow. So, in order for us to really determine what's going on with the disease

and especially to diagnose the disease, we must do a bone marrow aspirate and biopsy. Its very important. Now, you might say, “Well, I had a bone marrow aspirate and biopsy when I was diagnosed, but I haven’t had one since and that’s okay, but in order to get a diagnosis of myeloma you really need to have that bone marrow aspirate and biopsy done. If you have a significant measurable disease, as in your M spike, then you can just look at the M spike and determine what’s going on with your disease and not ask you to have a bone marrow biopsy done every three weeks or four weeks, that’s kind of crazy. But, small amounts of bone marrow cells can be withdrawn with an aspirate needle and we actually take small core of the bone and the marrow is often removed at the same time with a different type of needle.

Anne McNeill – So, when you go for a bone marrow aspirate and biopsy, usually the physician will go into the posterior iliac crest which is your hip bone. You might be familiar with that. They will do an aspirate. So, they will put a needle into the bone marrow. They draw out some of the fluid and with the same puncture, they will actually take a small core of bone for biopsy and both of the tests are to determine how much of the normal bone marrow is replaced by myeloma cells. So, there is a very specific percentage of all of the cells in your marrow. So, you have plasma cells, white cells, red cells, platelets, and all the different types of white cells. Every single cell has a normal percentage in your bone marrow and for all of us that do not have myeloma, the plasma cell represents a very small percentage, like 1% or 2%, in our marrow. For myeloma patients, it could be 10%, 30%, even as high as 90% or 95% of the marrow can be replaced by plasma cells. Okay?

So, not only are we looking for the percentage of plasma cells in the bone marrow, but very, very importantly we do additional specialized testing on that bone marrow sample, especially at diagnosis prior to the beginning of treatment and those tests are called the cytogenetics and the FISH testing and that can give us a lot of information about the biology of the tumor itself and what it does is, when we do these tests, it puts patients in a risk category. They can be either standard risk or high risk. Now, it doesn’t mean we don’t treat the patients who are high risk. We treat everybody. We have various effective means to treat every patient with myeloma, but we understand from experience that patients with high-risk disease can just be a bit more challenging. We might have to just keep right on our toes to determine what our next line of therapy is going to be because traditionally patients with high-risk disease don’t have those very, very long remissions that patients with standard-risk disease are likely to have. So, that’s what’s really important about the bone marrow biopsy.

A lot of times patients will come to our clinic. They have already had a bone marrow biopsy done, so we do have the percent of plasma cells, but then the physician says, “Well, they didn’t do FISH and cytogenetics, so we have to do another bone marrow biopsy.” So, that’s how important this testing is. We do a lot of genetic profiling. We do molecular studies. This is getting very, very advanced to determine exactly how much of a risk the patient is from their disease based on their molecular studies and this is all evolving over time. This is a new testing that we are doing for myeloma. So, I think that is my last slide and I know that was just a very brief overview of all the testing that we do for patients with myeloma, especially to diagnose you, to make sure you do have myeloma and then to hopefully monitor the course of your disease, whether it be with observation alone or with active therapy. So, I guess, Pat and Priya, I guess we can open it up for some questions that anybody has.

Pat Killingsworth – Awesome, Anne! That’s…, that’s… You can take a breath.

Anne McNeill – Uhmm… Yes.

Pat Killingsworth – You know, it isn't becoming. I hate on broadcasts when the hosts gush over their guests, but you are an incredibly good at this and I actually enjoyed listening to something that would normally be a pretty dry subject (laughter) and I don't know if I am speaking on behalf of the other questioners and I only have one question, but it could take a little time unfortunately, but I think its important because I interact with myeloma community down here 24/7 via email and comments on my blogs and broadcasts like these and the number one question I get and I can't answer it because I don't follow this ratio, this value. The number one question I get is about the serum free light chain assay and what the ratio means. So, they will say, you know, 24 or blah, blah, blah… and I am like, I have no idea because I just follow my M spike.

Anne McNeill – Sure.

Pat Killingsworth – Its so simple, but… I mean what do I tell these people?

Anne McNeill – Sure, Pat. Its really simple. When you do the free light assay, it consists of three numbers. So, you are going to get a serum free kappa quantification, then you are going to get a serum free lambda quantification and then the third number is going to be the kappa-lambda ratio. So, you can determine your kappa-lambda ratio by having just the other two numbers. If you have your free kappa number and your free lambda, all you do is divide kappa by lambda and you get your ratio. So, you might say what's the significance of the ratio. Really, I have to be honest with you. Some practitioners and some patients really focus on the ratio, but you really need to look at the absolute values of both the serum free kappa and the serum free lambda as well as the ratio. So, if the ratio is becoming very abnormal, you have only to look at the numbers, so it is very, very, very, very, high.

Pat Killingsworth – So… And what does the normal ratio look like?

Anne McNeill – The normal ratio, I don't have the normal…

Pat Killingsworth – I guess there might not be a normal ratio. Even I…

Anne McNeill – No, there is a normal ratio. The normal ratio is somewhere between 0.4 and 1.6, something like that. I don't have the lab… I mean I am at home right now. I don't have the… And also, you have to remember too, Pat, based on the lab, these values of the reference range will differ. So, depending on whether the person goes to LabCorp or Quest or Bio-Reference or GenPath or their local hospital, that hospital or that institution, that laboratory has to set their own reference rate. So, basically its within the same kind of numbers, but I think, what I am thinking of right now is anywhere, its like 0.4, I think, to 1.6, something

like that and we all, everybody has free light chain. That is the normal ratio for a patient without myeloma, I mean an individual without myeloma. There is a normal amount of free light chain in our blood. If that ratio is becoming very abnormal, then we look at those numbers and we see, well, you know, it is the serum free kappa going up and usually the patient has an IgG kappa myeloma, we will see a very, very abnormal kappa level and that once the kappa level goes too high, the lambda will then be abnormally decreased and you will get a very, very altered ratio. So…

Pat Killingsworth – I understand it and like other values and I am just cutting you off because we wanted to…

Anne McNeill – Okay.

Pat Killingsworth – …switch over to, so other people here have questions. So, it is like other values, say like an M spike, you are following this for months and months, right? Aren't you going… Aren't you looking at trend?

Anne McNeill – Yes, yes, yes. Absolutely, Pat. We see this all the time. We are looking for trends, but you have to remember this is a very sensitive test and I have patients who have come to me have and their, let's say they are an IgG kappa and their kappa level has gone from 21, let's say, I am making up numbers, from 21 to 30. That is the… Oh, my god, they are, you know, saying, "Wow, my level went up." That's really not a significant increase in the kappa level, like these are very small numbers and we typically look for pattern of increasing numbers and we look for big jumps. So, this is… Again, something like you should discuss with your doctor or nurse, but I want you to understand that these are very sensitive numbers and even very small increases may not be that significant, but its something to review with your practitioner.

Pat Killingsworth – Wonderful! That's very helpful and, Matt, are you with us?

Matt Goldman – I am.

Pat Killingsworth – Great! I am sure you are watching. I don't want to… I wanted everybody to have a little bit of time. Matt, you have a question or so for Anne?

Matt Goldman – Yeah, I do. Thanks for all of that. It feels great. For me…, for me we tracked my 24-hour urine and we looked at the total protein and then the UPEP, the paraprotein. We don't look at M spike and I don't understand the relationship between what we are looking at and the M spike. So, are they the same thing just being looked at differently or is it something totally different?

Anne McNeill – So, the M spike in the urine is also a measure of that abnormal protein that is spilled out from the blood. So, there are some patients where they are urine secretors. In other words, they really have more of a measurable disease in their urine, but yes, you are looking at the M spike in the urine. Now, you also want to look at both the total protein because that can be an indication of what's going on with your kidneys, but you really want to look at the M spike. You can follow the M spike in the urine also to determine whether or not the disease is being monitored correctly via treatment. You know what I mean? You have to be…

Matt Goldman – Uhmm…

Anne McNeill – …careful with your 24-hour urine. You have to make sure that the patient is collecting it properly, that the volume is recorded correctly, that the lab knows what they are doing here. A lot of… A lot of variables for the urine sample. So… But you can, you can follow the M spike, just that you follow the blood M spike. Yes, you can.

Matt Goldman – Right, but we never… We never knew about the M spike and I have always wondered why not. We only look at the paraprotein, that percentage of the total protein.

Anne McNeill – So, in your urine you mean?

Matt Goldman – Uhmm….

Anne McNeill – Yeah. So, in other words, so if they have a total protein and they have a percentage, that's the paraprotein, they are really looking…

Matt Goldman – Right.

Anne McNeill – …at the M spike. Yeah. Its just not a number, so… You can follow the percentage and some labs only report out the percentage and that's okay and some of the labs automatically will just do the math and give you an M spike that's actually a milligram to 24 hours. So, its easy just to kind of calculate it. You look at the percentage, in special cases you can follow the percentage. I think…

Matt Goldman – So, its really… I am sorry. So, really its the same thing just being looked at in a different way.

Anne McNeill – Correct. Correct. Percentage, absolute values, it really is something you… As long as you know that you are monitoring one thing, you know its the same. You don't want to, you know, if you are following…

Matt Goldman – Right.

Anne McNeill – …a percentage, you want to keep following the percentage. Don't go back to the absolute values, but yes, you have to.

Matt Goldman – Right. Like Pat… Like you and Pat just said, its all about trends and following the trend.

Anne McNeill – Yeah. Oh, yes, all about trends.

Matt Goldman – Yeah. Just one more question before we go to somebody else. Can that total protein number, can that jump or vary, you know, from month to month just based on even like diet and what sort of…

Anne McNeill – Yeah.

Matt Goldman – …protein or [00:41:00]diet.

Anne McNeill – Yeah. You know… Yeah. Not so much diet. I mean diet has little effect on the total protein, but when I see jumps in the total protein, I am always thinking about what's going on with the kidneys, so there are non-myeloma issues that can cause a jump in the total protein. If you have high blood pressure and you are on blood pressure medications, if you are a diabetic and you are on diabetic medications, if you are an amyloid patient, a lot of these issues can cause jumps with decrease of the total protein that may have nothing to do with your myeloma.

Matt Goldman – Uhmm..

Anne McNeill – So, its really important to look at that M spike in the urine as well as the total protein.

Matt Goldman – Okay. Got it. Thank you very much.

Anne McNeill – Okay. You are welcome.

Pat Killingsworth – Thank you. Well, there's somebody who has got a party going in the background.

(Laughter)

Matt Goldman – I am actually getting treatment right now, so my machine is beeping.

Pat Killingsworth – Oh! There you go!

(Laughter)

Pat Killingsworth – Now, that's a myeloma warrior.

Anne McNeill – That is... That is….

Matt Goldman – There you go.

(Laughter)

Pat Killingsworth – Awesome, Matt!

(Laughter)

Pat Killingsworth – Okay, Cindy, you are up.

Cynthia Chmielewski – Hi, Anne. How are you doing?

Anne McNeill – Hi, Cindy. How are you?

Cynthia Chmielewski – Okay. So, how many inches of snow did you get?

Anne McNeill – Oh, I think it was like 14 inches at noon. I believe it stopped. Actually, it stopped right now [00:42:18] I am hoping it doesn't start again. So, you are in Philly. No, you are not in Philly. You are in New Jersey also, right?

Cynthia Chmielewski – Right. Yeah. We got about 12 to 13 inches and they are saying that I always learn something new every time I listen to you, so I have two questions.

Anne McNeill – Aha?

Cynthia Chmielewski – The first question, I was wondering when we are looking at our lab results, is there like… Is there a relationship between certain types of treatments and how they look at certain numbers in the lab results, like if you are always taking blood, you should be looking at your red blood count because it affects your red blood count and if you are on another type of treatment, you should be looking at platelets.

Anne McNeill – Yeah.

Cynthia Chmielewski – So, isn't that relationship there?

Anne McNeill – Yeah. Cindy, that is an excellent point that I forgot to bring up when I was talking about the CBC. So, that's another reason why the CBC is so common with outpatients. Not only does it show us what's going on in the bone marrow, but most of our treatments will affect the blood count to some degree and in general…. In general, this is just, you know, a very wide statement, but in general, the proteasome inhibitors like Velcade or bortezomib and Kyprolis or carfilzomib, they will lower the platelet count temporarily and drugs, the IMiD drugs, the drugs like Revlimid and pomalidomide or Pomalyst, they will affect the neutrophil counts and lower those counts temporarily. So, it is very important… And of course, anemia can occur with these drugs also, but again its very important to get that CBC done frequently when you are on treatment because the treatments themselves can lower the blood counts and we have to monitor them closely. Very good point. Thanks, Cindy.

Cynthia Chmielewski – Okay and the other thing is kind of just related to me. When we are talking about, I guess, your anemia bothers your IgG or IgA, all those. My myeloma is an IgG myeloma. Yeah. My… My myeloma is now and my IgG is in the normal range, but my other two, IgA and IgD or whatever they are, I can't remember…

[00:44:33] (Anne McNeill) – IgA or IgM.

Cynthia Chmielewski – IgA and IgM, those two, they never recover. They are too low and its been years. Is that something common or…

Anne McNeill – Yeah, that's common. Now, Cindy, that… that… that… We have seen that. Sometimes even though the disease is under excellent control, we would like to see those uninvolved immunoglobulins, you know, normalize, but sometimes it just doesn't happen and its really no bad effect on you. Like I said, we would like to see them normalize, but sometimes it just doesn't happen and there's nothing we can do to make that happen. That's just your disease. That's just your… That's just, Cindy, Cindy's myeloma.

Cynthia Chmielewski – Right. Yeah. I always keep on watching and saying, "Oh, they are coming up and, yes, they have come up maybe from 7 to 8.

Anne McNeill – Right, right.

Cynthia Chmielewski – 10 to 15. Okay, but nowhere near to normal now, but I think… I catch a lot of, you know, illnesses. So, I guess…

Anne McNeill – Right.

Anne McNeill – No, I think… No. IVIG, we do not believe, we are IM, that is very effective. The only time we will use IVIG is if a patient is repeatedly almost half the life with very frequent upper respiratory infections and really truly has what's called hypogammaglobulinemia, which is a really significant decline in all of their immunoglobulins. You know, this happens with teachers and people who work in daycare centers and nursery schools. They are always around kids. They are always getting sick. They have very low immunoglobulin levels. These are people that may benefit from some of the IVIG infusions over the, but other than that it really has not seen a big effect on the reduction in infections with IVIG.

Cynthia Chmielewski – Okay. Thanks so much.

Anne McNeill – You are welcome, Cin. Stay warm.

Cynthia Chmielewski – I hope you… Yeah, I hope you don't get more snow tonight.

Anne McNeill – I am keeping my fingers crossed.

(Laughter)

Pat Killingsworth – Thank you. Thank you, Cindy. Nice to hear your voice.

Cynthia Chmielewski – Nice hearing yours too, Pat.

Pat Killingsworth – Great! Time has worked out, so that's good. Dana, you are up.

Dana Holmes – Hi, everyone, Anne and everyone, thanks so much for inviting me tonight to join your group. Anne, I am smoldering.

Anne McNeill – Okay.

Dana Holmes – I was diagnosed after an incidental finding by my neurologist who added Anesta really as an afterthought to the bottom of a laundry list of autoimmune labs. As all of my regular labs were normal, including my total serum protein, so I really…

Anne McNeill – Okay.

Dana Holmes – …had no red flags. My labs have remained pretty stable and I am monitored every three months. So, as a smolderer, an abnormal free light chain ratio is an important concern because from what I understand its an independent risk factor possibly for progression. So, I would like to know what do smolderers need to know about the variations that we tend to see in the actual ratio results from test period to test period? Is a solid upward trend or a big jump the key for smolderers as well because some of us actually see the ratio really bounce around a lot.

Anne McNeill – Right, right, right.

Dana Holmes – And secondly, which labs are the most important for those with the precursor state?

Anne McNeill – Okay.

Dana Holmes – Are they the same as a multiple myeloma patient we follow or do we need different monitoring?

Anne McNeill – Okay. So, the second question is a little bit easier. When you are a smoldering myeloma patient or an MGUS patient, then you get your labs done every three months. The values that are monitored are exactly the same as a patient with myeloma. So, we are going to look at the Ig, let's say urine IgG kappa.

Dana Holmes – Uhmm…

Anne McNeill – We are all going to look at the IgG level. We are going to look at the serum free kappa. We are going to look at the M spike. We are looking at the same exact lab values over time and its very important because I have patients who come to me in support groups and say, "Here are my labs. Tell me how I am doing." That is impossible for me or any myeloma practitioner to do, not knowing how they started off and what the course of their numbers has been over time. So, you have to flow these numbers for every single three months. You should keep a flow chart or, you know, your physician is probably keeping a flow sheet of what's going on with your numbers over time, but yes, the same numbers are monitored. Now, I have to be honest with you. If you are a smoldering myeloma patient, yes, the free light assay is important. Very frequently, like I said before, if we see significant abnormalities in that assay, sometimes we see them first before the M spike goes up and before we have other concerns with the other labs, but again there is a lot of research being done with smoldering myeloma patients at this time and I went to ASH in December and there is a lot of new information coming out with regards to managing myeloma patients who are smoldering.

Dana Holmes – Uhmm…

Anne McNeill – And right now, unless you are ultra-high-risk smoldering myeloma patient, we would not treat you at all unless you did develop a crab symptom. In other words, I am sure you are familiar with this, but you will…

Dana Holmes – Uhm…

Anne McNeill – …have to become more anemic, have calcium levels that are abnormal, kidney issues, and bone issues. So, regardless of your numbers, we are not going to say, “Okay. Dana.” Your name is Dana, right?

Dana Holmes – Yes.

Anne McNeill – Dana, what I am thinking is when you get an M spike of 3.0 or your kappa level becomes blah, blah, blah, your Ig, whatever it is, you know, then we are going to start treating you. That’s not the case. We are not looking for a number. Its not a number. Its how you get there. Not only is it how you get there, like, you know, the big spikes over a short period of time, but are your other organs getting affected, are you becoming more anemic, are you having issues with your creatinine or your calcium or your bones?

Dana Holmes – Uhmm…

Anne McNeill – So, its a much bigger picture with the smoldering patients.

Dana Holmes – And how important is a bone marrow biopsy in the precursor state? Can we just be diagnosed with labs only if we have low levels of M spike and immunoglobulins and a normal serum light chain ratio?

Anne McNeill – In order to be really classified as a smoldering myeloma patient, you need to have a bone marrow done actually for diagnostic purposes.

Dana Holmes – Uhmm…

Anne McNeill – You do not need to have a bone marrow done every three months or every six months. After you have the initial bone marrow done, you can then be followed with labs every three months, every four months, every six months, whatever you decide, you and your physician decide to do, but in order to be truly classified as an MGUS or smoldering myeloma or an active myeloma, you need to have the bone marrow biopsy and aspirate done. Period.

Dana Holmes – Okay. Thank you, Anne.

Anne McNeill – You are welcome, Dana. Is Pat there?

Pat Killingsworth – I believe, Priya… Thanks, that was… Dana, that was helpful. It was great!

Dana Holmes – Thank you, Pat.

Pat Killingsworth – In smolderers, by the way for the record, if I was to somehow, you know, quantify the emails, the questions that I get and could somehow measure, I guess as a former social studies, social science guy…

Dana Holmes – Uhmm…

Pat Killingsworth – …and we had to come up with a way to quantify angst, anxiety, and apprehension…

Dana Holmes – Oh, yes. Oh, yes.

Pat Killingsworth – …I have got to tell you smolderers I think worry more than a lot of patients…

Dana Holmes – Yeah.

Pat Killingsworth – …with active myeloma.

Dana Holmes – Absolutely. Its a double-edged sword because with the added worry, I mean I am wondering if I could feel lucky that I am being monitored and then on the other hand, you know, through this entire extra worry and to feel, but you know, honestly, even though I am not particularly fond of the watch and wait, although I realize its due to the chance I may never progress, I am trying to do my best to really be proactive in case I do.

Anne McNeill – Pat, also with the MGUS patients, not only the smoldering patients but the MGUS which is usually found incidentally…

Dana Holmes – Uhmm…

Anne McNeill – …the anxiety level every six months or so when they had their labs done and you can, you know, you walk in to the room and you can feel the tension because its so nerve wracking for patients. You know, it is very anxiety producing. It is.

Pat Killingsworth – Yeah. Very difficult. We should do a… We should do a show on that.

Dana Holmes – Oh! That would be great.

Pat Killingsworth – I am not sure, but I think that would be good. Priya, did you have a caller on the line?

Priya Menon – Yes, Pat. There is someone who wants to ask Anne a question. The person calling in from number 805-985, please ask your question.

Caller – Oh, hi there! Thanks, Anne, for your talk. I am a caregiver for a multiple myeloma patient and as you were describing the different types of multiple myeloma, his is a little different and I thought also the caller that said their M spike wasn't monitored maybe he might be in the same situation that my husband is in. He never has produced an M spike.

Anne McNeill – Uhmm…

Caller – So, he is technically called a non-secretor and his type of cancer is kappa light chain.

Anne McNeill – Okay.

Caller – So, the only elevation that's ever been detected lies with his free light chain test, so that's the primary test for him even though his levels were so low that they call him a non-secretor, but you know, yet he reached a stage 3, you know, cancer, multiple myeloma level with this cancer and they were planning that test…

Anne McNeill – Right.

Caller – …you know, for detection. So, they kept thinking everything was fine.

Anne McNeill – Right.

Caller – They did and he has never had any of his biopsies, have all proven to be negative and not shown any detection. So, its just an unusual situation and as I hear you explain the antibody structure, you know, I am just…

Anne McNeill – Right.

Caller – …interested to know how this variant in the cancer. How it differs, you know, without having the protein aspect or the M protein?

Anne McNeill – So, okay. So, let me ask you something. You are a caregiver. This is your husband, you said?

Caller – It is my husband, yes.

Anne McNeill – Okay. So, actually I just wanted to comment that before the advent of the free light chain assay test that we use in the lab now, before that became developed, there were about 10% of our myeloma patients were called non-secretors.

Caller – Uhmm…

Anne McNeill – Since we had the development of this test, it has gone down to 1% to 2% because most of our patients who were previously non-secretors, like you mentioned, can be monitored somewhat with this free light assay.

Caller – Yeah and he is kind of between the things where, you know, (laughter) they don't really want to say he is not a non-secretor because the level has increased what so little compared to…

Anne McNeill – Right.

Caller – …the _____ of his disease.

Anne McNeill – Right, right, right. But you said, he is a free kappa myeloma, a free light chain myeloma.

Caller – Right. So, all the other heavy chains that you mentioned are not applicable of him.

Anne McNeill – Right. Right. Right. So, this is not… Its not common. Most patients do have a heavy chain, but this is after IgG kappa, lambda, and IgA. We do have patients with either free kappa light chain myeloma or free lambda light chain myeloma. Like I said, not common, but we definitely need to use that free light chain assay to monitor their disease. Its very important and unfortunately patients like your husband may need more bone marrow biopsies in the future, like the serum free light chain assay is very important. This is an unusual presentation, a less common presentation, because the plasma cells are not producing an excess of the heavy chains, so he just has an excess of the serum free light chains and you know… Does he get 24-hour urine collections more frequently. He should be collecting urine samples more frequently than most of our myeloma patients. How often does he collect a urine sample? Do you know?

Caller – Actually, no. They do do the light chain, you know, his labs every month, but what they have been doing is a PET scan every six months.

Anne McNeill – Oh, yes. Yep. Yep. Yep. Yep. I was just going to say that. If you want bone marrow biopsy, then we will

Caller – But its interesting to see, you know, we have kind of thought, you know, oh, his light chain is in the normal range, so you know, maybe not necessary to do the urine, 24-hour urine test, but you know, perhaps that's not good thinking and that should probably course.

Anne McNeill – I like to do the 24-hour urine not with every set of labs but maybe every other, just to get an idea, you know, because sometimes you do get those abnormalities in the urine that you don't see if you are just doing the blood. You know, your husband is…

Caller – We didn't realize. That's a really good suggestion.

Anne McNeill – Yeah. I would… I mean it doesn't have to be every time but unfortunately your husband is in the minority, in the very small minority of myeloma patients that he is difficult to monitor.

Caller – Yeah. I don't think of bringing it up because in his situation he has had a plasmacytoma and…

Anne McNeill – Oh, yes.

Caller – …he was being monitored for the progression or, you know, the development of multiple myeloma by an oncologist and he was being seen every month for an entire year and of course, they were doing the 24-hour urine on occasion and the M protein and the regular, for instance, the regular assay and never with the free light chain test run and if it had been run, this would have been much earlier. So, I just cautioned that, you know, although its rare, its unfortunate that that test isn't used more frequently…

Yeah, yeah.

…for diagnostic.

Anne McNeill – Yeah. You are right. You know it is an extensive test and that may be the reason why a lot of practitioners are not routinely using it, but certainly in your husband's case it should be without issues, that its routinely a part of his lab, you know, evaluation.

Caller – Right and now that's definitely established. It was just in the diagnostic period. You know that's why his disease was allowed to get a little out of control, be it for…

Anne McNeill – Yes.

Caller – But I appreciate your bringing this up very much. I really enjoyed learning a little bit more about the lab results.

Anne McNeill – Oh! Thank you very much and good luck with your husband.

Pat Killingsworth – Thanks for calling in and, Anne, thank you for answering a question definitively. You don't always get that from a healthcare professional. They can be pretty good tap dancers.

(Laughter)

Pat Killingsworth – Priya, do we have time for one more quick question that was emailed in to us?

Priya Menon – Ah, yes, Pat, and I think we have a couple of minutes more. Anne, we have received a few questions. I will just quickly go through them. Kate wants to know why do we test magnesium for myeloma?

Anne McNeill – Oh, yes. Yes. I did see that. Okay. Very quickly. I did see that.

Priya Menon – Yes.

Anne McNeill – And you did send me that via email. Magnesium is an electrolyte that is frequently altered, especially low risk, in cases where a patient has nausea, vomiting, and diarrhea. So, in general, patients… We do monitor labs because the patient's treatment may cause these GI symptoms. They may have been post transplant and having issues with nausea, vomiting, and diarrhea. So, that is an electrolyte that we do need to watch out for. If those levels are altered, the patient might be dehydrating and we definitely don't want patients to be dehydrating. We want to check the kidneys, so we do check magnesium level. You deplete that very quickly when you are vomiting and having diarrhea. So, that's the reason why we check that magnesium level. Okay?

Priya Menon – Thank you, Anne. I think she had another question. She wants to know how do eosinophils relate to multiple myeloma? She has no allergy, but she checks her eosinophils every month is what she says. I think I have sent you this question in May.

Anne McNeill – Oh, yes, yes. I see. Okay. Oh, yes. I did see this email again. The eosinophils… Yes. The eosinophils were elevated on the patient's CBC and, yes, eosinophils are usually associated with patients who have allergies. If she doesn't have any allergies, the most important thing to look at on the CBC and I can't remember this email specifically, but its not to look at the percentage of eosinophils because its very important that when you do a CBC, you get percentages in the differential and you get absolute values. So, I would look at and pay attention to the absolute value, not the percentage because the percentages are just a relative measure. You want to look at not the eos percentage but the eos a or absolute and that number, I guess, is closer to the normal range than the percentage which might be altered significantly. It might be too high. Never look at percentages in a differential. Always look at the absolute values and every CBC will give you both. So, its very important because the… Depending on the total white count, the percentages can be very altered. So, you really want to look at the eos, the absolute value. Aside from allergies, I could not tell you if its truly an elevation in eosinophil count. I really don't know because the only thing I am familiar with is the allergies. So, I really can't answer that, but its important to look at the absolute values.

Priya Menon – Thank you, Anne.

Anne McNeill – Okay?

Priya Menon – Pat, would you like to add anything? I think we just have… We are almost over time, but would you like to say something, Pat?

Pat Killingsworth – No, I just… I just wanted to thank everybody for… Its hard to be a panelist on a show like this because often, since I have done that. I am panelist on some of the other Cure Talk broadcasts and you relegate it to the end and barely get any time. So, you just listen patiently and hope to get your question in, but I want to thank the patient panelists and, Anne, I want to thank you for taking the time to visit us a second time. I actually am so much more informed after this one, I thought the last one and I am a pretty knowledgeable patient. I thought that there was… There was too much, so this helps a lot. Thank you.

Anne McNeill – Oh, thank you so much, Pat. Thank you.

Priya Menon – Thank you, Anne. Anne is actually shifting her house and in spite of being so busy, she took time out for us today. Thank you very much for joining us and sharing such a lot of information with all our audience. Pat, Matt, Cindy, and Dana, thank you for your support and what you are doing for the myeloma community is invaluable. Pat is not feeling well. I hope, Pat, you get well soon and…

Pat Killingsworth – Thank you, Priya.

Priya Menon – We look forward to all of you joining us. Yeah. (Laughter) We look forward to having all of you joining us on 26th of Feb at 5 p.m. ET. We are having our show with Dr. Vincent Rajkumar from Mayo Clinic and we are going to discuss “myeloma – control versus care” and make sure you mark your calendar. It is at 5 p.m. ET, not our usual 6 p.m. eastern time and for registrations, you can always mail me or visit curepanel.carefeed.nic. For myeloma trials, please visit the MMRF trial search tool at myeloma.trialx.com/ask. The link for today’s show as well as link to Anne’s slides will be shared with everyone via email. Thank you so much.