Speakers
Selina Luger, MD
Emmanuel C. Besa, MD
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Emmanuel Besa: Thank you, Selina. What she just told you, I have to tell that to my new patient when they come in in a much shorter version without the slides, but it's very helpful that you understand your disease. I think that's the only way you and I can work together because if the patient doesn't understand why you're doing this and why… they're not going to cooperate. I'm the voice of experience. When I started studying this disease, we were calling it pre-leukemia. There was no such word as Myelodysplastic Syndrome when I got interested in this. My original interest when I was training and I trained at Penn, too, in this complex. It doesn't look the same anymore. There's new buildings now, but I was interested in low blood counts. Why do people have low blood counts and in my country where I came from, aplastic anemia was very common. We see a new patient for almost every month. So when I came to the United States, it turned out that aplastic anemia is very rare in… and so all my patients with low blood counts had very bone marrows that were full of cells and we couldn't understand if the cells are there why aren't they working and that's how we got interested in all this and used to collaborate with Dr. Peter Nowell who is very famous for discovering the abnormal chromosome in the condition called chronic myelogenous leukemia and called the chromosome Philadelphia chromosome which was discovered here in Philadelphia and he was working down the hall and I said, "Look. I have all these patients. Maybe we can find out what's going on by looking at their chromosomes," and because of that research, we now use the chromosome as a very important part because I would call him and say, "This patient with this particular chromosome, they develop leukemia very quickly." So, we could identify the high risk group from the low risk group. So, those are the things I'm just telling you how important research is in this condition because when I first started, there was no medicine or drugs that were working. I was working with no drug that was effective. Everything that we tried didn't work and I want to thank my patients who were just like you who agreed to participate in the clinical trial that Dr. Luger just showed you with Lenalidomide. My patients agreed to participate in that and you're getting now the benefits of those patients who originally tried. So, I think clinical trials very important for us to advance and the benefit by your participation will be the next generation of patients that are coming in. So, I would like to open your mind to such things as clinic. Don't be afraid of the word 'clinical trial.' These are very important part of developing better and newer treatment. What else? If you want to ask any questions, there are a lot of new things that we're not allowed to tell you, but if you're interested…

(Laughing) We can lock the door.

Q1: I know there's a clinical trial that's been going on for awhile where they're using oral Vidaza as opposed to infusion. Can you tell me where that might stand at this point in time?

Emmanuel Besa: I think they're just finishing the early data from the oral. I know Dr. Manero, Garcia Mannero, in MD Anderson did that original draft. It's still without know how well it's absorbed. I think that's what's important.

Selina Luger: The current study that's ongoing is a study in low risk disease. It's patients who otherwise would not necessarily need it because they don't know how it compares to standard IV Vidaza. It's a study that's being done. Patients get the pill and then they spend a lot of time getting blood work done to see how well the Azacitidine is being incorporated into their system and that's kind of a level where that (inaudible 5:20) right now.

Emmanuel Besa: But it's more than that. Yes.

Q2: Some of the foreign countries, if I recall having read this probably, were doing some research with high doses of vitamins, vitamin K and vitamin D.

Emmanuel Besa: It's interesting that you mention that. One of my research has been with what we call analog of Vitamin A which what we call retinoic acid and it was one of the trial that we did early on and since we entered everybody that was including… We didn't know IPSS score then we were treating everything and it didn't seem to work in the aggressive and, in fact when we wrote up the paper, we said it was negative. However in the early stage, there were a few patients that did well on it and I've been interested in… I noticed that some of you are early. You're not requiring transfusions. Most of our trials are patients who require blood transfusions or having bleeding and infections. We had strict criteria. So most of the time when you're early, we're just supposed to observe and watch how you're doing. My interest is can I do something early to prevent that? So, we may have to do a clinical trial where one group gets the vitamins and everything and the one group that doesn't, so we can see if it does make a difference. See, that's how we learn. We do clinical trials and that's why Selina and I are here because we do clinical trials and when I used to stand here and said there's no treatment available for MDS, now we're able to say hey, we have this and we have that and maybe coming… So whenever the patient gets depressed, I tell them, "Don't despair. Everyday we're still working. There are new drugs that are being developed and who knows you may benefit from it. You know? Today it's not available, but maybe in two or three months it may be available."

Q3: I have… I've been going to see a doctor treatment for my Myelodysplasia and my blood count is the criteria and it's been up to… It's down… It was down to 8 then it went back up to almost 11 was it?

Emmanuel Besa: Well, you're on Procrit?

Q3: I was on no drugs at all.

Emmanuel Besa: No drugs. Okay.

Q3: So then it started going down again, but it stopped. It was at 9.8 for quite awhile and then I had a CAT scan done for another reason and now it's down to 9.4. The point is that the doctor was… every time I'd go there to leave it up to me, but I'm supposed to be eligible for some kind of an infusion.

Q3a: Injection.

Q3: An injection. Yeah.

Emmanuel Besa: Probably Erythropoietin was ordered.

Q3: Yeah and so I did read that the side effects of that, one of the side effects is cancer. So…

Emmanuel Besa: I understand your problem.

Q3: I've had the answer twice already and I don't… I really don't know what to do about that problem of taking that trans…

Q3a: An injection.

Q3: The injection and running the risk of getting another cancer or whatever. This is a problem.

Emmanuel Besa: I think sometimes too much information is bad.

Q3: I do read up a lot.

Selina Luger: But the two things about that are that that cancer has been reported is not in this patient population.

Q3: I'm sorry. I didn't hear you.

Selina Luger: It's not in this patient population. It's when people were given that agent who had hemoglobins that were much higher. So, there's really no risk of cancer to MDS patients taking Erythropoietin.

Q3: No risk. Okay.

Emmanuel Besa: See, we're supposed to tell you all this even though it's not in the same context as yours and that's what the government requires us to do.

Q3: What was the drug that you had mentioned? You said you mentioned the name of…?

Q3a: (inaudible)

Emmanuel Besa: The retinoid is Accutane. It's used for acne. It's when we started because there were some data information that similar drug works for leukemia what we call acute promyelocytic leukemia and it's different… it makes the cell that Selina showed you from the immature cell to the more mature. So, it's what we call differentiating agent. I think… Well, I can't tell you if it works or not unless we do that.

Q3: He's a very good (inaudible 11:20) if he want to start have them very low doses and see what happens. It's down to 9.4 and if it doesn't go back up… If it goes the other way, I guess I'll have to (inaudible)

Emmanuel Besa: There's a reason why we call this pre-leukemia because even if you're low risk if we wait long enough more than five years it may take. Eventually in my mind if you don't die from other causes, will develop to leukemia because the change given the low risk, they get new chromosome abnormality along the way. So, I think we're missing an opportunity to do something early. The reason why we have a condition what we call 'pre' is it gives us a reason to treat or to make a difference in the long run. I think one of the objectives is to prevent leukemia. That's one of the things that we're interested in. Prevention. Yes.

Q4: Can you please clarify that so a low risk patient, my husband for example, he's had the RARS classification. He's been low risk because the percent blasts continue to be low, five percent, over time. He will also convert to leukemia because that's different than what we have learned so far in the history of his having the disease.

Emmanuel Besa: That's the…, I think maybe the Foundation should have a registry of all this early and see what happens to them.

Q4: He's been… So getting transfusions, he's been through a number of different drug protocols that both you have mentioned this morning, but we still thought he was going to be low risk (inaudible 13:19) throughout the course of his disease and not convert to leukemia.

Selina Luger: A good number of patients will never develop leukemia.

Q4: I misunderstood what…

Emmanuel Besa: What I said… A few (inaudible 13:30) you're all different from each other. They're not one disease and this the reason why it's so hard to tell you what's going to happen is because of that and I think that's the reason why we should continue studying this and learn about it is how do we tell which ones are going turn into the more… the worse form which is leukemia. Yes?

Q5: When I was diagnosed back in November '05, they did the typical biopsy bone marrow. I have not had one since. What is your position with respect to a repeat to find out what progresses happen, what the progress is?

Emmanuel Besa: See, we don't enjoy putting a needle into your body.

Q5: I didn't enjoy it either.

Emmanuel Besa: Well, it appears to be that I'm doing it for myself. It's not the reason. So, we need a reason to go back there and look. If there's something that's developed that's new, you used to have normal white count and now you're white count is starting to go down. I think that's the time when we say is it changing? Where are you in the IPSS? Are you going from low

to intermediate or intermediate to high? Those are the reasons why we repeat bone marrows. Now, we have a research. Sometimes we may ask you can we get some marrow because we're interested in your chromosome or something and we want to try putting a drug in there to see if it works. Those may be a reason to do it and… but we can't do it without your permission. When we started this with Dr. Nowell, the chromosomes were not being paid by the insurance companies because it wasn't routine part of treating and, well, we didn't call it MDS then. So, I used to draw bone marrow and carry it myself to the laboratory here because there's no laboratory that will do it. So, that's how we start. Now, it's routine to do the cytogenetics.

Q6: In one of the slides, it was mentioned that the number 5 chromosome is the most common defective one. Does each set of chromosomes have a different bearing on the blood deficiency?

Emmanuel Besa: Yes, yes. Definitely and that's what makes this what we call heterogeneous. You're not all the same. It's not five. It is different from a 5Q. In fact, we're learning a lot about 5Q that's very exciting how the mechanism is actually makes it die prematurely, the cells, and that's one of the reasons why you become anemic is the cells die prematurely before they mature. So, it's exciting to know exactly what happens when you miss, you lose that portion of your chromosome and why the drug particularly what we call Lenalidomide works very well with that. It actually suppressed that clone. Actually in some patients, the clone may disappear, the 5Q may disappear and to me that's the best response a patient could have. Now, we don't know if that's going to cure the patient or not, but that's one of the early signs that the… we can do something about the bad clone.

Q7: So far the question, is there any data for people that have had pre (inaudible 17:53) cancer treatments with chemotherapy and all the radiation to develop MDS if there's a (inaudible 18:01) and the second part of that is what can you do prior to that to prevent MDS? Is there anything…?

Emmanuel Besa: You mean while you're getting the chemotherapy and the radiation? I don't think we can do anything… This may develop years after chemotherapy and radiation. Maybe take 2 to 5 to 10 years later.

Q7: There's no real data on how many (inaudible 19:32) develop or (inaudible 18:34).

Selina Luger: I know that we're doing a lot of research there particularly in the breast cancer population looking at whether there… We're looking to see whether or not certain genes in patients predispose them to sensitivity of the chemotherapy that they're getting before the breast cancer. It's very much in the research setting. It may in the future make us choose other chemotherapy regiments for certain patients for their primary cancers, but that's something way in the future. It's an area of active research.

Q7: Thanks.

Emmanuel Besa: Yes?

Q8: Really for Dr. Luger. In the slide who, you mentioned 50,000 to 60,000 new cases a year. That's an order of magnitude of 5 (inaudible 19:17) a few years ago. Is that just better knowledge in the medical population?

Selina Lugar: I think it's a bunch of different things. I think it's… We changed the definition in multiple occasions. So, it used to be that, you know, we'd change the definition of MDS. We changed the definition of AML. It used to be MDS by standard criteria required that you have both… if you have more than one abnormal blood count and by the more recent WHO criteria, a single abnormal blood count qualifies you as having MDS. So, I think it's all of those things as well as… I don't think there's more MDS. I think…

Q8: But we're less of an orphan, so you get more money.

Emmanuel Besa: It wasn't classified as a cancer before and it's really changed since then because we can do a lot more research with funding. The other thing is since it's more common in the elderly, the population, the Baby Boomers which is a big population, is now reaching that age where we see it a lot and I think that's the reason why we all of a sudden the numbers have come up. Also, they… The WHO when they define what is MDS, they now have what they call minimal criteria that means we're looking at earlier and earlier stages of MDS and that's the reason why I'm interested. Can we diagnose them earlier and do something then. The minimal criteria has changed so that what we used to do call other names we can now call MDS because of that. Yes.

Q9: Why did they really consider it a cancer?

Emmanuel Besa: Because of the leukemia. Because in…

Q9: (inaudible 21:22).

Emmanuel Besa: Yes.

Selina Luger: When you find a chromosome abnormality that means that you got a cancerous cell in there. So since more than 50 percent of the patients are found to have that abnormality in the chromosome, that tells you it is a cancer.. It doesn't (inaudible 21:36) call a clone and a clone by definition is cancer. So, that's what allowed it to go into the cancer…

Q9: (inaudible 21:43) blood cells.

Selina Luger: No, you can have more abnormalities that are not cancerous but the finding of the abnormality in the chromosomes defines it as a cancer.

Emmanuel Besa: Aplastic anemia, for example, gives you the same thing, but it's not a form of cancer because it doesn't… Well, I mustn't say never because there's some MDS that they're very low counts… very hypocellular count… the marrow is empty and they can go to leukemia. So, I can't say perfect all the time, but I think the chromosomes is a one of the reasons we know will make it progress to leukemia.

Q10: I never had a chromosome test.

Q11: Any research being done to suggest that the body has some capability to adapt itself to the condition? Normally if you're seeing a decrease and George is only in the platelet cell line, normally intervention occurs at some point as those counts drop and then an intervention is done. Once the intervention is done, you now change the body chemistry. So, the body chemistry now adapts to that intervention. If you do nothing as he did, he went from as low as a 13 count many times being recommended to go into treatment, which he chose not to do. Now, he's gone back up to a 22 with no interventions and very stable at 22. So, my question is do we know whether or not the body have some capability to adapt itself.

Emmanuel Besa: You remember this slide Dr. Luger showed that one of the treatment is immunosuppression. So, some of these may be related to imbalance in your immune system. I have patients that usually they're much younger I've treated with the immunosuppression is you suppress the immune system of the patient and the patient recovers completely. So, there may be an immune part of all this and see it's very difficult sometimes to choose which ones because we don't know. We can't really tell right away what the actual mechanism is in the actual patient that we're seeing. That's why we're doing research is to figure out which ones to treat with the new one suppression and which ones to treat with the other treatment. We know 5Q-, you need the Lenalidomide because it works very well for that.

Sandy Kurtin?: I think the pace that which people's disease changes also is highly variable which is why often we take time to get a feel for how your disease changes over time. So with the exception of people with very high risk disease because we know they convert to leukemia very quickly and that's very serious. We usually take time to get trend. Your case is a little different because of the prior therapy that you had to the bone marrow producing regions and that by itself creates a different path, if you will. So, there's just a lot of variability. That's the study challenge.

Emmanuel Besa: One of the first thing that I talk to the patient is what is your objective for your future as a patient? Do you want to just be comfortable? See when we're trying to determine who we should be aggressive, I think Dr. Luger alluded to this. Who should we transplant because transplant is only option to cure. So, we need to have an understanding that one of your goal may be for a cure or do you just want to be comfortable and reach the certain milestone in your life and you'll be satisfied, but not everybody can go through a transplant, but it's very important very early in the disease especially in the higher risk that you go to see doctor or center the (inaudible 26:35) because there are a lot of things that needs to be done. It takes a long time to determine whether you are a candidate or not, whether you're a donor or not and if you're receiving a lot of transfusion, you may have too much iron in your body that you don't do very well with the transplant. So, those are the things that we need to see earlier than to come much later. So I'm just saying if you have a bad disease or you're in the high risk group that you go to a center, a center of excellence for MDS would be fine.

Q12: Is there a way of getting rid of iron in the body beside not using a magnet.

Emmanuel Besa: Well, we actually did a study with what we call XJ. What's the nontrade name of XJ?

?: Deferasirox

Emmanuel Besa: It's oral and it drops the iron and brings out in your poop.

Selina Luger: It's a big problem which is unfortunately…

?: What's it called?

Selina Luger: Deferasirox. It's called XJ. So, there's two issues with it. Side effect wise it affect on your kidneys, but the major issue is that's it often not covered by Medicare and it's a very expensive drug. So, that's why we have special pharmacies that deal with it. It's $40,000 a year. So, knew the situation. Ask your pharmacy. At your specialty pharmacy if they can help you through those financial hurdles if your doctor recommends that you take these prescriptions and I know Novartis also has assistance programs for that medication. So, I know financially it's always a hurdle. It's a scary thing to hear those numbers, but that there is help out there. So, don't just stop and say I can't afford it. Just look for other avenues for that.

Q13: I've been XJ for over a year and I'm Medicare and it's covered. Now if you have a supplementary plan, you still have to run through the deductible and XJ runs through the deductible very fast, but once you've done that, my coverage I'm paying 5 percent definitely $80,000 a year cost.

?: There are options. I can't just ask those questions at your pharmacy, in your specialty pharmacy in particular and they'll just stop from saying I can't.

Steve: I agree with her advice in terms of… my goal is always to get the cost down to zero dollar out of pocket if at all possible and one thing I would advise is that if you're ever denied coverage or if a corporate foundation says they're out of money, what you want to do is get that in writing and then if you can approach Novartis with that denial in writing, we may be able to get you covered with free drug. I can't guarantee it because I'm not part of that process, but I know that's an important step. So when she says don't take a no as I quit. It's just not no. It's just can I get that no in writing please and then we can continue. That's all.

Emmanuel Besa: Unfortunately, it takes a lot of time for my nurse to do it, but we do it for you. Any other questions?

Sandy Kurtin: Thank you very much both of you for your time.

(Applause)