

Forum Presenters:

Dr. Kenneth Meehan

Dr. Christopher Lowrey

Dr. John Hill, Jr.

Dr. Christi Hayes

Susan Brighton, APRN

Lynn Root, RN

Laura Blodgett

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Kate Wilcox, RN

Susan Hogan

Deborah Murray

Dr. Kenneth Meehan: We're going to go ahead and get started just so we can stay on track. Okay? So, this is an opportunity to ask any questions that you have. Again, just for formal introductions, I'm Dr. Kenneth Meehan. I'm a hematologist. I'm the Director of the Transplant Program and then next to me is....

Dr. Christi Hayes: Hi. I'm Christi Hayes. I'm one of the hematology and transplant attendings.

Dr. John Hill, Jr.: John Hill, transplant and hematology attending.

Dr. Christopher Lowrey: Dr. Lowery. Also... you know me now.

Dr. Kenneth Meehan: As I've been mentioning, we've had a number of questions submitted to us electronically, but we'd first like to open it up to the floor if you have any questions at all. We also have two nurses here, too, that would be happy to answer any potential questions you might have. Any questions come to mind? Yes.

Q1: Are there any clinical trials currently going on here?

Dr. Kenneth Meehan: So, the question is are there clinical trials in MDS that are... are there any clinical trials in MDS going on here at this point?

Dr. Christopher Lowrey: So, we just finished one recently. Some of the... at least one person here was on the clinical trial and we have another one that's moving to the approval process. I don't think we have any open at this exact time. They kind of come and go as they come online then we treat a bunch of people, the trial finishes up and we get the next one rolling.

Q1: How does one find out about them?

Dr. Christopher Lowrey: They're on our website, so you can see those. There's also an excellent website sponsored by... it's called clinicaltrials.gov. Clinicaltrials is all one word and it has every clinical trial in the United States. So, you can go on there and just plug in Myelodysplastic Syndrome and you'll see every trial on Myelodysplastic Syndrome.

Q1: Specifically for (inaudible 2:21). What would be the website to find out if there is one?

Dr. Christopher Lowrey: Norris Cotton Cancer Center.

Dr. Kenneth Meehan: The other thing is just talk to your hematologist because they know what trials are available, but also what trials are open and so as Dr. Lowrey mentioned and I can think of another trial that's about to be opened shortly, too. So, probably the best is the website and/or your hematologist.

Q1: Okay, but I'm currently affiliated with a hematologist who Southern New Hampshire Medical Center in Nashua and they're affiliated with MGH. So, is it possible that I could get a clinical trial here and not at MGH?

Dr. Kenneth Meehan: Yes. So, the trials vary. It may be that you need to be seen here, sometimes treated, sometimes you're just seen here and if it's a tablet for example, you could be treated. If that's not an option then either their center or MGH should have trials available.

Q1: Yes, but to get into MGH versus getting to Dartmouth is two different things.

Dr. Kenneth Meehan: Yes. One other advantage is you can always be seen here for a trial and there's also Norris Cotton Cancer Center in Manchester. So, we'll often see patients and if we want them to go on a trial or make treatment recommendations, they can sometimes, not all the times, but sometimes be treated at Norris Cotton Cancer Center in Manchester, too.

Dr. John Hill, Jr.: I think it's important to emphasize, too, your treating hematologist that you really want to come here for a trial. Otherwise, you might get steered towards MDH. If you say that's not as convenient and they have a trial open at Dartmouth and I'd like to try to see if I could get put on that trial then they would probably refer you for an initial consultation with one of us to see if that would work to put you on the trial and then we would send you back to them of the course for continued therapy.

Dr. Kenneth Meehan: Any other questions? While people are thinking, I'll actually go to the website and refer to some of the questions that were submitted. So, one question here is 'Can you please define what is meant by supportive care therapy for MDS?' Dr. Hayes, do you want to try taking that?

Dr. Christi Hayes: So, I think the two lectures kind of touched on some of the supportive care. So, supportive care can include things like transfusions for blood or platelets or injections to stimulate the production of blood or platelets. Sometimes, not strictly supportive care, but sometimes as mentioned MDS can just be monitored and treatment doesn't need to be started right away. I don't know if there's any (inaudible 5:17) comments on that process.

Dr. Christopher Lowrey: I don't think I have any to add.

Dr. Kenneth Meehan: Yes?

Q2: With regard to the transfusion support, other than that supportive therapy are there guidelines to determine when to use the EMACAR versus platelet transfusions? Are there like platelet guideline levels to look for?

Dr. Christi Hayes: That's a great question. So, I think it's partially clinical judgment depending on how low the platelet count is and also what type of bleeding a patient's having. If it's specifically nose bleeds and the platelet count is not very, very low then you can try something like EMACAR. So, I think it's a very individualized decision based on a specific patient's situation.

Dr. Kenneth Meehan: Another question is 'Why or how does MDS become leukemia and do all patients with MDS progress to leukemia?' So, maybe Dr. Lowrey, do you want to try answering that?

Dr. Christopher Lowrey: Sure. So, like Dr. Hill showed you with the prognostic scores, the IPSS, that helps predict what an individual patient's chances are of going on to develop leukemia. If somebody has the low risk disease, it's unlikely that they will progress to leukemia. Only a small number of those people will go to leukemia and it often can be on average years before they develop leukemia where to someone is in the higher scores and that means they have the higher blast count between like 10 and 20 percent. Those people are at much higher risk of going onto leukemia and maybe a third of those people, maybe a few more will actually end up going onto leukemia. So, often it really relates to that blast count thing.

Dr. Kenneth Meehan: Another question is 'Are most cases typical and follow a typical pattern or is there usually a wide variation between cases?' John, do you want to try answering that?

Dr. John Hill, Jr.: I think we're continually impressed by the degree of variability in our patients. That's why I emphasized that those prognostic scores are not black and white and so you have two patients that may come in around the same time with what looks to be sort of a similar prognostic situation and invariably they have totally different courses in many cases. I'll tell you a little story about someone a few years back an elderly gentleman was on Vidaza and said at one point, 'I'm just tired of coming in for my weekly infusions, weekly, every month. I

just don't want to do that," and the nurse practitioner and I working with him said, "That's appropriate. You should be in the driver seat in terms of having autonomy here, but we just need to tell you that your disease will very likely progress within the next several months," and for the next seven years he came in and joked with us about, "Hey, doc. I thought my disease was going to progress as soon as I stopped therapy," and something else carried him away at a much older age than he anticipated and it wasn't it his MDS and that's just an example of how... and it tells us, I think, how little we understand. We think we have some understanding of this disease that helps us to treat and prognosticate but there's so much that we don't understand. So, variability is absolutely the norm with this disease.

Dr. Kenneth Meehan: Yes, there's a question up there?

Q3: Two weeks ago I was diagnosed with a wet macular degeneration. Is there a connection between the MDS and the macular degeneration?

Dr. Kenneth Meehan: It's actually a great question and that was the next question. So, the question is so you were recently diagnosed with MDS and you just experienced macular degeneration in one eye. Is this related to MDS or could it be related to treatment?

Dr. Christopher Lowrey: As far as I know there's no connection between MDS and the macular degeneration or the treatment. Macular degeneration is a pretty common thing and most of those people don't have MDS. So, it's probably just kind of bad luck that they both happened. Would you agree with that?

Dr. Kenneth Meehan: Yeah. To be honest with you, we cheated a little bit because we had your question ahead of time, so we talked. So, none of us can come up with an association. So as Dr. Lowery mentioned, I think it's totally independent. We don't think it's related to therapy nor the MDS.

Yes?

Q4: That leads to another question which is are there associated diseases which MDS could be implicated in or not?

Dr. Kenneth Meehan: So, the question is are there other diseases that MDS is associated with...

Q4: Could be.

Dr. Kenneth Meehan: ... or could be associated with. That's actually a very good question. So off the top of my mind, there are some congenital diseases that peoples are born with that they have an increased risk to develop MDS or as Dr. Lowrey mentioned exposure or sometimes patients who have a cancer and they're treated with chemotherapy especially in association with

radiation. They have an increased risk of MDS. I can't think of any off the top of my head any disease that are associated with MDS.

Dr. John Hill, Jr.: We've had a few patients with MDS that have then developed autoimmune hemolytic anemia which is a different entity and yet we know that there could be some autoimmune influences on the MDS, but that's the only thing I can think of where we had another separate disease entity that we've noted some overlap in a small number of patients.

Q4: But the disease isn't heart, liver or vascular (inaudible 12:00).

Dr. John Hill, Jr.: No.

Dr. Kenneth Meehan: No, I can't think of any and there should be any association with that.

Dr. Christopher Lowrey: I can think of maybe one or two. So, some people have...

Dr. Kenneth Meehan: He's a molecular biologist, so he would know.

Dr. Christopher Lowrey: So, a lot of people that have MDS get transfusions over many years and that can lead to what we call iron overload because every time you get a transfusion it's like taking a whole bottle of iron pills essentially and iron can build up in your body and over years that can be toxic to the liver and to the heart. So, it's not a directly a result from the MDS, but it's kind of a side effect of the treatment and another thing are infections. People who have MDS are more susceptible to unusual infections that a person without the MDS wouldn't get. So, that's another thing that's kind of related, but not directly.

Dr. Kenneth Meehan: So, that brings up a good point. I apologize. I was associating the diagnosis of MDS with another disease. What Dr. Lowery was emphasizing is when someone's diagnosed with MDS what can happen over the course of time. That actually leads to a couple questions that are here, but first let me do the most pertinent and it actually asks the question, 'What about iron overload in MDS and what's the role of what we call chelation for iron overload?' What that means giving a patient a medicine to pull the iron out of their body. John, do you want to try answering that?

Dr. John Hill, Jr.: So, the first approach that we've typically used for iron overload has been something called phlebotomy, but as everyone probably understands that can be very difficult in patients with MDS that already have anemia. If you're already struggling just to kind of maintain a hemoglobin in the nine or 10 range the last thing we want to do is start taking blood off to take off iron while making your anemia worse. So, there are a couple of chelating agents that can be used. One is a traditional intravenous one and then there's a more recent oral one. They're not without their own risks in terms of risks to the kidneys and that sort of thing, but they can certainly be utilized as an alternative to phlebotomy in terms of trying to get that iron off

especially in patients that are manifesting significant liver abnormalities because they've got so much iron in their liver or other side effects. So, yes, it's an important question and especially then also if someone's going to a transplant. We know that the risk is higher for complications after transplant. If they go to an allogeneic stem cell transplant with iron overload and so that's an important consideration in trying to minimize the overload of iron prior to transplant and then in the post-transplant setting, too.

Dr. Kenneth Meehan: So, John, can you address what are your criteria for starting chelation of iron?

Dr. John Hill, Jr.: Great question. First of all if it's feasible in patients and they have to have a reasonable kidney status and it would be a scenario most likely in someone who was manifesting elevated transaminases or liver enzyme elevation so that you really felt like the risk benefit tradeoff was going to be in favor of doing it. It might be worth a little bit of a hit to the kidneys to do this to try to free up the iron from the liver and... or if there were other things like secondary diabetes that could be something that would then cause us to say that's an issue, thyroid disease, changes in gonadal function, that sort of thing. All these things could be affected by the iron. I'm not aware of seeing someone that's had a cardiac issue, but certainly the heart can be affected by iron overload. So certainly, if we had any sense that there was an iron issue that was so significant that the heart was beginning to be affected we would start chelation, but I think the most obvious one would be that we see the liver enzymes go up then it make sense to start.

Dr. Kenneth Meehan: Getting back to this previous question, 'I was recently diagnosed with MDS. What precautions should I take?' and then the second part of the question is, 'Are there foods, elements, surroundings and/or any situations that I should avoid with this new diagnosis?' Christi, do you want to try answering this?

Dr. Christi Hayes: So, in terms... the first one is addressing precaution. So, I think it's going to be individual to the patient and what specific how the MDS is manifesting in each individual. So obviously, if there's a low white blood cell count and specifically the low neutrophils that we were talking about then you may want to take extra precautions and you may be on medications to prevent infections in advance, so to prevent infections that haven't occurred yet. If your blood count is low you just may want to take precautions in the sense of just knowing that your red blood cells are low and not overexerting yourself while still trying to be as active as possible and just knowing that maybe that your platelets are low and that can affect what medications, other medications that you might be on for other things. In terms of foods and things like that, I think one thing in terms of if you have a lot of iron you just may want to not... I don't think you have to really be very restrictive in your diet, but you definitely wouldn't want to be, let's say, on iron supplements or things like that and your physician can kind of help with your specific situation in terms of foods or supplements and things like that to kind of guide what you can or should be taking or not taking.

Dr. Kenneth Meehan: And one issue that I wanted to get back to because now we've had three people ask the question is MDS a cancer? And I said no and Dr. Hill said, well, yup, maybe. So, I'd like to ask each of us to sort of give their opinion and with my patients you've heard me give this discussion or talk about this already and MDS as I've been saying from the beginning it's a spectrum of diseases. Way over on this end it's very early. Patients can live for years. We may see the patient every six months and just follow blood counts and there might be a slow deterioration in the count over course of years and then way over on this end it's very, very aggressive. It can convert into leukemia in a matter of weeks. As you heard Dr. Lowery mention we call this preleukemia. So, survival is short unless we proceed with a very aggressive therapy like a transplant. So, you have this whole spectrum of diseases and we as your treating physician need to determine where you fall on that spectrum. It's in my mind it's difficult to say someone who's way over here could live 10 or 15 years has a cancer. On the other hand it may be easier if they have something like preleukemia. So, that's why you hear the discrepancy. So, let's go just down the panel here and hear what their opinions are. Okay?

Dr. Christi Hayes: So, I think part of the confusion comes with a lot of times MDS is described sort of synonymously with preleukemia and I think that sort of raises a lot of confusion. So, I think it's very important in terms of like the risk category. So certainly, someone with a low grade MDS can live a long time and would not be on medications that are traditionally associated with, let's say, leukemia and then with the higher risk disease the treatment can look almost exactly like the treatment that would be given for leukemia. So, I think it's really important to sort of figure out where sort of on the MDS spectrum that each individual patient is because the treatment can be very similar to the treatment for leukemia and then on the other hand no treatment at all may be required.

Dr. John Hill, Jr.: So, you could tell that I was influenced somewhat by the question posed at our national meeting a few months ago with the sort of scolding of the participants that we needed to be more frank with our patients. I think that the best way to think about this or one way to think about this is we know that this is the disease that has two major complications, one being bone marrow... progressive bone marrow failure over time where the counts are dropping and the other being a propensity to develop into acute leukemia depending on the particular subset of disease and the patient and I think if you look at those separately we would say a bone marrow failure syndrome even if progressive is not in and of itself a malignancy, a cancer, and yet the other complication it's hard to say that that's not a pre-cancer or a cancer. So, I think if we divide it between those two complications because not everyone manifests both. Some patients... the majority of patients will oftentimes just have a bone marrow failure syndrome without the propensity to go to leukemia. So in that sense, I think we can say that's really hard to say that's a cancer and in the other setting it's hard to say that it's not. So, I think that's my best take on it.

Dr. Christopher Lowrey: I don't like the word 'cancer' for a lot of blood diseases at all. When a lot of people think of cancer they might think of metastatic lung cancer or breast cancer or colon cancer which is really serious and usually the person who has one of those things doesn't have long to live whereas I've had patients with certain forms of leukemia alive for 30 years and never needing treatment and should we call that cancer? I hate to use that word. I'd like to say you have chronic leukemia. It's not like those other cancers and a lot of patients with MDS, it's not that way either. It's not like we think of cancer... the connotations of just that word are so difficult and can just almost change your outlook on life once you have that applied to you. So, I like to think that you have MDS and then we can discuss you know what your individual MDS is like and maybe not even think about the cancer thing, but that's just my approach.

Dr. Kenneth Meehan: Any other questions from the audience? Yes.

Q5: Back to graft versus host. Sorry. Can you explain and I'm not sure if any of the patients here have had this treatment, the ECP treatment. How effective is it? Is it worth going through which is just your opinion? How long does it take? That's pretty much it on that one.

Dr. Kenneth Meehan: Let me just give some background because we like to use a lot of acronyms. So, graft versus host disease is a disease that happens after a bone marrow transplant and what happens is the graft, the cells we give to the patient starts rejecting the patient. So, it's the graft versus the host and it can manifest in a number of different organs. The way we treat that is we suppress the person's immune system. One possibility something called ECP, extra corporeal photopheresis. That's why I went to medical school. ECP.

Q5: As being a technician in the medical field, I still cannot pronounce that.

Dr. Kenneth Meehan: And I can't spell it, but I can write ECP. So, what ECP is is a complicated treatment. What it basically does and someone experiencing graft versus host disease are hooked up to this machine and it's almost like dialysis. It's painless. The blood comes out of their body. The blood is hit with sort of type of radiation and then those cells go right back into the body and the radiation is specific to a type of cell that causes graft versus host disease. So therefore, it suppresses graft versus host disease and it's a little more complicated than that, but that's the way I think of it because there's medicine involved, etc. Your question is more complicated because what's the response of ECP? It works real well because it will kill the cells that manifest or cause graft versus host disease. The responses differ depending on what therapy you've received before, the progressive different therapies, what type of graft versus host disease. The downside is you have to come here at least twice a week to get put on the machine.

Q5: But if you come here on Wednesdays, it's wing day.

Dr. Kenneth Meehan: But the advantage is unlike the medicines we use that are nonspecific that really suppress your immune system this procedure is just specific for graft versus host disease.

Q5: So, what you're saying it does suppress your immune system?

Dr. Kenneth Meehan: Nope. ECP will not... ECP is the only therapy that won't suppress your immune system. All the other medicines will, but it's effective in treating graft versus host disease.

Q5: Okay. I'll be here Wednesday for (inaudible 26:15).

Dr. Kenneth Meehan: Any other comments on that?

Dr. John Hill, Jr.: I won't reiterate because I agree with everything Ken said. It is we do emphasize to our patients that first and foremost it's a logistical hassle. You have to get used to that idea. That being said depending on the circumstance, how many other treatments you've had, how resistant your graft versus host disease is it may be a life saver. I mean, it may be a real key to your responding to that treatment and in addition to the treatment benefit, it also enhances the ability to come down on steroids and for anyone who's been on long term steroids and realizes... understands what an adverse outcome that has on your quality of life, muscle weakness and all sorts of stuff, if you can have a treatment that helps you come off steroids so much the better and so the other thing I should just say about our ECP staff that's made up of nurses, some of whom have been hematology oncology nurses and we never ask you to come in twice a week for your ECP and also come in for your appointments here. We'll see you down in the ECP suite. So, everyone tries to do their best to minimize the additional hassle of inconvenience and most of our patients after a few weeks they really feel plugged in and, again, it's easy for the doctor to sit here and say that most of the time it goes well, but in any event that's our take on it. So when it's recommended, it's something to really seriously consider.

Dr. Christopher Lowrey: I'm sitting here thinking as we talk about this GVHD, the graft versus host disease and the ECP that there may be many people in the audience who haven't gone down the transplant pathway and are kind of wondering what the heck are they talking about. So, let me just take a minute to give you kind of a hint about that. So, the whole cool thing about a transplant is and the reason that it can cure MDS and leukemia and other diseases is it doesn't work like chemo. Chemo kills the cells, but at least for MDS it won't cure it, but a transplant what you're effectively doing is taking somebody else's immune system, their stem cells and putting them in the patient's body and you reprogram the person with MDS, you reprogram their immune system so now they recognize the MDS cells as foreign and their new immune system kills off the MDS cells. So, it uses their new immune system to cure the disease, but what can happen is the new immune system can get a little out of control and start attacking the patient's own body. So, it can attack the liver, the lungs, the skin, pretty much any part of the body. That

is what we call graft versus host disease. So, the graft is the new immune system and the host is the person who got the transplant and this ECP is just a way to kind of quiet down the new immune system so it's not attacking the host anymore. Does that make sense?

Dr. Kenneth Meehan: This brings us to our last question and I think that's why we work so well together. The last question was, 'What's the role of bone marrow transplantation in MDS and who should receive a bone marrow transplant?' So, I think just in follow up to Dr. Lowey's comments, age is a major criteria. So often we can't talk about MDS in patients based on their age. Performance status is another one and we only talk about transplant in those patients on this end of the spectrum where they're progressing towards leukemia where we know it's going to convert into leukemia or a complete bone marrow failure in a matter of months or so.

Are there any other questions before we take a break?

Q6: What's the youngest patient age wise that had MDS?

Dr. Kenneth Meehan: So, the question is what's the youngest patient that we've ever seen who've had MDS? So, I had a patient mid-20s who had MDS. What's interesting is we'll often see patients and this gets back to the other question. We'll see patients who could have a congenital abnormality born with something and develop MDS and was actually there from birth and it just starts manifesting in their 20s. So, we'll often analyze new patients in their 20s do they have MDS or not, but the strict diagnosis of MDS the earliest I made was a young woman in her mid-20s.

Any other comments?

Dr. John Hill, Jr.: Someone in their 30s and then I was just mentioning to Ed we had an interesting scenario a few years ago where a young person came in probably in his early 40s, had MDS, had seven siblings. We knew that he needed a transplant. We started to do HLA typing on the siblings. There were about three matches and we brought in the first patient, the first sibling, to screen him as a donor and lo and behold his platelets were low and we... and so we ultimately ended up doing a marrow on him and he had MDS and so we brought in another sibling and her platelets were low and the bottom line is that we ultimately got every sibling in and we sat... they sat around in a circle in the room and they recounted a story of having grown up on a farm and every day dad would bring out this really caustic substance and they would have to clean the horse stalls and everything and it would get all over them and it was spraying all over everything. So, the best we could tell was that it was a genetically familial situation, but it was an environmental exposure that they all had at a pretty early age and probably over and over and over and whether that cleaning substance contained benzene or whatever. It wasn't clear, but I think that's a scenario and that probably accounts for why when we see an occasional young person come in with MDS there's probably some environmental exposure that's occurred.



Dr. Kenneth Meehan: Thanks for all the questions. What we're going to do in the interest of time is take a 20 minute break to 12:30. At 12:30 we'll have a patient and caregiver forum. In the meantime, the MDS Foundation was nice enough to sponsor lunch. You all take a 20 minute break, you can eat outside and hear whatever you'd like to do. Thank you, everyone.

(Applause)