



Speakers:

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Bart Scott, MD: Alright. So, (inaudible 5:06) keeping this on schedule I'm going to go ahead and get started on the next talk. So, if everyone could have their seat please that would be appreciated. If you want to go up in the back and get something else that's perfectly fine.

So, I have the pleasure of introducing Dr. Ueda who is new to our faculty here. I believe you did your internal medicine training here and then went away for a fellowship and is now back as an attending physician, but I asked her to speak today because she's doing a lot of interesting work that's looking specifically at patients and their mutational analysis and how it might impact the therapeutic choices for them and also another interesting aspect is following people over time and their mutational analysis and how they do. So, I think it's very interesting work. I think it's kind of what the future will hold and I'm very excited that she's going to be speaking about that today. So, thank you very much.

(Applause)

Masumi Ueda, MD: Good afternoon. Thank you, Bart, and (inaudible 6:17) to the MDS Foundation for inviting me to speak to you today and thank you all for being here on a sunny day of Seattle.

I'll be talking about patient chemotherapy pertaining to MDS. The objectives for my talk are to understand what various factors that may impact a person's response to MDS therapy and in discussing one of these factors I'll (inaudible 6:43) go over how the common drugs for MDS or hypomethylating agents Dr. Scott had earlier talked about Azacitidine and Decitabine, how they work and then ultimately understand how patient tapered therapy can really improve treatment and lead to more successful treatments for more patients.

So, I thought I'd start off with two cases to illustrate our point. Patient A is a 69 year old man who presented to the doctor with fatigue and is found to have low blood counts and he was ultimately diagnosed with MDS, bone marrow at diagnosis was that he had five percent blasts or leukemia cells or MDS cells (inaudible 7:24). He got standard treatment with Azacitidine seven days every month and after a few months miraculously almost his blood counts were actually normal and subsequent bone marrow show that he had less percentage of blasts, only two percent, and he went on to have a very good response for over two years and had a fairly normal life during that time.

Patient B, similar aged patient, a 69 year old man with the same diagnosis, had five percent blasts at the time of diagnosis presented with a similar kind of low blood count and treated with the same treatment, Azacitidine seven days every month. However, after three cycles his blood counts are still low. They never recover and a bone marrow subsequently show that his blasts had increased, doubled from five to 10 percent.

So, I think one of the most interesting questions in medicine and most blood cancer is why two people with seemingly similar disease and similar presentations, why do this respond so differently to the same treatment and I think the answers lie with two main things. The first is that MDS is (inaudible 8:37) cancer cells are genetically different such that their DNA (inaudible) could be different for one person, patient A and patient B and this (inaudible) differences in their response to standard treatment for MDS. The second part is that each person, each individual's body processes drugs differently and that patient A and Patient B after they received the same drug their chance of those drugs hitting the right target may be different and that ties into my research (inaudible) talk about (inaudible), but I think the key challenge in MDS and also in other cancers is that we often don't know which of the possibilities or maybe both is there a reason that it's not responding to treatment.

So, what is patients (inaudible) therapy. To me I think that therapy should be individualized in this age to 1) the cancer cells being age specific, DNA fingerprint of each person's specific cancer cell and 2) therapy should be tailored or individualized to each person's body and how they process the drugs and we sometimes call this pharmacodynamic and thirdly and probably most importantly we always try to tailor our therapy to an individual goals, beliefs, lifestyles and their background.

So, I'll be talking about the first and second points spending more time on the second point.

So, first of all cancer cell genetics. Just to illustrate the fact that this is a very complex field this is an example of a study actually that Bart showed earlier of nearly 1,000 patients with MDS and they checked for 100 areas in the genome for a specific mutation and actually they found that 90 percent, nearly 90 percent of patients had at least one mutation in this area in the cancer cells and actually on average each person had about three mutations although it ranged from zero mutations for patient (inaudible 10:42) patients for patient. Furthermore, there are about 47 genes that seem to be repeatedly mutated in a significant number of patients over greater than 10 percent. So, this really gets at how MDS can be so diverse between two individuals. To illustrate the point if you have three people with various types of MDS. One person can have mutation A and B, the next person can have mutation A and B also, but maybe they have two problems of the mutation B and the third patient may have mutation A and B, but also mutation C and D and so there are so many permeations of this that you can come up with and this is why you need genetic diversity in each person's MDS is so different and this probably (inaudible 11:35) in their response to treatment.

So, this gets at the idea of cancer genomics. This is a slide that Bart loaned to me, but this is the area research where we're looking at really specific sequences and fingerprint of the DNA within each person's cancer cells and we're using that information to really tie it into or translate into patient care in terms of deciding their best treatment and also in helping with diagnosis and also predicting how well they'll be able to. We talked a lot about cytogenetics which really means the chromosomes or the clumps of DNA in the cells that can help us sometimes decide what therapy is best, but the field is moving more towards what we call whole genome sequencing and that's looking at the billions of code in the DNA and looking at specific changes within those that can help us or (inaudible 12:33) us to what therapy may be best (inaudible).

So, the main point of all this is that tailor... we should be tailored and a key to each person's cancer and each person's cancer DNA. An example of this is that we find that you have a patient with gene A. We know that you are more likely to respond to drug A, so we should give you drug A. In other words if you have an occasion gene B, we know that you're not likely to respond to drug A, so we should probably try something different and I think this is the direction that cancer research in general is going but for MDS in particular there have already been a number of genes that have been associated with response or nonresponse to the class of agents we've been talking about, the hypomethylating agent, Azacitidine and Decitabine, and they're listed here and I think going forward there will be more and more studies like this that will help us really determine what mutations will predict a response for therapy.

So, this first part is tailor the therapy to cancer cell DNA. The second part which is my area of interest is looking at this concept of pharmacodynamics and this is based on the fact that each individual person's body probably handles the drug and delivers the drug to its target in a different way and it would be nice if we can tailor therapy to these differences. So, in talking about that I wanted to go over the basics of how these hypomethylating agents, the Azacitidine and Decitabine work. Here we have a diagram of DNA. There's two strands of blue and within a particular section of the DNA you have a gene one and in normal circumstances with DNA decoder a series of proteins can come together and produce and resolve a protein in this squiggly line and the cell can functionally and come normal blood cells. In many types of cancer and specifically in MDS there is a phenomenon called methylation and what this means is basically there's a stop sign that's placed in front of the gene such that the decoder, the DNA decoder, cannot get to the gene and make the protein that would otherwise help the cell function normally and we think that the classes proteins called DMNT in the (inaudible 15:10) brings a stop sign in places that scientists in front of the gene and this leads to what we call silencing of the genes, the proteins that need to be made where the cell functionally are not made in the cell may become dysplastic as in Myelodysplastic Syndrome.

So, knowing that how do we... the hypomethylating agents work? So, Azacitidine and Decitabine they can kind of sneak their way into the DNA strand and at the opportune moment they can attach themselves the DMNT, the blue box, and they can actually remove the stop sign or the (inaudible 15:49) in front of the gene and get rid of it and this allows the cells to go ahead

and make the protein like it was supposed to and allow the decoder to get to the gene. So, that's a simplified version of how Decitabine/Azacitidine work.

So, that's all good and done. However, the drug has to get from point A which is in the bloodstream after it's given to point B which is the target of DNMT and actually there's several obstacles that the drug has to encounter before getting to point B and the difference is among (inaudible 16:26) individuals probably exists in these different obstacles as I'll show you. So, I have here in the red or the orange circle the drugs Aza and Decitabine. The first obstacle they encounter really are these scissors in the (inaudible 16:41) of the bloodstream (inaudible). Bart had talked about this a little bit earlier, but these are (inaudible)-like scissors I can chop up the drug and actually only a small percentage of the drug actually can escape the scissors and make it inside the cell and you can imagine that maybe same two people maybe can have more CBA than the person next to you that you may see less drug inside the cell even if you're given the same dose and actually we've seen in some reports that men and various women have higher levels of CBA enzyme and perhaps they need more of the drug to get inside a cell, but at this time we give everybody the same scheduled dose.

So, once the drug can escape this enzyme and make it inside of the cell there's a second obstacle is that they have to be shaped in a way that they can actually go inside the DNA. This is called (inaudible 17:39) and a series of steps have to take place for this to happen, a series of proteins that helps to do that and then thirdly the third obstacle is more of a timing issue in that the DNA can only (inaudible) now transform drugs into the DNA at the specific time when the DNA is open. That's probably only 15 percent of the time. So, there's so many obstacles for the drug to get from point A to point B and but after the drug is in the DNA, only then can it bind to the DNMT and lead to its destruction. So, as you see there is so many steps to achieve the target and along away there's probably individual (inaudible 18:27) between patient A and patient B (inaudible) anymore. That probably leads to differences in how well we are able to achieve the targets even if you're given same doses of the drug. So, a simplified version of this is did the drug really get to where it needed to be. So, you can imagine before treatment you may have a fair amount of DNMT floating around and then after treatment with these hypomethylating agents, a person may have significant decrease in the level of protein as shown here and you can guess that this person will probably respond to the drug. The other possibility is that the drug doesn't get to where it needed to be. You still have a lot of DNMT floating around in this person does not responded to the drug. So, the real problem is if the drug hasn't reached its intended target, the DNMT, it really has no or little (inaudible 19:28) regardless of if you have a mutation or not that may otherwise predict that you'll respond to the therapy.

So, that's my research question, 1) can we first monitor the levels of this protein, DNMT1, inside cancer cells to really make sure that we're achieving the intended target of these otherwise pretty effective drugs and if that's the case does the decrease in the DNMT over time of treatment does that predict your chance of responding to one of these drugs and then most importantly if we can successfully prove these first two lines can we individualize both the dosing and frequency of

drugs so that we can make sure that a person that we're achieving the DMNT1 level depiction and the goal of all of this would be to try to make treatment more successful and also safe for a patient and we talked about earlier these drugs can also cause the blood count and bleeding and infection risk and it's possible that the doses that we use now are maybe a little bit too much and we can achieve adequate DMNT depletion without causing side effects, but it would only be possible if we can monitor the levels of DMNT1.

So, we actually now I'm on a project where we're actually testing this and after (inaudible 20:58) of DMNT and it uses a technology called flow cytometry is actually routinely used for (inaudible) MDS also, but it's a machine, a very specialized machine that can take blood from bone marrow samples. You can stain the cells with (inaudible) antibodies or dyes. You (inaudible) the machine and the cells individually line up a single cell at a time and a laser will hit it, excite the (inaudible) in there and give an output into a computer of how much protein is inside each particular cell. So, it's a cool technology and what we're doing alone is currently is going a step further and trying to measure the DMNT at specific times when the cell has its DNA open. In this case, the (inaudible) a lot more sensitive.

So, this is my complicated slide and this is what the output (inaudible 21:57) flow cytometry looks like. It looks like abstract art perhaps, but there are cycles individual dots in the graph represent one single cell and depending on the cell it... depending on the location of the dots in the graph we can tell if they're (inaudible) for something or how large the cell is. For this particularly (inaudible) the dotted square there and they represent the cells that are undergoing (inaudible). So, the DNA is open and we expect the drugs to be working and the top two panels represent before treatment with Azacitidine and the bottom two panels represent blood samples from after treatment and you can see that the number of cells actually decreased with treatment as we expect, but also the number or the level of DMNT that we're measuring also decreases before and after treatment as we would have expected after treatment with Azacitidine. So, we think we have a way that we can actually measure that target of the drug before and after a treatment and to really ensure that we're achieving the necessary target of the drug.

And this slide is courtesy of my collaborators back in Cleveland, but this is a panel of patients that we've already tested where we've take the blood from it with the flow cytometry machine and before and after treatment we can actually show that there are decreased levels of DMNT1 telling us basically that the drug thought to where it needed to be which is helpful to know, but what is more interesting is that the degree of decreased among these five patients are very, very (inaudible 23:50) and also the starting level of DMNT1 among these five patients are also very, very (inaudible). Again it just goes to show you that each person is different, each person's cancer cells different and so our goal is to try to understand these differences and how we can monitor and tailor the dosing frequency of the drugs to really make sure we're actually hitting the target of (inaudible) the DMNT.

So, I have this research (inaudible 24:20) open here at Fred Hutch where we're asking volunteer patients to donate blood for being these agents Azacitidine and Decitabine. We're taking blood sample at specified time points throughout their therapy. A type of their otherwise getting blood or bone marrow done and the goal is to (inaudible 24:42) DMNT if the people who respond to treatment have a lower amount of DMNT at the end of their treatment and if somebody's not responding to therapy perhaps they have similar amounts of DMNT than when they started treatment.

So, the goal of all of this is really to have patient tailored drug dosing for hypomethylating agents and I hope that by monitoring DMNT levels we can tailor the dosing and the frequency for each individual person to make the treatment more effective and safe.

So, to go back to the initial question of why two different people with the same disease may respond differently to the same treatment I hope I've been able to show that 1) cancer cell genetics in the DNA and there are differences between two people is very important and 2) just as important each person by the process of drug treatment so two people given the same dosing of drug you have differences in how well they target these drugs, the (inaudible 25:50) of the drug and I think as we can work on these two points together we can really tailor therapy to each person and to each person's cancer and lead to more successful (inaudible) in the future.

So, that was a quick overview, but I'm happy to take any questions.

(Applause)

Q1: What was your sampling rate from a timeline perspective? How often are you sampling?

Masumi Ueda, MD: Yeah. That's a great question. I think that's one of our research questions for the initial dataset we were... remembering when we have two time points before treatment like a baseline sample and any time after a treatment has begun, but really at this point we don't know when is the most important time point to check to see if there's (inaudible 26:39). So, that's one of our research questions and therefore in our project we're looking at least twice per cycle to see if you can pick an optimal time that you go for.

Q1: Thanks.

Q2: At the beginning you mentioned two patients, number one and number two. Could you just tell us what exactly happened with according to your... by your research what patient one or two and 2) and what did their (inaudible 27:15) who survived, who not and how long and how your doses those patients. What's the clinical... any clinical application or starting which you're tailoring doses (inaudible) medication.

Masumi Ueda, MD: Well, I can tell you patient A is a real patient I met when I was training in Cleveland, a Vietnam War veteran who was diagnosed with MDS and he had already been starting on Azacitidine when I met him and probably almost a year into his treatment I saw that his blood counts suddenly dropped and at that time it was hard to tell if there was that the drug toxicity that we've been talking about that Azacitidine caused myelosuppression or is this a progression of the disease. I had been working on this project already when I was there, but I wish that there was a way to see if we were actually targeting DNMT1 in his blood cells adequately to see why he had suddenly taken a turn in his response and, I mean, what happened to that patient he was doing well for two years, but afterwards his disease progressed and for various reasons he did not get a transplant and he since passed away. Patient B was made up.

Q2: So, patient two died sooner, yeah?

Masumi Ueda, MD: Patient B is a (inaudible 28:49) I made up for this (inaudible). So, a real very real patient that (inaudible).

Q2: But no clinical implications on the dosage and choice of drug? It just what you presented see (inaudible 29:06) your ideas.

Masumi Ueda, MD: Right. Ultimately, that's the goal is to try to adjust the dose of the drug based on...

Q2: But you actually adjusted... have adjusted dose? Not the imaginary patient but the real patient?

Masumi Ueda, MD: Yeah. We do adjust doses at least I have in the past, adjusted doses of Azacitidine based on one's blood (inaudible 29:32) other side effects from it. There actually been studies that have looked at lower doses of Azacitidine, not 75, but using as low as 32 milligrams per liter squared particularly in patients who are post-transplant and (inaudible) with Aza and then they're recovering from transplant they may need more. So, (inaudible) myelosuppression and low blood counts and in that setting we actually do use a lower dose of Azacitidine.

Q2: What's going to do these patients responded to Vidaza? You continue and what's the end point? Death or what? Or are you may discontinue early when it work, doesn't work? What's the criteria for the continuous long term use of Vidaza?

Masumi Ueda, MD: I think on average most patients who are on Azacitidine and do not conform with a transplant, the average time that they responded is about two years.

Q2: They respond you stop it or you continue?

Masumi Ueda, MD: If they're not responding to the drug then you would need to go the next therapy or a clinical trial.

Q3: You mentioned that patient one is a Vietnam Vet. Is there some special significance? Is there some relationship between those who served in Vietnam and developing MDS later in life as there are with many other diseases?

Bart Scott, MD: Right. So, there's a difference between what you think and what you can prove. So, I'll answer your question in that way. So, thank you so much.

Masumi Ueda, MD: Thank you.

(Applause)

Bart Scott, MD: So, the next talk is going to be by Dr. Salit and she's going to speak about an unusual (inaudible 31:32) about Myelodysplastic Syndrome overlapped with myeloproliferative (inaudible). So, thank you very much.

Rachel Salit, MD: Thank you guys for inviting me here today (inaudible 31:44) MDS Foundation. So, I'm going to talk to you today about MDS and MPN overlap syndrome and this is actually really made as a diagnosis in 2008. So, it's fairly new. So, I'll go through the diseases and then see if anyone here is actually some (inaudible 32:26).

So, since we've been talking about MDS this whole, I just thought I would do a brief overview of what is myeloproliferative neoplasm or MPN. So, while MDS is usually dysplasia or decreased production of blood cells, in myeloproliferative neoplasm it's usually (inaudible 32:45) making too many cells. So, common symptoms of making too many cells are headaches, shortness of breath, dizziness, itchiness, fatigue, weakness and weight loss and often abdominal pain and difficulty eating from enlarged spleen that happens trapping all these cells.

Some of the common Myeloproliferative Neoplasm that you may have heard are CML or chronic myeloid leukemia which is an overproduction of white blood cells, polycythemia vera which is an overproduction of red blood cells, essential thrombocytopenia which is an overproduction of platelets, chronic neutrophilic leukemia which is the overproduction of neutrophils, eosinophil leukemia which is an overproduction of eosinophil and then primary myelofibrosis which is when the bone marrow is gradually replaced by fibrous bone tissue and disrupts normal blood cell production. So, we often see polycythemia vera and essential thrombocytopenia can turn into primary myelo or secondary Myeloproliferatives over time.

So, comparing the features of an MDS versus MPN, the MDS we saw were ineffective blood (inaudible 34:01), low blood counts and abnormal blood cells called dysplasia whereas in MPNs

we see super effective blood making leading to increased blood counts and increased spleen size with no dysplasia.

So, what is an MDS-MPN overlap? So, in patients with this condition, they have some problems with blood cell formation from MDS and then some from MPN and these are the best defined entities and we'll talk about four of the five of them today. I chose to leave out the juvenile since we're all adults here. So, CMML is the most common. There is atypical CML. There's an MDS/MPN with ring sideroblasts. Sort of like the MDS of ALS, but with also thrombocytosis, so overproduction of platelets and then an MDS/MPN unclassifiable which is sort of a wastebasket for all the rest of the commonalities. Does anyone here have any of the overlap symptoms? Yes. Are you CMML or something?

Q4: The second from the bottom with the T.

Rachel Salit, MD: With the T, okay. Okay. Okay.

So, I kind of like this slide for fun. You know, when I was a little stem cell I didn't know what I want to (inaudible 35:31) and the stem cell says but I'm so confused. So, that sort of typifies this condition. So, it's really a pathology I noticed and I went and spoke to the pathologists who were giving this talk because although I am (inaudible), I don't evaluate pathology and I do find it is very confusing when you look at these slides to tell the difference. So, this would be more of a classic Myelodysplastic Syndrome. So, you see dysplasia. So, a bunch of abnormal cells with some myelofibrosis running through it. There is... where there is myelofibrosis you would see mostly fibrous tissue with some abnormal cells (inaudible 36:14) and in the middle is this MDS/MPN overlap which is the dysplasia with the fibrosis but not one or the other. So, the most common condition of MDS/MPN entity is CMML and the main feature is that you have too many monocytes which is a type of white blood cell in your blood. So, the bone marrow is hypercellular. So, it has monocytosis which is the MPN component, but there has to be dysplasia of at least one cell line which is your MDS component. In this condition your spleen is often enlarged and, again, 15 to 30 percent of the patients do go on to develop AML. There is gene mutation that people have been talking about seen in greater than 90 percent of the patients the most common of which is a TET2.

So, what are the symptoms of CMML? So, having too many monocytes really thickens your blood. So, it can cause any of the symptoms with CMML. These monocytes can settle in the spleen or in the liver making these organs large and leading to weight loss and decreased appetite from sort of a crushing of the stomach as well as some (inaudible 37:37). Patients with CMML may have low blood counts in the other areas like anemia or low platelets and interesting in this condition people who have flu or other bacterial infections can have elevated monocytes and so if you're receiving a diagnosis of CMML the doctors will first rule out infection.

So, this is what a CMML person's blood would look like on the left. You can see there's these large kind of funny shaped nuclei and here is when they're clumped and darker and in the bone marrow aspirate you would just see these big clusters of monocytes all bunched up. There's three categories of CMML, There's (inaudible 38:28) 1 and 2. Right now there's a CMML-0 and the categories are based on how many blasts are in your blood and how many are in your marrow. Also (inaudible) we look at white blood cell count. They're sort of an MDS type of CMML that has less than 13,000 white blood cells and in a myelofibrosis type CMML that has greater than 13,000 white cells. Other core prognostic features could include the hemoglobin level, the platelet, having abnormal chromosomes and an ASXL (inaudible 39:05) mutation.

So, this is just sort of depiction of what people can expected from prognosis of CMML and I have a... or down low left hand column here CMML-0 is less than five percent blasts, CMML-1 is five to nine percent blasts and CMML-2 is 10 to 19 percent blasts and then 20 percent or greater would be AML and then across the top it shows CMML the MDS type meaning less than 13,000 white cells and the MPN type which is greater and you can see the survival with the MDS type is actually better. So, the CMML-0 is core here survival is only seven percent of paper progressing to AML in two years versus the CMML-2 group that has approximately 17 month overall survival with a 36 percent progression to AML at two years.

So, what therapies have been tried in CMML? So, the low risk patients can get agents like (inaudible 40:13) or Hydroxyurea to just lower the monocyte count, but the most common treatment for the CMML-1 or 2 patient is the Azacitidine and Decitabine. They've been seen for MDS. These patients about (inaudible 40:28) percent respond and the complete remission has really varied between 10 to about 60 percent in various studies with an overall survival of one to three years and some of the factors that have been shown to be predictive of how long you will respond to the Azacitidine are bone marrow blasts and elevated white count as I showed earlier and better overall survival is a lower monocyte count and lower peripheral blasts.

We're still here unfortunately we do have transplant and it has been shown to be a cure for CMML. There have not been any randomized trials. Initially, transplant was prohibitive as was talked by Dr. Deeg earlier mostly because we only had high intensity conditioning, but now that we have reduced intensity conditioning patients are having much less treatment related toxicity for transplant for CMML. We did a retrospective analysis here on 85 patients that were treated for CMML and this was published back in 2011 and the 10 year overall survival was 40 percent for these patients. So, the patients who are (inaudible 41:45) as their CMML are having long term survival and improved survival was associated with the opposite, younger age, lower comorbidities, and (inaudible 41:59) cytogenetics. The European Bone Marrow Transplant Group did a retrospective analysis in 513 patients. So, a much larger group. Ninety-five of those patients had already transformed to AML and in that group the four year overall survival was about 33 percent and the only significant prognostic factor was that they were in complete remission at the time of transplant and it was likely from hypomethylating therapy.

So, the (inaudible 42:31) I'll talk about is the atypical CML. So, atypical CML is similar to CML but with no Philadelphia chromosome. So, if you heard about patients with CML, it used to be one of the most common indications for transplant, but since it came out of agents like Gleevec or imatinib or TASIGNA which is Dasatinib we've been able to essentially cure or long term treat patients with CML. Unfortunately, atypical CML does not have a Philadelphia chromosome, so it can't benefit from these drugs. It is a fairly rare disease with less than two cases for every out of 100 cases of CML and it is a (inaudible 43:16) agent (inaudible) with a male predominance and, again, patients present with fatigue, night sweats and increased spleen. The diagnosis is really pathologic. So, how are you going to tell atypical CML from CML is not going to be what the patient looks like, but what the pathologist sees in the lab and the treatment of choice for atypical CML is bone marrow transplant.

So, what do we commonly see in the lab with CML... with I'm sorry with CML is these. Pelger-Huët which looked like sunglasses. Hyperlocomotion compared to a normal neutrophil that has maybe three clones in its nuclei and also hypogranularity. So, the cytoplasm looks very white.

And here's slides, again, CML versus atypical CML and to me they look very similar, but to a pathologist they look very different. So, when I show these to the pathologist I said how would you tell that this was atypical CML versus CML? She said well, look at how much more lobulated it is in the atypical CML compared to the CML and also the (inaudible 44:40) cytoplasm is more (inaudible) in atypical CML than CML. So, not having the Philadelphia chromosome is probably the most revealing. The largest (inaudible 44:54) that has been looked at for atypical CML is 55 cases. So, it just shows how rare the disease is. In that group the median survival is 25 months, about two years and about 40 percent of those patients transform to AML and the prediction for shorter survival of older patients, female gender higher white count in the presence of (inaudible).

Now, we told the pathologist a lot in terms of saying this is atypical CML versus CMML or another entity is a mutation called SATPV1 and this is seen in 30 percent of atypical CMLs. In this study that was published in 2013 they actually showed that there are the different (inaudible 45:43) so whether you were SATPV1 positive or not. So, (inaudible) negative had a 77 month median survival versus patients that were SETPV1 positive with the mutation who had less than two years survival.

Okay. So, now were at the MDS/MPN/RST. So, this is very much like the RARS in MDS. So, it is considered a (inaudible 46:20), but in this case you also have too many platelets. So, patients who we divided into low risk and high risk really based on if they're over the age of 60 or if they have a history of blood clot. So, low risk patients can benefit from just the low dose aspirin therapy. The biggest risk is that the patients will develop blood clot. Bone marrow transplant would be the treatment of choice for in these patient, but it's reserved for patients who are not responding to the transfusions or patients who have progressed it to an AML.

So, here's some of the features of that MDS/MPN/RST. Patients have increased platelets and abnormal neutrophils. The bone marrow aspirate shows red blood cells that have a lot of abnormalities in shape. The bone marrow aspirate shows clusters of large platelet making cells and also these ring sideroblasts which is the iron deposition around the nucleus of the cell.

So, MDS/MPN/RALST has a mutational finding in 72 percent of patients of (inaudible 47:48) and there's (inaudible 47:52) significance with this mutation. Patients having a 6.9 year versus 3.3 year survival at your positive or negative for FSPB1. They can also be distinguished from RARS by a JAK2 mutation. So, 60 percent of patients with RARST have a JAK2 mutation in terms of zero percent of patients with RARS. In patients with a JAK2 mutation also had a better prognosis. So, there been kind of a two headed hypothesis for RARST, but the FS3B1 that they talked about with MDS is the first hit and then the second hit, the JAK2 mutation, leads to the T. So, there is the combination of the MDS and MPN.

And the last one, the MDS/MPNU, is the wastebasket sort of where all of the other MDS/MPNs that we're not sure what they are.

So, what are the features? So, you still have to have a dysplastic feature in one type of blood cell. Platelets have to be greater than 450 and a white count higher than 13 and you shouldn't have any history of any other MPN or MDS either individually or together. You couldn't have received any chemotherapy in the past. That is secondary condition. You can't have a BCR (inaudible 49:24) or a Philadelphia chromosome and you can't have any of these genetic abnormalities. So, really it's a (inaudible) disease that had missed features that it don't fit in any other category.

So, there's been one theory that patient describes by MD Anderson. Eighty-five patients with this MDS/MPNU and they treated their patients with hypomethylating therapy, (inaudible) therapy like a Lenalidomide or stem cell transplants and the median outcome was one here. Favorable outcome was with younger aged, higher platelet counts, (inaudible 50:03) circulating blasts and less than five percent bone marrow and they basically show in this series that MDS/MPNU patient had a worse survival than patients with MDS or MPN. They are studying right now combination therapy with Ruxolitinib which can commonly use in MPN drugs which is (inaudible) and Azacitidine together to see if they can get a better response from (inaudible).

So, what is the future of treatment for MDS and MPN? There is really a rare disease. It's reasonably been described. In other than CMML, we don't really have any studies of MDS and MPN as a disease. The goals of therapy are to cure a disease. We do want to reduce symptoms (inaudible 50:54) myeloid as well as (inaudible) blood counts and to get people into cytogenetic and molecular remission and the ultimate goal when we're talking about treating any of these diseases is really to halt the progression to AML.

So, there was one study that has looked at these MDS/MPN patients 2012. They enrolled 28 patients and they did a combination of Thalidomide, arsenic, dexamethasone and ascorbic acid and they called this the TADA Study and 15 of patients had MDS/MPNU, eight patients had CMML and five patients had (inaudible 51:34) and they actually showed about 30 percent response to this (inaudible). Now, (inaudible) not a common (inaudible) regimen and probably means (inaudible) very often, but what's interesting is at 24 months the median progression (inaudible) survival was 14.4 months and overall survival was 21.4 months. In this was 15 of the patients were MDS/MPNU which in the last slide I was telling you only had a one year survival. So, they essentially doubled the survival with this regimen.

The other therapies that we talk about for these conditions are these targeted therapies. So, I mentioned sort of as we went along some of these mutations that you could possibly have. So, one possible mutation is the JAK2 V617F and this is a common mutation see in the MPNs. In the RARST 60 percent of patients had a JAK2 mutation. So, Ruxolitinib is the very exciting opportunity to treat that disease. The RAS pathway there's a new drug called Trabectedin which is a meth inhibitor can be used to predict CMML as 25 – 35 percent of patients have CMML and 25 to 55 percent of atypical CML patients have this mutation. The SF3B1 we talked about as well. Seventy-two percent of patients with RARST have this mutation and there is a drug whose mechanism I can't clearly explain called (inaudible 53:27) that traps all three (inaudible) called Luspatercept that is sort of coming down the pike right now in phase one and phase two trials. There is another drug called H3B-8800 and I'll talk about that. We're opening a study here which can target CMML. Fifty percent of the patients have an SRSF2 mutation and the last one is a drug that we commonly use in Hodgkin's disease called (inaudible) which is an anti(inaudible) in 30 to 40 percent of CMML patients actually (inaudible).

So, currently here we have the study of Guadecitabine that Dr. Scott talked about earlier and that study is open to patients who have MDS as well as CML. The H3B-800 study will include patients with CML and the (inaudible 54:30) is a Southwestern oncology group study which may open here which would include patients with CMML as a (inaudible).

So, in summary I hope I did justice to this complicated (inaudible 54:51). I think that it's really a work in progress in terms of limiting how these diseases are separate from each other and what are possible ways that we can treat them either individually as a group. So, we know that they have features common to MDS and MPN, that the diagnosis is often made in the laboratory or by a pathologist because a lot of different presentations of the diseases are very similar. The facts that we see increasing of some counts then decreasing of other counts can make it difficult to treat because you're working at not dropping one line while you're trying to drop another cell line. The hypomethylating agents are most commonly used, but probably had to have optimal efficacy compared to what we've seen with MDS and transplants really are preferred treatment and so for younger patients, higher risk disease, people with low comorbidities transplants really the cure for these diseases. We talked about mutations that may provide targeted opportunities

for targeted therapy and we're trying to open clinical trials which are really recommended for these type of rare diseases, so we can learn more about what they respond to.

So, with that I'd like to acknowledge the people at this meeting as well as Cecilia Young who is a pathologist who helped me run through all these slides and (inaudible 56:29). He works on our molecular profiling and the SSDA and the patients and caregivers.

I'll take any questions.

(Applause)

Either I confused everybody or I was very clear.

Bart Scott, MD: Thank you, Rachel. That was a really outstanding talk and I do have to say that those groups of disorders are really difficult to convey to patients (inaudible 57:16) in doing that.

So, Sandy is here. Sandy Curtin. I've known you for a long time, about 10 years I think.

Sandy Kurtin, RN: I know. Yeah.

Bart Scott, MD: She's going to talk about quality of life and then patients support group that's coming in around 3:00 but I did want to remind everyone that there will be an iron overload talk sponsored by Novartis following that. So, thank you.

Sandy Kurtin, RN: And I think we'll probably get done before 3:00. If you need to stand up and stretch for a moment, this is has been a really long, very (inaudible 57:47) for a day. So, you might want to just shake your head a little bit and let it all settle in there. It's complicated for us. So, I can only imagine what it's like for you. So, if you want to take a minute to get up and stretch that might help.

Alright. We'll go ahead and (inaudible 1:01:30) in here so we can get you out to the sunny Seattle day which I know that doesn't always happen and the weather lately has been very crazy up here in the Northwest.

So, I'm Sandy Kurtin. I am a nurse practitioner. I work at the University of Arizona Cancer Center in Tucson, Arizona. We have a number of Seattle... What do you call yourselves? Seattle-ins? Seattleites like socialites but Seattleites. That's very nice. I like it. So, we have a number of Seattleites that spend each part of the winter down in sunny Tucson where we have far less humidity. It's a little toasty down there right now, but I'm glad to be here. I have been doing this work for 32 years. I have had the great fortune of working with remarkable people over the course of those years with MDS and also I'm a member of the Board of Directors for the MDS Foundation. It's an international national organization. I just got back from our

international meeting which was in Valencia, Spain which was very molecular and the moral to that story is it is not going to get any simpler. So, it's hard to hear. It's hard to say. We're really working hard to help you all to better understand things at this level of complexity because that's the way medicine is moving in this precision personalized care and so part of our goal this afternoon is to go back through a little bit of that and then the second thing is to really focus on how you can stay well so you've heard Dr. Deeg and you've heard Dr. Scott and you heard Dr. Ueda and all of them to say people who fit. So, part of the huge part of the battle, if you will, is to be well enough to be eligible for whatever it is that's coming next and there is a lot happening. We have not had a new drug group in the studies for over 10 years. It's been way too long. There are a lot of very exciting compounds that are moving forward and there are a lot of really smart people at global level working together to try to understand this disease at this very complex level and (inaudible 1:04:04) such variability from person to person and then how we can best exploit each of those little abnormalities for therapeutic benefit. So, our goal this afternoon is to have you... you're digesting all this stuff you've heard this morning, but hopefully to instill a little bit of hope in that there's a lot of really good work going forward. We would never have a drug without a clinical trial. So, then we'll just echo that sentiment right up front that if you have the opportunity to participate in a clinical trial we always prefer that because my way of practicing is never exclude a treatment option and if there's a trial and I'll (inaudible 1:04:51) an option that you would otherwise not have we can do whatever we want with FDA approved agents. We don't have any of them, but the only way we find new drugs is through clinical trials. So, I'll just echo that sentiment.

So, I just have a few slides. I also chair the International Nursing Board, Nurse Leadership Board. So, we have members all over the world as we do with our Centers of Excellence. They're all over the world. So, we're putting our heads together and trying to come up with things.

So, some of the people in the group said they haven't required transfusions. So, one of the first questions we say is when do we start treatment for MDS. We know that transfusions and we know that growth factors can help with symptoms, but they really don't treat the underlying disease. They are not disease modifying therapies. So, what clues us in to treating somebody actively with a disease modifying agent is that you're transfusion dependent. It means your bone marrow's not doing that job by itself and it needs some help and transfusions over time you'll hear a little bit about iron overload, but there are some other things that we suspect that come from those (inaudible 1:06:04) transfusions. If your blood counts, these cytopenias, low counts means cytopenias are becoming worse. That's another indication that the bone marrow's not working. The blasts are going up. That means you're moving. If you think about the lowest risk disease here and AML over here if you're moving over here you're not to jump the fence and become AML then we say you know what? It's time to do something disease modifying or in people who simply just have to... more things in the worry bucket than the big bucket. So, when I talk to people I say well, here's things in the big bucket and here's the things in the worry bucket and if it's on the scale and this bucket's too full we need to do something to change that

disease and we're going to look at you as an individual. Are you fit or frail? So, we get back to this whole question of fitness, look at your comorbidities. So, we want you to work just as hard with your cardiologist or endocrinologist or primary care doctor to fine tune your diabetes or your heart disease so that you can be as well as you can. So, it really does take a team and you are all part of that team. You heard about the risk stratification based on the IPSS-R. We'll come back to that. What is your lifestyle and what is your personal choice because that matters. You can then tell us what you want to do. We have, as I say, people come down to Arizona in the winter from places like Chicago and Minnesota, don't you know, and they want to play golf and they want to play golf and they want to play golf and they don't want to spend all their time with us and so we negotiate. So, you have to say here's my goals and one of those is to be alive, but you don't want to spend all your time with us as great as we might be.

What are some the principles? You heard about allogeneic stem cell transplant. So, with MDS you can't get your own bone marrow and that's true of myeloid diseases in general. So, we have myeloid diseases that are in one part of the bone marrow tree and then we have lymphoid diseases things like myeloma and lymphoma where you can have your own bone marrow. When you get your own bone marrow you don't deal with the same level of toxicity and primarily you get graft versus host. So, it's a very different situation and because of that that age cut off varies. So, you may be sitting in a waiting room and see somebody who had a transplant and they make it look like a piece of cake and that's probably because they have their own marrow. So, that doesn't really apply in myeloid malignancies of which MDS is a part of that as well as the crossover disease that you just heard about.

Age alone, so chronological age alone is really... it used to be that the cutoff for allo transplants was 60 and then it started creeping up and creeping up and creeping up and if you're here at the Hutch where they do more transplants than most anybody in the country and they get good... they're good at it because of that experience. If you're fit, if you're a good 75 you can get an allo transplant. If you're... you can be 40 and not well and you're not eligible. So, it's not about the number of really chronological. It's about physiological age. So, again, staying well is really key. We'll talk a little bit about the time it takes for things to work. You heard a little of that from Dr. Scott about the minimum of three months if you're on Lenalidomide. Some of us would say even four months and a minimum of four to six months before we call it quits on the de-methylating agent, Azacitidine and Decitabine, because this whole process of correcting all those abnormalities that we been talking about takes time. You have to kind of reprogram the cells, recalibrate the factory, the bone marrow, if you will and it isn't something that's quick. So, when I see patients, I say you know what? I need you to commit to four to six months. We're going to have to stick with this, give it time. It's often difficult because early on there's side effects. The counts actually can get worse before they get better and that's often you've heard that sometimes that means we're actually doing the work we expect and if you give up too soon then you really only expose yourself to toxicity with no (inaudible 1:10:37) therapeutic benefit. So, we really try to get people to stick with it and stay the course as long as there's no... somebody was saying they got all puffy and swollen and rashes and so there are some people where a certain drug is

not really the one for them. So, we make our plan and we stick together and work as a team to try to get people through those early months of treatment so that you have the potential for therapeutic benefit.

So, this is one of my favorite little slides. I call it the ravine slide. So, if you think about this is your bone marrow and it has MDS in there and it's a little crowded and there's some abnormal cells we actually make that worse initially when we start treatment and then it starts to get better, but it may never actually look like it did in the beginning. So, before you became diagnosed your counts may have been normal, but at the time of diagnosis they're out of balance and there are people who never have a normal platelet count again and that's okay as long as you're not having problems. So, we tried really hard not just treat the little computer in the little graph, but to treat you. So, you can do fine with your platelets, no bleeding. You can also do fine with a lower blood count and not be affected. So, we really try to focus beyond just those numbers and to understand that it may never actually get back to normal again. You kind of get reset if you will.

These early toxicities require management. So, we have to work as a team and recognizing what those are and treating them very proactively, but sticking with it to get your through that so that you can get to the other side basically. Understanding that that best response may not happen till later. So, even four, six, nine months down the road. So, giving these drugs when you only have a couple drugs to use we want to give each one of the best possible opportunity to work and I'll share a couple case studies. These are patients that I've taken care of. This is a younger patient who came to us with low platelets. So, the platelets here are in the goldenrod color here and white blood cell counts in blue and the red blood cells are in pink. Don't know why I didn't do red, but it's pink and you can see the ups and downs and so this is a person on Azacitidine who has low red blood counts to start with and you can see it gets worse. They need transfusion, transfusion, transfusion, transfusion, oop, up we go, four cycles. So, if we stop way over here because the numbers weren't getting better and they were getting worse we would have simply made you worse and not better. So, it's really important if you haven't started therapy or if you haven't started one of these therapies to understand give it enough time and you just support people through that, but transfusions are just part of care so that they have the opportunity to actually have a response. Now, this was a younger patient who happened to have a sibling donor and went onto have a transplant, but it took that long to see those numbers improve.

This is the famous Chet chart and this is actually not the most recent. So, this is a patient I took care of for a very long time. We had a lady here who was also on Revlimid for 12 years. He was a 5Q- who had several prior therapies with experimental drugs, but you can see... and he's a rocket scientists, so he built rocket engines for NASA so he actually created these charts because I'm not smart enough to put them on two different axis. So, (inaudible 1:14:30) can I just use yours and put the numbers in (inaudible), but you can see early on he had very short drop in platelets and then this would go out to 2014. He actually died of heart disease not of MDS. Still on Revlimid at that time, but he did not... here's 100,000 and the lower (inaudible 1:14:57) for

platelets is 150,000. He had two normal platelet counts for more than 13 years, did fine, didn't bleed. His white blood cell count which is here. So, here's 3,000 which 3,500 is generally the norm, very few numbers that were normal, but he was never hospitalized. So, it's okay as long as you avoid people who are obviously ill and do those kinds of things people can do well and their counts are abnormal. It's okay.

So, we have to sort of rethink our goals in what we're trying to achieve and the people that are able to stay on long term therapy part of that is you being a partner. So, taking control, being here is the first step. So, that's great, trying to gain knowledge and really learning how to manage your disease. So, maximizing each treatment option, becoming a partner. Caregivers, can't do it without them. There's no way. So, I always said when you get married and the last part there says in sickness and in health and then the fine print that you can't read says including, but not limited to... medication administration, shots, line care, like we don't train you for this. We go to school for years to learn how to do these kinds of medical things and you guys just get signed up. If you come to with the patient to a visit you're a potential caregiver. We sign you up and we say blah, blah, blah, blah, bye (inaudible 1:16:36) in a few weeks. Good luck. There's a lot to take in and there's a lot of responsibility. So, we try to really have caregivers also take care of themselves really, really important and part of that is asking for help. We're going to talk more about staying well. You all got a little packet. So, one of the things that we did as the Nurse Leadership Board is we created the *Building Blocks of Hope*. This was... I have two children that are 30 and 28. This is my third child, but really... and we're revising this and I'm going to show you my fourth child shortly, but the idea is that if you go online and you can get an interactive version where there are live links and it'll take you a lot of information. The idea is to just begin to learn about your disease and what kind of questions you need to ask so that you can empower yourself. How to track your progress. How to see are my counts are getting better or how much transfusion am I needed and now we're going to have for us understanding the profile of your disease. So, what are your chromosome abnormalities? How many of you know your IPSS-R score? There you go. So, there's a few. So, really important to know where you fit in this scheme of things. What's the signature of your disease and that's going to matter and as these newer drugs are coming out it's going to be really important to know do I have a this or a that in my profile? So, understand your disease. Get the tools to track them. Take your medications as prescribed. Keep your appointments. I'm always... I get messages to say so and so didn't come because they didn't feel good. Well, they probably should have come because they didn't feel good because that's sort of our job is to help figure out why you don't feel good and make you feel better. So, we try to have... when you don't feel good that's probably the time to go to see your healthcare team, your provider, or at least to call them and have a conversation. So, if you got like food poisoning so please stay home. Tracking your symptoms. So, being able to come to us. So, if you're seeing the provider once a month you may not remember what's happened that whole month and then you have your visits and sometimes they're very brief and it's difficult to get organized and know what to convey in that time because what decided to do as clinicians with you is based on what you tell us from visit to visit. We can only help you with whatever information we gather from you. So, I often encourage people to bring a caregiver or an advocate

what I call the truth squad so that when you sit there and say I'm great and they're going mmm mmm, no, no. They're sitting on the couch all day. They're not eating. They tell on you, but that's good because we need to know that so that we can make adjustments as we need to. Be your own advocate. Ask questions. Really make your wishes clear. So, this is really important and now there's really a mandate with the what used to be called the Institutes of Medicine which is now the National Academy of Sciences saying that you have... we talk about advanced directives and what would you want if this happened and it's really important to get that out there and then you check it's done, the works done, you put it away. That's okay, but knowing people's wishes were really, really important. So, the best treatment for the patient is gained through shared decision making. So, we have a conversation about your disease, what the possibilities are, what the potential risks are and then basically you get to decide but it's something that should be done collectively incorporating these preferences that we talked about. Prepare for your visits. Set an agenda. Say what do I really need to get out of this visit? Write it down. Keep track of it. Take it with you and if you only get time to ask three questions think about what are those three questions I really want to ask and if it can't happen with the provider then there's a whole gamut of people involved in your team that you can work with to ask those questions. So, we encourage you to do that. You can always call Audrey, our patient liaison who triages a lot of these questions out to various people experts that will give generic answers. It's always best to talk to the people who are actually taking care of you though. So, make that list of questions so that you remember. Bring that support person with you. Update your provider on anything that's happened since the last visit. People are in a multitude of medications they get from 25 different people. They're not great at taking them away. They're very good at adding to the list and sometimes you may have two drugs that are the same or that they're in conflict and that's not good. So, we really count on you to keep track of that information and let us know if you're taking stuff that's over the counter or you're trying alternative therapies. We need to really know that. There are certain things that we prefer you not do that might interfere with your therapy. So, the last thing you want to do is take something that's going to negate the benefit of your therapy. Certain things (inaudible 1:22:12) science and that's okay, but just let us know so we can have a conversation. Keep your transfusion records. So, we already talked about your whole team and then if there are things that you really don't have clarity about after your visit write that down so that you can ask again or talk to the nurses or research coordinator is always a good person if you're on a study. Be sure that you're involved in asking those questions and any question's okay. You got to just ask them and we'll do our best to answer those.

I mentioned the caregiver. So, I'll leave it at that, but there are a lot of resources that are specific caregivers and so we really emphasize to people you got to have a break. Get somebody to come and fill in for you if you need to, but being a caregiver is a very stressful thing and we don't want you to get sick also. So, we need to take care of the collective group. There are a number of resources that are out that are pretty cool. There's this thing called Lots of Helping Hands. So, it's an organization that works within communities and they give you tools to basically bring people together with a shared calendar. So, they have a help calendar and you can post it and write people, your friends and family to do tangible things. You just say you I need somebody to

go the dry cleaners on Tuesday. Very specific requests. I don't go to the dry cleaners. If it needs to be ironed or dry cleaned I don't buy it because I hate to iron and I don't like to go to dry cleaners, but so that's the other solution, but it gives you a tangible way so if people are asking what can I do to help? You say you know what? Here's the list. So, it's actually really meaningful help and this is just kind of how that looks. So, it's just an example of something that's out there for you.

So, let's shift a little bit to say what can you do to stay healthy? So, a balanced diet. There is no special magic diet. There isn't. We've gone through every fad, (inaudible 1:24:30) a very strong cancer prevention program and then there was a time when everybody came in and they were literally orange because they were eating and drinking so much carrot juice and they had orange palms and orange eyes and guess what? It didn't matter. It didn't work. And then we all ate oats till we were like oated out. That didn't really matter. So, we've gone through all these fads. Sometimes it's magic diet. There is no such thing. So, it's really balanced is the key. Eating fast food every day is not good for you. Can you have it once in a while? Yes. So, balance is the key. Things in moderation. Some things in excess (inaudible 1:25:18) like chocolate because you got to have a little fun because what's the point. If eating becomes work and it's really stressful it's probably more harmful than good to you. There's this whole (inaudible) big thing is sugar. Well, you know what? If you're eating ice cream and cookies and brownies, whoops, every day, but I'm sure you balanced it out with a salad and a whole grain bread, but if you're eating junk food that's not good for you loaded with sugar. Can you have some sugar? Sure. There isn't anything to say that people (inaudible) a little bit of sugar do much worse. So, if you hear all these fad (inaudible 1:25:55) people are making a lot of money selling these various things. It's a business and the reality is that balance is really the key. If you smoke, you quit. So, the single worst thing you can do for your body. We know that tobacco is connected to MDS actually now then something that's been studied. Limiting alcohol. So, moderation, again. Be active as much as you can. If that means doing a chair exercise to keep your strength up that's better than nothing. It doesn't mean you have to go to the gym and work out for two hours. You just a little bit walk around the block, up and down the hall, in your house if that's you can do, but do something. Be active. Get some exercise band. I have people do that all the time. There's one... if you do one thing you can get an exercise (inaudible 1:26:47) and roll it in your hand, the flat ones, the rubber band and you put... I'm probably going to fall. You put it under your foot and sit in a chair and do this but if you do one motion you push and you pull at the same time and it strengthens all of your proximal muscles. So, this is what you need to wash your hair, brush your teeth, get dressed, these are your quads are what you need to get in and out of a car, up off a chair, up off the commode. When those muscles... when you're not using them the muscles get weak very quickly and then you can't do anything. You have no stamina. So, if you just do a few of those a day, sit and do whatever, watch TV, don't watch the news because that'll stress you out. Then we all need therapy. Just like really? Are you kidding? Wow.

Avoid infection. So, I've had... so there's a whole another level of safety when you've had an allogeneic transplant, but in the general population people with MDS don't get (inaudible

1:27:58). Most people it's like an infection in the blood because we're not using those drugs that cause that. So, the big thing is avoid people who are obviously ill. Don't go to the buffet though I hate to say. Don't play in the elevator. Don't go to the mall on Saturdays with everybody else. So, be sensible. Wash your hands, avoid people who are obviously ill. Drink enough fluid. Get some rest, but be active and so I had one patient who actually got that yellow tape and put it all around her house and because they heard somebody say you can't do all these things and they were so depressed because they couldn't see their grandchildren. I said, "Oh, my gosh. No. You can see children." If they've had a live vaccine probably not a good idea right at that time. If they have a runny nose or those kinds of things you don't want to snuggle so much, but it doesn't mean you can't be around them. So, those are things that bring you joy and we want you to have joy.

We talked a little bit about keeping track of your symptoms. Taking care of your emotional state is also really important. So, if you're having trouble feeling depressed or anxious ask for help. There's a lot of people out there that have training in ways to help you with those emotions. It's very natural and we take this as seriously as we do physical findings. So, very, very important to keep that going. There's the exercise. I talked about the exercise bands. Getting enough rest. So, if you're not sleeping talk to your healthcare provider. There's a lot of simple strategies. They say eat light before bed, avoid reading backlit devices like your phone. Before you go to bed create a dark and (inaudible 1:29:55) environment. You can sit down and relax, meditation, breathing. There's a lot of things other than medications that can actually help you with sleep. So, talk to your healthcare providers.

Water. You got to drink it. It's good for you. Not everybody's a water drinker. In Arizona, our humidity is close 06 percent. It's really dry and so people get dehydrated very easily and so we say 2 ½ to 3 liters a day. That's a lot of liquid. Non-caffeinated beverages because caffeine goes right through you. So, you have it, but you can't count it. So, it's hard to remember. People think they walk around with this cup and they never actually empty it. So, I have them do a very initial thing. I say you get three little containers if you're doing three liters and you fill them up in the morning and if they're not empty at the end of the day you did not drink them. It's that simple because it's very visual. Now, you're not trying to remember did I, did I. So, staying hydrated is really important to your health and particularly when you're getting treatment getting rid of these metabolites and other things. I think we talked about the food enough.

Now (inaudible 1:31:12) is the other thing that's really important. So, the CDC says treat the hurt. So, we want to treat the masses because that's who you're exposed to. So, the only exception to that is live vaccines which the most common one is the shingles vaccine. So, it's a live virus and if catch it you're really sick when you're compromised. So, we don't have people who are immunocompromised get the shingles vaccine, but you should get a flu shot. You should get a pneumonia vaccine. It may not work quite as well if your lungs not as great, but they generally will not hurt you. Washing your hands is probably the very single most important thing that you can do. Avoiding bleeding has everything to do with your platelet count. So, if it's

below 50,000 that risk goes up really the risk is highest when you're below 15 or 10,000, but if they're lower we're going to have you not be taking aspirin. If you're on blood thinners we're going to work with your cardiologist or whoever has you on blood thinners to say when if they're below 50, we're probably going to have to hold those drugs. So, again, it's really important to keep track of who the mentors of your team are and how they could work together to make sure you're not at increased risk. We talked about stay connected to your healthcare providers to manage those comorbidities. There is palliative and supportive care. So, palliative care used to mean going to hospice. That's not what it means anymore. It means doing supportive care and that can be anything from relaxation and meditation to other kinds of wellness activities. So, we really try to get you connected to the right people in the team to help you with all of those symptoms.

Now, these *Building Blocks of Hope*, there's book five which is really about your plan, keeping track of your counts, knowing the characteristics of your disease and that's basically in that booklet that you all received. We have now taken this and created an app and I'm going to just touch on and this is now we launched this at the meeting in Valencia last week, or is that two weeks ago, and you should have a flyer in your (inaudible 1:33:31) but let's see if we can get this to work here.

(Video)

MDS Manager is a newly developed (inaudible) health application designed for smartphones and tablets that includes a variety of features to assist the patient caregiver living with MDS. This innovative tool represents a digital adaptation of book five of the Building Blocks of Hope. MDS Manager empowers users to more effectively manage their care, improve communication with and among providers, track the response are treated and access the latest scientific data and resources. Users can track a variety of important data such as blood counts, treatments, symptoms, provider and caregiver information, medication, appointments and more. Users will also have the ability to download, print and share this information with selected individuals and finally using two way communication technology MDS Manager provides tailored support for patients and caregivers by providing symptom management strategies, links to resources and information about clinical trials. This app provides a tangible and meaningful strategy for improving health self-management. You can find out more about MDS Manager by visiting the MDS Foundation website at www.mds-foundation.org.

Sandy Kurtin, RN: And you all should have a flyer in your packet that gives you a little bit more information about that. There are tutorials that are in process. I'm going to show you one briefly. This can be on an Apple iPhone or (inaudible 1:35:14)

(Video)

This video provides an overview of the MDS Manager app. After the second medical disclaimer statement you'll be taken to the home screen of the app and from here you will have access to features such as your MDS profile, medical professionals, clinical trials, additional resources, a symptom tracker, medicine, a calendar, notes and your personal profile. From this screen you can also access additional information and settings by touching the three bars at the top left hand corner of the screen. This is known as a (inaudible 1:35:49) and it is a quick way to get back to the home screen, reviewing messages, change your settings, contact us and to view the privacy policy. To close this menu, simply click outside of the menu area and this will close the menu.

Sandy Kurtin, RN: So, that's just a quick overview. The idea is that you can use all the features, you can use part of the features, very quickly links you to all of these resource in digital format. It takes you to pages for individual symptom management that then give you additional information on how best to manage those. If you do enter your disease profile there is a confidentiality feature that is in the compliance so that none of your identifying information really transfers to anything, but let's say you put in your molecular profile in your IPSS-R score and if there is a clinical trial that's available to you where you are based on your location basically that information will be pushed to you to say this is a new trial that might be an option for you. So, it allows you to access information and keep track of information and share that with your providers. It's obviously a lot easier to see and read on an iPad, much bigger screen, but I have it on my phone and on my iPad and so we're working hard to try to make all of these features very useful to people and to connect people in that way.

So, really that's all that I have in terms of a formal presentation. I think the goal right now then is to really just open this up to questions, trying to clarify things you heard this morning, things you want to share or add and just really have an open discussion to try to help people work through all the information that you take in today which is a lot. So, yes?

Q5: So, all your slides in your presentation are they available in the booklet?

Sandy Kurtin, RN: No, the slides are not in the booklet but they will be available on our website. So, if you go to www.mds-foundation.org if you have it on your paper still it should take you... Oh, I guess (inaudible 1:38:24)

Audrey Hassan: We'll get the presentations on our website right under the patient forum probably about a couple days after we get back and get them loaded down.

Sandy Kurtin, RN: Yes and that kind of information will also be... you can access it through... if you download the app you can access all the things that are on the website right on your phone or on your iPad, either a tablet or smartphone.

Q5: Secondly, if I'm shortness of breath, how can I keep up exercising and keeping in shape?

Sandy Kurtin, RN: So, that's a very, very good question. So, if I'm short of breath how can I exercise? Well, the only treatment for fatigue is exercise. There's no magic wand. There's no magic pill. I always say I'm fresh out of fairy dust and it seems like it's backwards because I'm telling you to try to move and you're saying I'm too tired and so sometimes that shortness of breath if you don't have an underlying heart disease or lung disease comes from this lack of endurance which comes from not being active which comes from being tired and so then you rest and then it becomes a vicious cycle that when you do try to do something you can't go very far. You've lost your stamina. So, I say to people start with chair exercises because then you're not afraid to fall and you would be surprised on you build those bigger muscles then you're able to actually take more activity and you just build up slowly, go slowly. If you feel unsafe, have somebody with you so you don't fall. Use a walker. Get one of those that has a little bench on it so you can go a little while and then you sit down on it and go a little while and sit down, but try to get moving because it won't get better if you keep... just rest. It's hard. It's hard work, but is the only way to make it better.

Q5: I get tight chested and shortness of breath.

Sandy Kurtin, RN: Well, tight chested. So, if you're having chest pain or tightness in the chest then you need to talk to somebody about that and make sure you don't have an underlying heart problem. Sometimes you didn't have it to start with but you can develop that. So, those are symptoms... that's what I'm saying you got to write that down and say you know what? When I try to walk from here to there I get tight in the chest because maybe then you need an echo or something to evaluate your heart to make sure there isn't any problem. So, you got to talk to people about it. Write down, make a list, talk to people about it.

Yes?

Q6: I've had enough interest in exercising through life. I've had things like a Garmin watch (inaudible 1:41:09) so it knows what your heart rate is while you're exercising. So, 10 years ago I could ride a bike, run, walk. The first minute you might go over what's the maximum heart rate and that's a different opinion and now today I'll do that walking what I used to do or couldn't do running. So, then I would get a little I'd feel like wow, I think I feel so... before I would go I'd take an aspirin and I just wondered if by pushing it is that putting a demand on the body to produce more red blood cells or is it overtaxing? Is it helping it? Is it hurting it?

Sandy Kurtin, RN: So, there's probably not one answer to that. Exertion, exercise doesn't... your body does try to get what we call boxcars like things to carry oxygen which are red blood cells. So, (inaudible 1:41:59) red blood cells as being box cars carrying oxygen molecules, just a visual. If you don't have enough box cars you're anemic then you may become where your body's like okay where's the oxygen and so to me then you say you know what? I... this is a

different time in my life. I'm not going to shoot for that maximum heart rate. I just want to be strong and be healthy. There's a different.

Q6: Well, it's not shooting. I go beyond it. I just go beyond it.

Sandy Kurtin, RN: Okay. So, then you're doing just fine. Right? So, don't be a showoff.

(Laughter)

Sandy Kurtin, RN: Right? Because I could... (Inaudible 1:42:42) so you're obviously very fit. So...

Q6: (inaudible) but you're in pain too.

Sandy Kurtin, RN: Well you know what? I push to the point of pain. I guess that's my point. So, we're not trying to make you a marathon runner. We're trying to make you fit, fit enough so that you can have these therapies that you heard about all morning and be considered well enough to have a transplant to go on this trial because they... that's part of the criteria now not just your disease features, but how well are you and can you tolerate these if you have side effects are you going to be able to tolerate them. So, keep it up. Don't push to the point of pain is what I would say to you because that's not the idea. You want to hurt yourself, but a little bit each day matters and so it's whatever works for you it's going to be the way to go.

Yes?

Q7: So, back in the early part of your presentation you're talking about all the information and trying to keep up with it. We found my wife's doctors that it was just overwhelming the amount of information that we were getting and her doctors have recommended and they just have us use the recording function on our iPhone. Are there people doing that also or...?

Sandy Kurtin, RN: Did you guys all hear that? Recording the visits. So, if you ask people do that with me. I think the other thing that's the thing. So, I'm actually finishing up my PhD and my PhD is in health self-management with a focus and.... Well, nursing, but my focus is health self-management because I think we put so much on all of you and it's getting really complicated. Like we are having trouble figuring this all out and then we're having you say okay just keep track of this. I think it's a lot to ask of people and then my minor's in health technology because that's the way forward, but I have people who do face visits. So, they say let me call Gretchen in New York and Gretchen's in the visit and the little two year old's running in the background. So, it's time is short obviously, but if you ask permission people do that in our visit. They say can I tape this visit and I say yes. Some people might say no but you can ask. So, I think that's not unreasonable and then you can listen back to it and see if you can digest it a little bit more.

Yes?

Q8: You mentioned you have a patient who are coming for their winter months from Minnesota, Illinois to Arizona. How are they managing with the insurance coverage? What kind of insurance do they have?

Sandy Kurtin, RN: Yeah. So, insurance causes high blood pressure.

(Laughter)

Sandy Kurtin, RN: For providers, for patients...

Q8: And they cross the state line.

Sandy Kurtin, RN: Oh, my gosh. This is where you want... I want one of those Looney Tune phones that goes pow. Like it would make me feel so good because this drives us crazy. We have to do all this arguing and peer to peers and try to get things approved. So, there are sometimes limitations. Medicare is obviously probably one of the easier ones, but there are certain plans where they will not pay out of state, but what I tell people is because we have a lot of winter visitors that do their treatment in both places which then it's even more important for you to keep track of your stuff because you're doing part here and part there is to get on the phone, ask for a case manager in the insurance company so that you are not just a number talking to a different person every time. Just say I have a complex disease, a rare disease which technically this is considered. I need a case manager signed to my case so I can work through that and that's what I tell people to do. You have to be on hold a lot, but it can be done and we have people who are able to do that successfully. If you're getting a drug like Revlimid, we have people where they are still getting it from us, but it's being shipped to wherever they are and then the go to whatever's (inaudible 1:47:04) Quest or whatever to get their labs while they're away. We try to get them set up with a local provider if we can so that somebody where they are knows them if something happens. So, we co-manage patients not infrequently. So, it takes some work but it can be done. It doesn't always work with certain insurance providers.

Q8: Should the provision with the plan is the people have plan...

Sandy Kurtin, RN: It's all by individuals.

Q8: Or you are just each time asking for a favor for the particular treatment because of the disease or what type of...?

Sandy Kurtin, RN: So, every state has a different Medicare fiduciary. So, there's different (inaudible 1:47:52) Medicare is by state. Some share it. So, there's that's an issue. Certain

insurance providers are only in a certain state. So, it's all really driven by the individual plan and then who can you see under that plan. It's very complicated. There's not one answer. So, it's complicated.

Did you have a question down there?

Q9: When (inaudible 1:48:14) and (inaudible)

Sandy Kurtin, RN: So, the question is caregiver support. So, I mean, I just think that it's very... I've been a caregiver. I had two in-laws who died of cancer that I took care of. My niece died of pancreatic cancer. I was her primary caregiver and I have a lot of experience and it's stressful. So, you have to work on diet and exercise and time away to make sure that you're not getting burnt out. It's really important to be a husband or a wife or a sister or a brother or whatever it is and not just a caregiver because it changes the dynamics of the relationship and so we really encourage people if they need to seek counseling, but just take advantage of some of these strategies that are out there to help you in a very tangible way.

Other questions? Yes.

Q10: If you're traveling and say going on a trip for a week or two do you need have some blood testing done during that time you're out of your area and you're thinking of... but you also need to have a blood transfusion. Trying to figure that out.

Sandy Kurtin, RN: So, that takes planning. I've arranged for blood transfusions in Singapore. It can be done. It's a lot of work, but so I would say if you're planning a trip we double as travel agents. We're not very good ones, but we try and so really as soon as you know you can let your team know so that you can try to work it out. Most of the people and certainly a big center like this have colleagues all over the country and so if you're going to visit family somewhere and I say ask that person where you go to the hospital and then find out if there are people, care providers there. There are lab networks in Northwestern (inaudible 1:50:20) being the two most common that are all over the country that you can get blood drawn and have it sent back. So, it's a doable thing. It's not necessarily easy and it takes planning. So, you got to have enough time. So, we try to get people to let us know, keep reading me, let's start working on that looking at what our options are, but we've done that actually quite a lot because we have a big population of what we call snowbirds.

Q10: So, the transfusion side it takes (inaudible 1:50:49) finding out what's the most possible, where you could get it done.

Sandy Kurtin, RN: Yes or do they have the infusion center where they give blood and that city. If you're going to a tiny little place somewhere it's a little bit more complicated, but we work hard... or if you're just going for a week we say well you know, let's just tank you up before you

go like let's see you right before you leave, load you up. We try not to do it the day before you travel because we've had people get clots. So, a couple... trying to gauge how often do you need transfusions and can we give you a little and send you back and then have you see us when you get back, but it takes planning. So, but that's why you're trying to stay alive so that you can do these things that are important to you. So, you just got to bring it up and ask. So, you're not tethered.

Q11: Do you have any recommendations for patients who live some distance away from a major medical center and now must rely on I guess what I would call rural medical providers?

Sandy Kurtin, RN: Yes. So, we have a lot of those. We (inaudible 1:51:58) in Southern Arizona, so we have people that drive even two hours, sometimes more than that to the center because they want to be affiliated with the Center of Excellence and I do think that matters. I mean, understanding all of this is difficult and if you are someone who's (inaudible 1:52:20) colon and you see three people with MDS it doesn't mean you can't do it, but you may not be as current with all this information because there's just as much science happening in all those other diseases. It's a crazy good time, but it's a crazy time as far as the information goes. So, we tried really hard to co-manage and either we do that with the primary care provider or perhaps a community oncologist, but getting people to work as a team. So, if you're in a clinical trial you got to go to the center. That's just the way it works, but we also try to do whatever supportive care or interim kinds of things as much as possible where you are. Some people move quite honestly just so they're closer to where they can get that kind of care.

Q11: So, would you recommend remaining connected with a center like here in Seattle?

Sandy Kurtin, RN: Sure.

Q11: Not going back to one's small community?

Sandy Kurtin, RN: No, I'm not... we don't want to have people stealing people because that makes people mad.

Q11: I mean just going home and relying on the medical care in your small community.

Sandy Kurtin, RN: I think what you have to do is say okay, (inaudible 1:53:35) and then you have to decide where am I comfortable getting my care. It has to be a personal choice and that may be logistics like you simply just can't drive. It costs too much money, whatever. There's resources for that, but it ultimately comes down to how comfortable are you are with the care that you're getting where you are and there's some really great community oncol... I mean, there's some great people in rural areas that work in those areas that are actually quite good. It really comes down to a personal choice and feeling comfortable with you being able to ask the

question and can they answer it. That's what I would say. So, we do it a number of ways. We have a lot of people that we co-manage with their local providers.

Q11: I'd like to say I've been rather blown away today by the level of expertise of each of the presenters here and to go someplace other than here sort of seemed like it would be a drop off.

Sandy Kurtin, RN: It's getting very challenging in oncology because every disease is at this level now and when you have a rare disease which when you think about the incidents of MDS compared to say colon cancer or prostate cancer or lung cancer is a tiny little piece of the pie which is just as complicate. So, it's hard to keep up with all that science and it's hard for you, it's hard for us even as people that have been doing it forever. So, ultimately it comes down to your personal choice.

Yes?

Q12: I can see that people with MDS in Arizona are very lucky to have you there. Could you give us the name and phone number in Fred Hutch for as good as you are (inaudible 1:55:31).

Sandy Kurtin, RN: I'm going to turn it over to Dr. Scott for that. I'm not moving to Seattle, but we have... there are good people all over the country that are really committed, nurses, physicians, others.

Q12: For physicians we know we are just as lucky as could be, but that what your expertise is and what's your level of care. You say you are really (inaudible 1:56:02). we just want to know probably at Fred Hutch has somebody.

Sandy Kurtin, RN: Yes.

Q12: Or maybe even department but kind of...

Sandy Kurtin, RN: I'm sure they do. I'll let Dr. Scott answer that question.

Q12: But anyway you are presenting here from Arizona.

Sandy Kurtin, RN: I have great passion for this work.

Q12: It shows.

Sandy Kurtin, RN: A journey and I was lucky enough to work with as I say remarkable people. We did the original trial for Revlimid at the University of Arizona. We were the only site in the world and this graph that I showed you was one of the very first patients that had a response and you see that happen and you go we made them go back and get his blood checked again. We

were like that can't be right because we never expected it and so when you're in a setting of research there's nothing more rewarding than to be able to do things that help people and that's why we do this work. So, I feel fortunate to be doing what I'm doing.

Other questions that you have about this morning or other things? Yes?

Q13: I was diagnosed two years ago at 37. I have a 10 year old daughter at home and my quality of life has changed quite a bit. I'm just wondering if there's anyone in your realm. I'm also a nurse. It's very frustrating to be on the patient side.

Sandy Kurtin, RN: I can only imagine.

Q13: Is there anyone in your world that I could talk to about quality of life in juggling a home and a family with young children and working as a nurse? Do you have any of that (inaudible 1:57:40)?

Sandy Kurtin, RN: So, we have... I'm going to refer you to Audrey. So, we sometimes are able to get people connected because it is very different. Obviously being 37 that's incredibly rare and difficult, obviously, with what you're juggling. So, yes. I think the best thing for you... the other thing I would say wherever you're being treated and ask if they also have anybody else in your same age group that we've been able to (inaudible 1:58:20) people up in that way too (inaudible). We can say what we think, but we're not doing it ourselves. So, it's different when it comes from someone who's actually living with that. We could say here's what we've seen and this is what I've been told, but it's not the same and I know it's hard to go to support groups generally in centers where you might be the only one with MDS and everybody else has this or that and so that's not always the best answer either, but I would first ask people in your center. Social workers often have really good (inaudible) and physicians, obviously, the other providers and then I would give Audrey a call.

Other questions that people have? Yes?

Q14: I sent up during the middle of the week and I heard when month schedule instead of E-mail online I called to New Jersey and got signed up and a comment was made that last year there was a low turnout. This year with 65 people here. What's the difference between last year and this year?

Sandy Kurtin, RN: That man right there.

Q14: And part of my comment on that is just high speed. I probably came here with (inaudible 1:59:34) only that I have (inaudible) okay. So, I have the (inaudible). I've got a great guy at SCCA that I believe in and I could have been doing other things today, but I said you know what? My fear was it was a fraud, a scheme, a scam and... because...

Sandy Kurtin, RN: (inaudible 1:59:52) over here.

(Laughter)

Sandy Kurtin, RN: He looks like a car salesman.

Q14: And I love his accent. I would come for that as well. What a difference this year with last year, but also have you break that. Like I've worked with a doctor here that I really admired, SCCA. Okay. And so I'm satisfied and then this came up and I'm a mechanical engineer by history. So, I'm scientific. My wife's an RN. I'm interested. I got the problem and so okay let's go, but it really is like the results are overwhelming. I expected it to be something commercial. So, what did you do this year that you didn't do last year? So, what I say to my kind of a doctor. I don't want to tell you his name. I don't need to. I'm not promoting my doctor. He's busy enough already. And he just sent an E-mail and said, "John, you might be interested in this." Wow. I'd have come without fear and trepidation, but I didn't get that.

Audrey Hassan: We didn't do it last year. It was a couple years ago that we didn't have a big turnout. So, we had we were like (inaudible 2:01:06) at like 20 something and we contacted Dr. Scott and he did all the promoting to let the rest of the patients know about it but it wasn't... it was a couple of years ago that we had the low turnout.

Q14: See, my point is if you have a doctor within the group of four and Seattle is unbelievable. I mean, I happen to be lucky to live here, but I didn't grow up here. So, I mean, it's unbelievable. Seattle for this kind of a problem with the four COEs or however many there are. When she asked me she said this E-mail thing. Said please respond. Said absolutely I will. It said are you in a COE group? I said no, I was a CEO but I'm not a COE. (inaudible) what is a COE? I mean, just tell me so I said... I made it and said yeah I am, SCCA and I didn't even know what I was saying. It was just like... but I want this to succeed. That's all I'm saying.

Sandy Kurtin, RN: I think he was very intense. You're one of the guys that comes to clinic and has the color coded tabbed and (inaudible 2:02:08) (Laughter)

We can see you from across the room.

Yes, sir?

Q15: It seems though you're from Arizona you kind of understand what I'm going to say. I'm transplant. I'm seven months through.

Sandy Kurtin, RN: Great. Congratulations.

Q15: My big break out happened two years of dealing with this was to move down to Arizona and (inaudible 2:02:30). Well, I didn't realize and neither did my doctors was that going from sea level at 4,000 feet in California, going to 7,000 feet in Arizona, I ended up contracting cellulitis in my left leg. So, my blood normally here is 97 percent. I was getting 83 down there. So, that was something that wasn't even thought of.

Sandy Kurtin, RN: Just don't try going to Denver. So, we do have to think about that when you're somewhere may have some blood disorder. The altitude is a backdrop by itself and whether you're going to be able to tolerate that (inaudible 2:03:20). So, yes. It's very important to talk about that kind of things, but we don't always think about all that stuff, practical stuff. If you talk about it it's more likely that they'll say you know what? There might be an issue, but yes.

Q16: That's an excellent point you brought up. We were happen to look at taking a trip as well and then we realized what about the effects of elevation and what I'm wondering if there's probably all kinds of things like that that we should be thinking about when we're planning things, but what are they?

Sandy Kurtin, RN: I don't think they always know, but you could... if you can just give us as much description as possible like if you tell me I want to go out on a houseboat on Lake Powell for a week. I'm going to say uh uh, can't go. If you're cancer really bad because what are you going to do out there on the boat. You're floating around in the middle of nowhere in these little caverns. Not such a great idea. If you're going somewhere where you counts... I mean, if you're well that's fine you could go. You have to wear sunscreen, but and a hat and long sleeves. So, but those are the kinds of things where are you going, who's going to be there with you, what's the closest major city so that if something does come up you have resources.

Q16: And if you wanted to travel out of the country.

Sandy Kurtin, RN: And we have people who do that, but we talk about it. So, I had just a little lady that went to the Delphi... not Delphi. Oh, the coast of Italy that's all up and down and I said how many stairs have you climbed lately and she realized she's not going to have a very good time because there are no elevators. There's nothing but steps and you can't get around very easily there and so they kind of rethought the vacation because she would have had a horrible time. So, it's just little things like that to think about what to plan and getting enough time so that if you do need a little tune up, if you will, get a little tune up before you go that we have time to do that.

Q16: (inaudible 2:05:34)

Sandy Kurtin, RN: And then say can you really be gone for 12 days? Maybe it's only eight and so be practical and then you're going to be able to have some fun, get away, but not be end up in a hospital in Italy which has happened to some people.

Other questions that anybody has about stuff you heard this morning, things you haven't heard about, things you wished we would do other than find a cure. We're all working really hard on that.

Q16: I would like... I'm glad that you're going to post things online because some of the slides you went so fast. I was trying to kind of jot down things and I had trouble. Some of them I could, some I couldn't but know that they'll be available.

Audrey Hassan: So, I'll get an E-mail out to everybody with slides.

Sandy Kurtin, RN: So, just make sure that you left your E-mail with Janice and with Audrey.

Audrey Hassan: I have everybody's.

Sandy Kurtin, RN: Oh, you do.

Audrey Hassan: Yeah (inaudible)

Sandy Kurtin, RN: Okay. So then that's done.

Q17: As a rural nurse and dealing with patients with cancer, you've got to have a primary care provider in the area. You can't call the ER and have them (inaudible 2:06:44).

Sandy Kurtin, RN: No and so the problem today... So, if you can see me like that day. If you want to see a (inaudible 2:06:55)ologist of any kind give maybe six weeks. So, there's... we have a problem in our system right now. It's hard to get in to see people. We are having trouble just with PCPs. People are stressed out and a lot of the workforce is getting older and retiring and so they're not going to rural America to practice. So, we, the healthcare system in general, is in a state of flux and meanwhile we have the Baby Boomers. I'm at the tail end of that. Not the beginning. Just so you're clear that this huge population of people need care. So, there are a lot of the issues, but you have to just be vigilant and persistent and keep at it so that you can have a team. It takes more than just one group. It's really important to stay connected to your primary care doctor. We're not experts in diabetes. We're not experts... we know a little bit, but we're not the expert. So, we want you to stick good to your primary care doctor as well so they can help you stay well and you got to get all things in balance not just the MDS so that you are able to get the treatment.



Anything else that you guys... questions, concerns. Alright. Well, I thank you very much for your time. I encourage you to reach out to us. Use those tools that I mentioned, download the app, take a peek at it. If you got questions call us and then we are going to let Dr. Scott get started so you can get out and enjoy the rest of your sunny day in Seattle. So, thank you guys very much.

(Applause)