Speakers:
Emily Knight, RN, BSN, OCN
Rafael Bejar, MD, PhD
Peter Curtin, MD

Emily Knight: Hello. My name is Emily. I'm a nurse from the Mayo Clinic in Scottsdale. I just want to welcome everyone and thank you all for coming. I work with the MDS Foundation and we're happy to have everyone here today. Just want to introduce Dr. Bajar (inaudible) who will be the first speaker and then we'll go from there. We'll keep it pretty informal.

(Applause)

Rafael Bejar: Thanks and you may want to wait till I hear what I have to say.

Thank you all for coming on a beautiful Saturday morning. We're overwhelmed with the attendance and the crowd. It's very impressive to see you all here today. So, I'm going to speak first. My name Ron (inaudible 0:57) Bahar. I'm a physician researcher here at UCSD. I have a lab here in the Cancer Center and I also see patients and after me it's going to be Peter Curtin who is the head of our Trans Method in here at UCSD for an… a specialist in MDS. We're going to break up the talk into two different parts. I'm going to first talk a little bit about some MDS basics, things that you may already know, but I'll try to speak to everyone who may not necessarily have all the information and then talk a little bit about what's new in MDS, about what we've learned over the past few years that have changed, how we think about this disease, how we approach it and how we treat it and I'm going to say a few words about novel therapies that are both on the horizons and a little bit further coming down the pipeline.

So, I want to start talking about normal blood development instead of MDS. So, this is a diagram that describes how one cell here at the beginning, a stem cell, is ultimate responsible for producing all of the blood cells that we see in our peripheral blood and this is the cell, or one akin to it, that we think is the problem in MDS. This is where the disease begins. Give you a more schematic version of that. We start with that initial cell. It has a very unique characteristic. It has the ability not only to turn in all the blood cells that we need to survive, it also has the ability to make copies of itself and this is a great good thing because we need these cells to be with us for entire lives. So, this balance of whether the cells decides to differentiate, to turn into these normal peripheral blood cells or make a copy of itself and it divides very important. If that balance is thrown off, the cells could either extinguish themselves or divide too much and overcome the bone marrow. In MDS it's that latter situation that happens. At some point, a mutation, a genetic abnormality, forms and if it's just the right… in the right place and just at the right time, it can cause the cell to divide more than it should an expand. We call this clonal expansion and if this cell grows to outcompete the normal cells in the bone marrow and unfortunately since this abnormal cell doesn't function like it should, it isn't as good at making the blood cells that we need. So, we call this inefficient differentiation and this is what gives rise to the low blood counts that we see in patients with MDS. This also is not a static process. It doesn't just end here. These mutations can continue to accumulate and you see the patients can have two, three, four or even five mutations and some of these mutations will give these cells a

greater clonal advantage. They'll expand even more and become less efficient at producing the cells that we need and unfortunately in some patients, this actually can proceed all the way to secondary acute myeloid leukemia where if these cells don't differentiate at all and really grow very rapidly and take over the bone marrow. So, I'm very interested in how these mutations change the behavior of these cells and actually create the disease and lead to its progression, but from a clinical standpoint, I also want to know how these mutations impair the cell's ability to produce the mature cells that we need. So, this is where I think the patients really feel the impact of this disease. They feel it with the low blood counts, the need for transfusions, the complications that can arise from that, like iron overload, the need for platelets and the risk of infection. So, I'm very interested in how these mutations can affect this process because our therapies can do two things. They can either try to kill these abnormal cells or they could try to coach them into doing a better job of producing mature blood cells.

So, I have this slide here to remind that myelodisplastic syndromes is really a plural term. It describes a collection of different disorders that have some similarities and the really important similarities are that inability to produce blood cells normally. This clonal expansion of abnormal cells, there isn't something wrong with the patient. There's something wrong with the abnormal bone marrow cell that's taken over and that they have this risk of transformation to acute leukemia, but how this manifests in patients can vary quite a bit. Some patients can have relatively mild symptoms that don't progress over a long period of time and other patients can have more aggressive disease where they normal six months ago and now they're not. It's not rare. It affects a large number of people every year in this country.