The Latest Myeloma News from the American Society of Hematology Meeting
Webcast
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James Berenson, M.D.
Sagar Lonial, M.D.

Introduction

Andrew Schorr:
Hello, and thank you for joining us for another in our series of live web casts about multiple myeloma. I'm Andrew Schorr broadcasting live from Seattle, but I just got back as our guests have too from, I would say, a very exciting week in Atlanta. The temperature was great, and the temperature was high inside the Georgia World Congress Center as myeloma was very much on center stage.

There were five phase-III trials about multiple myeloma. There were poster sessions. There were over 21,000 scientists and physicians from around the world there, and many of them were focused on multiple myeloma. Maybe you saw, just even the other day, on the NBC Nightly News they focused on multiple myeloma and the story of a younger patient with multiple myeloma, and maybe that's why some of you are with us today.

So, we have the past programs we have done, and please look at those on www.patientpower.info under the special edition section, and two of those programs were with our guests today, and then we're going to add someone new. So, we have three expert physicians in multiple myeloma. We're going to get to as many questions as we can, but we want to explain the data that was presented in those studies and the relevant importance of each one. Could they mean longer survival? Could they mean time when maybe you don't need to take medicine? Could they mean changes in the medicines you take? If you're headed for a transplant, could there be different medicines to make that transplant more successful and maybe alleviate the need for a second transplant that some people have had? We're going to go through all that.

Let me tell you who some of our honored guests are today. We have with us again Dr. Brian Durie from Cedars-Sinai Comprehensive Cancer Center in Los Angeles, but beyond that Dr. Durie is the chairman of the board of the International Myeloma Foundation and its medical director. Brian, you and I have done programs over the years, and I know you're also I think co-chair of the myeloma group within the Southwestern Oncology clinical trials study group. Thank you so much for being with us again Brian.

Dr. Durie:
My pleasure to be with you again, Andrew.

Andrew Schorr:
Okay, and also across town there in Los Angeles is another myeloma expert who has been with us previously on Patient Power, and that's Dr. James Berenson. He is the Founder, President, and Chief Executive Officer of the Institute for Myeloma and Bone Cancer Research, and Jim, thank you for being with us again.

Dr. Berenson:
Thank you for having me this morning or afternoon, depending on where you are.

Andrew Schorr:
Where you are, that's right. Joining us shortly, if he's not with us yet, is we're going to go back to Atlanta and one of the doctors who didn't have to get on a plane is Dr. Sagar Lonial, and Dr. Lonial is at the Winship Comprehensive Cancer Center at Emory University. He is an assistant professor there, and he is Director of Translational Research B-Cell Malignancy Programs, and he certainly treats a lot of multiple myeloma and when appropriate helps people with transplant. So, lot's to talk about.

Dr. Durie, you got that title as Chairman, so we're probably going to start with you.

We will take some calls after we talk to the doctor, and you can e-mail our producers behind the scenes at myeloma@patientpower.info. One other point, I know right off the bat we will not get to everyone's questions today. We're going to cover what's important, so if we don't get to the area that you think we need to discuss, we will welcome your questions either now or in the next few days, and we're going to do a follow-up Q&A. Not a live webcast, but I'm going to interview him and record it with Dr. Tom Heffner, who's also from the Winship Comprehensive Cancer Center at Emory University in Atlanta, and then we'll post that a week from today. So, there's a lot going on, ample access to myeloma experts.

Positive News from ASH for Patients with Multiple Myeloma

Andrew Schorr:
We're going to start with Dr. Durie for a minute, and Dr. Durie, as with each of you, I'm going to ask you gentlemen a couple of key questions. So, first of all, how big a deal was the data presented at ASH today for people living with multiple myeloma who are either looking to start treatment, in treatment, may need a transplant? I know the data came from around the world, a lot of it from Europe. Also, one of the questions would be evaluating do you simply; you all have these terms, very good,

partial remission, VGPR, PR, and CR, complete remission; and get your perspective on what's important, and maybe we'll even have a debate about that.

Dr. Durie, first of all, overall how big a deal was this meeting as far as people living with multiple myeloma and what drug therapies might be available or transplant for them?

Dr. Durie:
Andrew, I think that this was perhaps the most positive ASH of all times for myeloma patients. We saw for the first time the three main novel agents; Velcade, Revlimid, and thalidomide; which have been used in relapsed settings moving into the front line. As you mentioned, there were phase-III trials looking at different combinations of these three novel agents in the front line setting. I would say that perhaps the greatest enthusiasm was for a trial called the VISTA trial, which was comparing the combination of Velcade with melphalan and prednisone to melphalan and prednisone alone, and it has been quite remarkable to see the synergy, the added benefit, of combining the Velcade with the standard melphalan/prednisone regimen. The results of this trial showed remarkable responses up front as well as continued benefit out through the first couple of years of this trial.

So, the synergy, the added benefit of combinations, was a key feature of this meeting. We saw also the combination of Velcade with a variety of other agents. You mentioned the role of stem cells for patients looking to do stem cell, and this is clearly still a standard of care for transplant-eligible patients. An important trial was from France comparing Velcade/dex with VAD as front line therapy, and the remarkable thing in this trial was that patients taking Velcade/dex as the first strategy only 30% of them needed to go ahead with a second transplant, which is the normal standard in the French trials. But other combinations were also exciting with Velcade. Velcade combined with thalidomide and dex compared with thalidomide/dex alone from the Italian group with Michele Cavo, M.D., very strong results with the Velcade/thalidomide/dex combo, and then Paul Richardson, M.D., presented Velcade/Revlimid/dex, and our own group that I'm involved with based in Los Angeles with Aptium Oncology; we presented Velcade, Cytoxan, and dex. So very, very strong data with Velcade combinations in the front line setting.

And then obviously another area of interest and excitement for followup was to look at the Revlimid and dex combinations front line, the followup of the ECOG trial, Revlimid/low-dose dex versus Revlimid/high-dose dex was presented by Vincent Rajkumar, M.D., and for the Southwest Oncology Group a very important trial, Revlimid/high-dose dex versus high-dose dex alone was presented by Jeff Zonder. So all of these bits of information are very important, but I think also a lot of numbers, and it's going to take everyone a bit of time to sort through well what does this mean for me and a very important time to think and discuss the options for patients under age 65 who might be eligible for transplant versus those in an

older group who might be looking for the best regimen to control their disease chronically long term. So, perhaps I'll stop there.

Andrew Schorr:
I was just going to comment as sort of the reporter on the scene, and just say clearly folks, I saw the myeloma experts excited, and they have more going on than every before, but it does take this time. If you're not seeing one of the folks with us today or another myeloma super subspecialist, it may be that for your community oncologist there is a time when all this sorts out, and if they're going to be changing what they do when, you know, that takes an active discussion with them and them maybe even listening to a program like this or one specifically for physicians. You can play a role as a proactive patient saying, 'What about this that was presented at ASH? I don't claim to know all the letters and numbers, but what does that mean for me?'

Let's go on to Dr. Jim Berenson, also in Los Angeles. Dr. Berenson, am I right? It was an exciting meeting at myeloma, and is there something to be done differently now in your opinion?

Dr. Berenson:
Yes, I think it was a very exciting meeting. I think we really corroborated a lot of preclinical work that we and others had done to demonstrate the synergy of bortezomib or Velcade with a variety of chemotherapeutic agents, and now even synergy with a now-approved Velcade with drugs that aren't even approved yet, the histone deacetylase inhibitors, the heat shock protein inhibitors, and a variety of new agents that are now being looked at with what we now consider a good old standard almost, Velcade, and I think what we view myeloma now is as more of a chronic disease and more of a marathon and a sprint, so I think in terms of these combinations, the real beauty is that Velcade can be a platform for a variety of drugs. For example, Brian mention Cytoxan, which we have had very good luck with as well in combination with Velcade even among people who failed melphalan and Velcade, and several years ago one would have never dreamed that a drug that's as similar in activity and mechanism as Cytoxan to melphalan would work in a melphalan/Velcade failure. The recent approval of Doxil and Velcade. We in our own group are using a combination of Doxil, Velcade, and very low-dose Decadron, very active, and I think that's the true excitement right now is that these drugs can be given long term with good safety and really importantly in my clinic, good quality of life for the patient, much different than we've observed in the past with more intensive therapy than drugs that were fraught with lots of quality of life issues.

Dr. Lonial's Comments on Transplant Therapy

Andrew Schorr:
Wow. Very positive. Now, Dr. Lonial, you are involved in transplant as well, and I know there was data saying, and I think Dr. Durie was just talking about it, could there be new combinations to prepare someone for a transplant, make that transplant more effective, and where otherwise maybe there's the worry would they need a second transplant, maybe make that less likely? Could you comment on that?

Dr. Lonial:
Yes. I think, and Dr. Durie hit on a lot of the major issues in this topic, historically it has not mattered what you gave patients prior to collecting stem cells and moving forward with high dose therapy and transplant, and this ASH was one of the first meetings where we saw that that may in fact not be the case, and there were two trials, both from Europe, one from Italy and one from France that looked at bortezomib-based inductions in the newly-diagnosed patient setting, and patients were randomized to either bortezomib and dexamethasone versus VAD, which is a European standard, or in the Italian study Velcade with thalidomide and dexamethasone compared with thalidomide and dexamethasone, and in both those trials, the two arms that contained Velcade in the induction not only had higher response rates up front but also had higher response rates and complete remissions following high-dose therapy in autologous transplant. I think we have to step back a moment and realize that this is really a landmark finding because up until now it didn't matter what you gave patients. Their post-transplant response was always the same because transplant was doing most of the work at generating the remissions or the complete remissions, whereas what we can see from these two large European studies, what you give in the beginning, the Velcade-containing regimens up front, really did seem to make a difference in what happened after transplant, and I think a number of us still want to see whether that increased rate of remissions translates into a longer duration of remission. That really is one of the big questions that I think we have answers to as yet.

Defining PR, CR, and VGPR

Andrew Schorr:
Okay, I'm going to work backwards here through you, our panel of experts, and just pose this to you first, Dr. Lonial. So, it seems like there's debate in the myeloma area. How big a deal? You look at certain results of trials. You look at how many people had partial remissions, or there's this other term, VGPR, I think very good partial remissions, almost a complete remission. You look at complete remission. You look at how long somebody lived, survival, and the effectiveness of the drugs where they had a response. There are all these different factors you look at. You look at side effects. What is the significance now where we're seeing

numbers boosted in some of these trials of CRs or "complete remission." How much weight should that be given versus a very good partial remission?

Dr. Lonial:
Yes, I think it is a confusing issue, and I think it's important to realize that very good partial remission is not some arbitrary, abstract definition. A very good partial remission means that the protein is 90% lower than it was at the time of initial diagnoses, so a 90% reduction is the very good partial remission area, and this actually came to us from the French group, the IFM, that has done a number of large landmark studies in myeloma, and the reason that they use this cutoff is first of all in their experience very good partial remission seems to track similarly to complete remission in terms of long-term outcomes and second because there is so much fluctuation when the protein gets that low in the measurements of these numbers, and so they wanted to take some of that fluctuation out and just set a bar at a certain level, and that became the very good partial remission.

I think that both of them are probably important, and I think what is impressive with our current novel agent-based therapies, whether in the induction setting or in the relapse setting, is that both VGPR, very good partial remission, and complete remission rates are going up dramatically more than they had been before, and I think that that's a great sign because 30 years ago when all we had was alkylating agents, or what I like to call combinations of marginally effective drugs, we didn't get very many CRs, and we didn't get very many VGPRs, and we had to rely on the transplant to get us there. What we may be doing now with these new drugs or new combinations of either novel agents with new drugs or novel agents with chemotherapy agents, we may be able to get to those same benchmarks without necessarily needing a transplant.

Pros and Cons of the Various Combination Drug Therapies

Andrew Schorr:
Right, and Dr. Berenson, on our last program we did with you, you think transplant is history already, but related to one of the trials that I think is like phase-I/II both up front and then for people who need treatment again, it makes sense that I know Paul Richardson's group has been studying can you combine Velcade with lenalidomide, or Revlimid, another very powerful drug, and do those two new agents work better together, would that become the new standard? Do you have any feeling about that early data?

Dr. Berenson:
I would say that it looks promising. I'm concerned about side effects with that combination, particularly effects on marrow function. As I say, myeloma today is a marathon, and if we give treatments that give us amazing complete remission rates

but with little marrow function left in a disease that still remains incurable, we've done a real disservice to patients. So, I think the ultimate goal here is longest life possible with best quality; that is least side effects from treatment or disease. We often miss that message when we look at large pieces of data because we're not in clinic looking at real human beings and what they're experiencing. Obviously, Andrew, you know being a patient what that can be like. So, I'm often mystified about some of the toxicities that are reported compared to what at least I see in my clinic with some of the agents that are out there today.

I think we need more data to convince me that Rev and steroids and Velcade is going to be a good and safe combination and lead to long-term, durable remissions because it's notable that some of these new agents can lead to remission rates that are extremely high, but the length of the remission is extremely brief, and in some of these newer drugs, there is some concern that we may be inducing a pretty bad, ugly clone, and I think you have to be very careful in interpreting what a complete remission means because I know, having done with Dr. Vescio a lot of molecular work to measure minimal residual disease, but these patients really are not in molecular complete remission. Complete remission here is to find an absence of protein in a bone marrow which appears to not show increased plasma cells, but we all know that this is a patchy disease, and with more sensitive testing there still remains, if you will, in the words of my old mentor, Carl Sagan, billions and billions of cancer cells left. So, these are not Gleevec complete remissions, the drug used to treat CML, where they are really very deep complete remissions.

Andrew Schorr:
Okay, let's pose this to Dr. Durie. So, Dr. Durie, we've talked in a very positive way about what came out of ASH, and Dr. Berenson is there and wondering, 'Well, okay, you can use powerful therapies, but what works best long-term?' What's your feeling about your newer agents and combining them in new ways and being able to manage side effects, and maybe you'd comment on also the data that came out about using a lower dose of dexamethasone? I think you mentioned Dr. Rajkumar, and I know I went to a news conference there. Some people are having that; Revlimid, or lenalidomide, and dexamethasone. I know he studied lowering the dose of dexamethasone and could it be just as effective, but basically, management of side effects so that somebody can really do well long term. Maybe you could comment on that.

Dr. Durie:
Right, well I think that that's obviously what it's all about. Patients want to live longer, and when we're talking about indicators, I think that a good paradigm right now is that survival is the best indicator of survival. You know, is CR an indicator? Well, I think that what we're focused now on is the patient alive early on? Is the patient alive at one year and two years? And being alive and doing well is truly the ultimate end point.

So, to achieve a good survival, we're balancing the benefit, the efficacy of the treatment, with the side effects and the quality of life, and one very interesting thing has emerged from the comparison of the low-dose dex with the high-dose dex, so that if you look at the ECOG data, the interesting thing is that is with the high-dose dex, the four-day pulses, there was a higher response rate up front versus the low-dose dex; however, if you look at the survival at one year and then at two years, it turns out that the survival was 96% at one year and 87% at two years with the low-dose dex, and so what has accounted for this difference if there was more response early on with the high-dose dex?. One is that obviously if you hit the disease harder, then it will knock it down more initially, and this has shown up in the longer-term followup with Revlimid/dex in the relapse setting, you need to be able to continue on therapy, and for me there was a very interesting parallel study presented at ASH by Jean-Luc Harousseau looking at the long-term followup with Revlimid and dex in the relapsed refractory setting with the studies MM-009 and MM-010, which were both recently published in the *New England Journal*, and what they commented on is that for patients who were able to reduce the dose of dex and stay on the Revlimid and dex longer term, there was I think it was 45% of the patients reached a VGPR and a CR not right away but over time, out to 12-14 cycles.

So, it's a matter of trying to have an excellent response, but how quickly do you need to achieve that, and how long can you maintain it? So, it's about therapies that can do an excellent job initially and in the short term but perhaps more importantly looking towards achieving a more chronic control of the disease to maintain that response, and I think that that's a very important new paradigm moving forward.

Andrew Schorr:
You're sounding like Dr. Berenson there. We're all running a marathon there. There you go.

Dr. Durie:
That's right.

Andrew Schorr:
Dr. Lonial, I have a question for you though. One of the things that's come up with Velcade or bortezomib is can you knock the disease way back and then just go off treatment for awhile versus with Revlimid and some of the other medicines, you know, they're pills, but you keep taking them. So, do you have any feeling about that or what discussions you have with patients about that?

Dr. Lonial:

Yes. I think there certainly may be benefits to treatment-free intervals and the absence of maintenance therapy contributing to morbidity and mortality, but I think in order to do that, you have to really get to the best response before you try and give patients sort of un-maintained remissions. I think the other piece about whether or not a patient may go without any treatment in many ways is dependent on their risk stratification. So, if you have high-risk myeloma as defined by a number of different groups, whether it's Dr. Shaughnessy's definition in Arkansas or the definition from the Mayo Clinic or other groups, there clearly are subsets of patients of a very high proliferative myeloma, and for those patients the absence of therapy may not be a good thing, whereas for other patients who have low-risk disease, they may actually gain great benefit from an absence of therapy, and so I think it's not just the depth of response, but it's also the phenotype, if you will, the biology of that specific tumor that may allow patients to either go with long treatment-free interval or stay on some type of suppressive therapy over a long period of time.

Does Age Play a Role in Deciding Treatment Options?

Andrew Schorr:
How important now, and I know they do this in Europe a lot, a lot of the studies I saw showed they were studying people 65 or older and then others were related to people under 65. How important is that cutoff? What if you're 64-and-a-half or you're 70, but you play tennis every day, or you used to before your myeloma diagnosis, and you're trying to get back to that? Where does age come into it, at least the way we practice medicine in the U.S., Dr. Lonial?

Dr. Lonial:
Well, I think that the Europeans have created this arbitrary demarcation between transplant-eligible, and non-transplant-eligible, and I think most would argue that that 65 age limit probably doesn't make a whole lot of sense. Even the Europeans would say that doesn't make a lot of sense, but those are the rules they created, and they try and play by those rules. I think that in this country we probably base it more on performance status and comorbid illnesses rather than on a certain age, so I don't think of age as being a qualification for treatment one way or another. I think about how well a patient is and whether or not I think they could tolerate the kind of therapy that may or may not involve high-dose therapy. If they are, then I would consider whether or not dexamethasone would be an option for them. If they're not, then I consider prednisone or melphalan and prednisone based regimens. So, I think it’s a little bit different in terms of the spectrum as we don't use an absolute age cutoff.

Andrew Schorr:

Okay, and what about you in Los Angeles, gentlemen? What about age? That's so important. How about you, Dr. Berenson, first, just related to age, what's your view of that?

Dr. Berenson:
I think age is one of the many factors that comes into play in terms of what decision I make to initial treat a patient with. So, basically I draw a Venn diagram, which is three circles. The extent of disease; that is, how much is it affecting bone marrow, is the patient significantly anemic, how much is it affecting the kidney, how much is it affecting the bone, what are the cytogenetics, and what's the patient's current quality of life as the disease is affecting them? Secondly I look at the patient's work and lifestyle. Are they, for example, a surgeon or a pianist like my wife so that neuropathy is going to be an issue? Are they very active in terms of their lifestyle. Then, third, what are the comorbid conditions? Do they have diabetes? For example, a patient I saw an hour ago has diabetic neuropathy, nerve problems, and so issues of using drugs like thalidomide are certainly important to recognize. Does the patient have heart failure?

So, all three of these come into my decision making in terms of how I'm going to treat a patient. We really try to individualize therapy here and not just "one size fits all." So, I don't use age as much of a criteria. I think it's a minimal criterion for me in terms of what I'm going to give a patient.

Andrew Schorr:
Any comment from you, Brian? I know people hear all this, and they say, well how does this apply to me, and some of these studies, again, use age as a demarcation point.

Dr. Durie:
I think age is actually very important, and I've been impressed with the data from the IFM group and also from the Italian group where they have shown that actually the 65 cutoff does influence both the benefit and the side effects from the therapy, and one important trial was to compare thalidomide and dexamethasone, which we use widely for both younger and older patients versus the melphalan/prednisone/thalidomide and melphalan/prednisone/Revlimid combinations, and what the French group showed was that actually melphalan and prednisone, and certainly melphalan/prednisone/thalidomide, is it's better than thalidomide and dex for the older patient in terms of not just lesser side effects but actually efficacy. The inclusion of the melphalan, which is a very important synergistic agent gives a better outcome, and so I actually find it helpful to look at the 65. It is an arbitrary cutoff, but positioning in that over-65 group we can look at combinations, which are particularly well-tolerated for that group, which goes up to 75-85, but also which works well. One of the strangest things is that we actually have some fantastic synergistic combinations, which have been evaluated in this

older group, which are looking pretty good for our younger patients too. So, things are moving in the opposite direction. What's working well for older patients can work well for younger patients, and that includes the Velcade/melphalan/prednisone that we were talking about but also melphalan/prednisone/thalidomide. So, I think that it is helpful, and I think that increasingly I can see that the therapy will be divided in some way like that.

Andrew Schorr:
Brian, and you and I march towards that cutoff age, we think about it. Okay, we're going to take a break. I know people out there have questions, and we've kind of set the stage here.

We're visiting with Dr. Sagar Lonial from the Winship Comprehensive Cancer Center at Emory University in Atlanta, and Dr. James Berenson from the Institute for Myeloma and Bone Cancer Research, and Dr. Brian Durie from the International Myeloma Foundation and Cedars-Sinai Comprehensive Cancer Center in Los Angeles. We'll be right back with more of Patient Power.

Andrew Schorr:
Here we are, we're back live with our web cast, world wide special edition of Patient Power discussing multiple myeloma with three noted myeloma experts, Dr. Lonial from the Winship Comprehensive Cancer Center at Emory University, Dr. Berenson who's with us from Los Angeles with the Institute for Myeloma and Bone Cancer Research, and then Dr. Brian Durie from the International Myeloma Foundation.

Okay, so we're starting to get questions, and we got some, a lot of them. I should mention, by the way, folks listen to the replays of our previous programs. Among them there's one with Dr. Durie after the big meeting of only the myeloma specialists at Kos, Greece. Another program on side effect management with one of the nurse practitioners who's an expert in myeloma and dealing with the side effects, and then also with Dr. Berenson earlier just several weeks ago.

The Complexities of Determining Treatment Options for Patients

Andrew Schorr:
So, here's a question from Russell in Waverly, Pennsylvania, and he says, 'Why are there so many varied opinions on the treatment of multiple myeloma and conflicting ones as well?' He's not just talking about some of the cancer fighting treatments that we've talked about now, such as Revlimid and Velcade and thalidomide and melphalan and prednisone, you know all this that we try to understand as patients, transplant or no transplant, but also even drugs to help, the bisphosphonates and others related to bone complications. Dr. Lonial, and I'll from all, I imagine that if

you put your scientists in a room and you have a lot to argue about, but for us as patients, why isn't there more clarity yet?

Dr. Lonial:
I think it's because over the past 20 years we've not had a lot of really effective therapies until the last four or five, and I think that that's the reality is we're now struggling to try and determine how best to use all these new tools that we have, the many developing tools that are in the pipeline and that don't have a lot of large randomized phase-III data. I think it's not like lymphoma where there's one quick and simple answer because there's nothing else that's been proven any better than that one quick and simple answer, the CHOP for myeloma, if you will. We don't have that in myeloma, and I think that's what we're really struggling to do, and so for instance, the three-drug combination that you mentioned earlier, the combination of lenalidomide with bortezomib and dexamethasone that Paul Richardson presented both in the newly diagnosed and the relapsed refractory patients at ASH. We're participating in both of those trials with him actually, and I've been struck by how well tolerated those regimens are and how deep and quick the responses are. It's really quite striking, and my thoughts, my hopes are that that kind of a regimen using the most active drugs we have, like we do in CLL, like we do in lymphoma, like we do in many other diseases, we'll form the backbone of some consensus regimen some time in the next few years, but we just don't have enough data to really say that at this point.

Andrew Schorr:
Dr. Berenson, so you have strong opinions, and I know you have arguments with the other doctors in the field. Would you agree with what Dr. Lonial said that we still need yet some more definitive trials, or where are we? It looks like some of the data presented at ASH, like for instance this VMP, the VISTA trial, a phase-III trial, I think it was 1600 patients, that seemed to be a pretty rigorous trial.

Dr. Berenson:
Yes, I would agree with you. I think that was a very well run, very well designed trial. I personally use Velcade at a lower dose and use the melphalan on a four-week schedule with a lower dose and give the Velcade only four days a month because I do believe in our phase-II trial, which we presented at ASH over the weekend. We see less neuropathy and a better tolerated regimen, but I think in general the combinations of these newer agents with the tried and true is very important. One of the problems with myeloma is its rarity. Compared to breast, prostate, and lung, this is a relatively uncommon cancer, so the ability to conduct large, randomized trials quickly is not so easy, and in addition differences that are said to be really monumental and important in breast cancer, for example, the role of chemotherapy up front in which the difference is truly in terms of absolute percentage advantages are in the single digits. In myeloma we have to show bigger differences because we can't do these giant trials. I would say, however, really

importantly for patients, don't give up the ship if what you try the first time doesn't work. I really believe that heartily. As I like to quote my daughter's principal at the school, he was talking about education, "There's a smorgasbord of new opportunities." Boy is that ever true in myeloma. So, I really want patients to get the message that this is a chronic disease, and there is really a rare patient that if you do get therapy and it doesn't work one way that you won't try something else and it will work great and be well tolerated. There are just so many options today. That's really the positive message.

Andrew Schorr:
It sure is. Brian Durie, so there you chair the Medical Advisory Board of the International Myeloma Foundation, and I'll give out that hotline number in a minute because what a wonderful service you provide for people one-to-one. Do you think we're moving; Sagar said, we've got a little ways to go for a consensus yet, but boy we have a lot to talk about, but for those of us, you know, we can say it's like; I always feel like Rodney King, you know it was the day after the riots in Los Angeles; can't you all get along? So, that's really what we want. We want this clarity. Do you see it coming some day soon?

Dr. Durie:
Absolutely. I think that we're getting closer, and it's just a matter of time. I think it's good news. I think there are lots of options, but we are limited by the fact that the outcome that we're looking for is a long outcome. We're expecting patients with myeloma to live for 10 years, to live maybe 15 or 20 years. So, you can't know if these new regimens are going to do that kind of a job for many years to come, but we have some very good hallmarks right now. For example, the IFM presented their transplant followup from their 99 trial, so that a study that was started in the late 1990s, and they have a 7-year survival in the 80-85% range so that in these single and double transplant protocols, in excess of 80% of their patients are doing well at seven years. Now, with the novel agents, we have patients doing well at two years, three years, and four years, but what we don't know is without transplant are those patients going to continue well at seven years, 10 year, and beyond 10 years? It's just going to take us time to see what will be the benefit with these novel agents with and without transplant. It may be that the answer will be novel agents plus maybe one transplant or maybe some new vaccine that we come up with, but it's going to take time to know so that the options are there. The advice is so important, and one of the things that I feel strongly about for the International Myeloma Foundation is that we can try to help people sort through what might be best for each one of them depending on their situation. Sagar Lonial mentioned that if you have abnormal chromosomes or some poor risk features, it may be that one option is better for you versus others maybe including Velcade as part of the combination.

Within all of this, we need to balance the short term benefit with the toxicity and expectation of long-term benefit, so good news, but it's going to take still time to sort out.

Treatment Considerations for Older Patients

Andrew Schorr:
Okay. My friends in the audience are calling, so we're going to start with some calls, gentlemen, and aim them at you, and whoever wants to take them. I'll aim it at somebody, but if someone else wants to chime in that's fine too.

I want to give the number for the International Myeloma Foundation, the hot line, because obviously you say what does this mean to me? Now, you're going to discuss that with your doctor, maybe you're going to get a second opinion, but use them as a resource too. Here's the number if you don't already know it: 1-800-452-CURE (1-800-452-2873). They're in the Los Angeles area, so think Pacific time when they're at work. Give them a call as well.

Here is a question from Carol. Carol, you're joining us from somewhere in New Jersey, and you're on the air. Where are you exactly, Carol?

Caller:
I'm in Cape May.

Andrew Schorr:
That sounds nice. I hope the weather isn't too bad there down on the water. You're living with multiple myeloma yourself?

Caller:
I'm a smoldering myeloma patient.

Andrew Schorr:
Smoldering is good. What's your question?

Caller:
My question is, just a few minutes ago, if I heard correctly, a completely sort of opposite view given by Dr. Berenson and Dr. Durie as far as you're approaching age 65 and how these treatment decisions should be made for patients approaching that cutoff age. Since I'm almost approaching 65, I'm very active, you know that's going to have a bearing on how I approach things and how I approach talking with my doctor.

Dr. Berenson:

I would comment that is that, and Brian and I certainly agree on, is that the data from VISTA was robust and that the melphalan/Velcade combination looks like one that can be given to older folks. The average age in that trial is 71, and I am certainly a big advocate of that combination up front, so I heartily agree with Brian that the thalidomide combinations in the older population are not well tolerated, and I'm certainly not using those up front except rarely, for example, in patients who require radiation in which there can be devastating consequences from Velcade in the setting of central radiation, so I think Brian and I actually agree on this. I don't know Brian, if you want to comment further.

Dr. Durie:
Right, well I think that the 65 cutoff is obviously arbitrary, and I think that for example a case could be made if for example the prognostic factors were good, normal chromosomes, and you're in excellent shape, and upfront induction of what we call front-line therapy with perhaps a Velcade combination followed by an autologous transplant might be excellent, even although you've crossed that magic number of 65. So, this is one of the things that you need to discuss on an individual basis with your physician, but on average, we do all get older and over the age of 65 you're more likely to have some heart problems or lung problems or kidney problems where on average it might not be quite as easy for you to go through the transplant, and the beauty of the available options right now is that we have excellent treatments. Jim mentioned that perhaps reducing the dosage slightly on the VMP regimen could make it a little more tolerable and a very excellent synergistic regimen. I hope that helps.

Andrew Schorr:
Thank you. Carol, my dad was 92 and still practicing law, and I think he looked about 75, so there are other factors that come into play and the other conditions some people may tend to have 65 or older, but it sounds like you're doing well, so that's the discussion. You can call the hotline at the International Myeloma Foundation 1-800-452-CURE or also obviously discuss it with your doctor or even seek a second opinion too in that you're smoldering now.

Determining a Treatment Course for the Newly Diagnosed

Andrew Schorr:
Let's take another call. This one is from Henry. Henry, you're in the south up the road from Dr. Lonial in Georgia. You're in South Carolina?

Caller:
That's correct.

Andrew Schorr:

Where are you, sir?

Caller:
I'm in Charleston.

Andrew Schorr:
I love Charleston. Spoleto Festival, right?

Caller:
Yes, we love it too.

Andrew Schorr:
Okay, what's your question, Henry?

Caller:
Okay, Wednesday of this week, December 12th, I was diagnosed with multiple myeloma. I'm 62 years old. The information in mind, I'm stating it from a layman's perspective of course, but he said I had 15-20% of the issue, and you would know and understand what that meant, and my blood cells were described as being larger-than-normal red blood cells and some of them sticking together, and that's of course what moved to the diagnosis and then with the bone marrow exam.

My question is, my hematologist oncologist is recommending that is use the Revlimid with the dexamethasone by mouth or I can take it intravenously coming to his office. Of course, there is a considerable difference in the price, but that's not the big question. My question is, what do I do?

Andrew Schorr:
Okay, now let me make a couple of comments. We're going to go to another southerner there first, Dr. Lonial, because he's closest to you, but what I would comment is first of all for all of our questioners, obviously it's impossible for us, not me but our doctors, to practice medicine over the internet, so obviously you're going to have a discussion with your doctor, and I would recommend, I'm just going to tell you were I'm coming from, is I think it's great to get a second opinion in a fast moving field that we've been describing today with new very powerful data. For instance, would it be that combination, would it be the results of this trial with Velcade and the VMP trial, does that have any impact on you? What does it mean?

Dr. Lonial, so for someone just diagnosed a couple of days ago and with this sort of late-breaking news, how would you recommend Henry look before he leaps, if you will?

Dr. Lonial:

I think it's a real challenge, and even as you hear from the three of us on the call, there are often differences of opinion, and I think it doesn't necessarily mean that one of us is right and the other two are wrong. I think it just means that there are lots of different ways to approach this. So, I think that there are a number of factors that go into this. The first question that I think of when I hear at least part of your story is, do you even need treatment right now? Is there something in there that says this is symptomatic myeloma as opposed to having picked up an M protein very early on in the disease course, in which case we would want to just observe it for a period of time to see how it does, and there are a lot of factors that go into making that decision. It's a clinical decision. It's one that you make with the patient in front of you and not necessarily one, as Andrew mentioned, that you can make over the phone or over the internet. I think that our approaches in terms of how to decide which regimen is best for a given patient depends on how far the patient has to travel, what kind of risk factors they have, with what level of aggressiveness their disease presented, age, comorbid illness, and all sorts of other things go into that decision about whether you're going to use Revlimid, as your doctor is suggesting, or Velcade, which is also what your doctor suggested, or whether it would be VTD, Velcade with thalidomide and dexamethasone, or RVD, Velcade with Revlimid and dexamethasone. There are a lot of different issues that I think go into it, and I agree with Andrew also in the sense that I think it makes a lot of sense to potentially get a second opinion because there's not any downside; I mean, when I see patients for the first time, if they want to go for a second opinion, I encourage them to do that as well because I think you want to make sure you hear information from as many different people as you can before you embark down the road of treatment.

Andrew Schorr:
Hopefully that helps you Henry. Good luck to you. I'll just tell you, now my disease has been different, so I don't want to make too many parallels, but chronic lymphocytic leukemia, I had never heard of it when I got it, and in that particular case it was sort of smoldering for a while like Carol was saying earlier, and so I actually didn't have treatment for a very extended time, and when I did, by the way, I was in a phase-II trial, so have part of your discussion be based on the results of these trials, is there something that you would offer me that makes sense, and second of all is there anything in research that may be should be discussed as a possible treatment option too. Like you heard, there is earlier data now with Revlimid and Velcade used together. Does that make sense? Maybe Dr. Berenson would say no yet while toxicities etc that's being investigated, but the point is that's part of the discussion too. That's just the counsel I would give you as somebody who has been down the road of treatments with something I had never heard of before.

Andrew Schorr:

I want to get to some e-mail questions, and we'll fire them off to our west coast doctors too. This is from Barbara from Richmond, Virginia. She says, 'Would you recommend a delay of a stem cell transplant if I'm asymptomatic and my M protein level is 5%? I'm currently taking dex and Revlimid, and I was diagnosed in September.'

Let's go with Dr. Durie, since you're involved in transplants some. What about whether she delays or not? Any thought on that just generally?

Dr. Durie:
Sure. I think that it's very reasonable, and I think that this is obviously a common question. If you're in remission, and you're doing well, it's hard to look at doing a significant procedure like an autologous stem cell transplant, and so the compromise position, which I think is particularly helpful on the Revlimid low-dose dex, is to harvest the stem cells and to save them so that you do have them available for the future, and that is actually what were doing in an upcoming Southwest Oncology Group trial where after four cycles of Revlimid and dex, we are harvesting the stem cells and then having patients continue with Revlimid and dexamethasone. As we touched on earlier, I think a particularly important part about the Revlimid and dex is that you certainly can stay on it, and the level of benefit does improved and increase over time, and so there's definitely and opportunity to stay on that, and then if you have your stem cells, those can be available for a transplant later on, so that would be the way that I would look at it.

Are There Dietary Supplements for Fighting Multiple Myeloma and Helping with Side Effects?

Andrew Schorr:
Thank you. Okay, Jim Berenson, any patient, and I'm sure you get this question a hundred times a day, wonders about what else they can do themselves, and we got this e-mail from Heather from Indianapolis. She says she's a nursing student, and she has a friend who was just diagnosed with multiple myeloma just a couple of weeks ago, and she wants to support her, and she is wondering is there any evidence of help from supplements or other forms of nutrition that could slow the progression of the disease?

Dr. Berenson:
Obviously there are a number of things that are being tried. I can't tell you we have good clinical trials. I would say in terms of side effects, I certainly would highly advocate alpha lipoic acid in terms of neuropathy. I think that's been very useful for my patients. On of the Millennium MSLs turned me on to that about a year and a half ago, and even one of my patients in this morning who has myeloma, the

husband has diabetic neuropathy and has started benefitting from that use, so in terms of helping with side effects, I think that's been useful. Other little tidbits that will be useful to you guys out there; cramps, believe it or not, dill pickles are extremely useful to overcome cramps, and in fact football players on the sidelines take pickle juice, so try that. You'll like it, and it will help. In terms of directly attacking the myeloma: Well, as you know there have been attempts to use curcumin, and there are people working on that. There are others, and I certainly can't say I have had patients who have had direct benefit from that, but I've seen some pretty amazing responses with some pretty, if you will, alternative things. For example, I have patients who have done work themselves with homeopaths with mushroom extracts that have actually led to responses. I wish I knew what it was in those extracts, but I can't tell you these have been studied in really any large clinical trials.

Andrew Schorr:
Right. I mean, I'm impressed. Let's just say so everybody gets it, not everything is equal. So, for instance, in the different trials we've discussed, some had 40 patients, some had 1600 patients, and in this area of supportive efforts in nutrition, unfortunately we often don't have the big trials. So, that's a discussion that Heather will have with her friend. Is there anything you'd want to call out though, Jim, that you would warn people against where you think it works against the myeloma effective treatment?

Dr. Berenson:
Actually, that's a very good point Andrew. The recent use of vitamin C, which we've shown very active with both melphalan/Cytoxan as well as arsenic actually works against Velcade. Actually, is was Sagar's group who directly showed that vitamin C inactivates Velcade, so we warn our patients who are receiving Velcade avoid vitamin C on the mornings you're receiving Velcade; however, that being said, if there's been several hours away from the Velcade administration, you can take the vitamin C. It's an immediate interaction, and one of the lead scientists at Millennium also believes it's an immediate effect. In addition, our own laboratories recently demonstrated that what I just advocated, the alpha lipoic acid, we also tell patients to avoid it on Velcade days because clearly it inhibits the ability of Velcade to kill myeloma in our laboratory, but again it's when they're in the test tube together, so we believe that if there's a separation there that we will not observe that effect, and we certainly haven't seen any negative impact.

Andrew Schorr:
Folks, this is the active discussion you need to have with your doctor for yourself or Heather for her friend as well.

We're going to go just a little bit over. If we don't get to your question when our doctors have to go, we're going to have a colleague of Dr. Lonial's from the Winship

Comprehensive Cancer Center at Emory with us next week, and I'm gonna just grill him with questions that you send in, and then we'll be posting that next Friday, and that's going to be Dr. Tom Heffner who has a lot of experience in transplant as well as all these drug therapies used by themselves.

The Differences Between "Smoldering" Myeloma and High-Risk Disease

Andrew Schorr:
Dr. Lonial, here's a question we just got in from Jeanne from San Diego, and she says, 'Please define the term "high risk myeloma" that you may have used in this broadcast earlier.' What does "high risk myeloma" mean and maybe what does "smoldering" mean on the other side?

Dr. Lonial:
Yes, so let's start with smoldering first. Smoldering myeloma is by the new definitions is essentially what we call asymptomatic myeloma meaning that you have more than 10% plasma cells in the bone marrow, but you don't have any of the four cardinal symptoms that we use to distinguish symptomatic from asymptomatic myeloma. So, smoldering myeloma is in many ways a sort of pre-myeloma state where similar to the CLL that you were describing, we observe patients, and we don't treat them until they have true symptoms of active disease.

High-risk disease is really again it's a definition that nobody has clearly agreed upon, but if you look historically, patients with elevated beta-2 microglobulins, a marker that we use, patients with deletion of chromosome 13 by routine cytogenetics are considered high-risk disease, patients who have abnormalities of what's called the translocation between chromosomes 4 and 14 are considered high risk; patients who have what's called a removal of part of chromosome 17 are also considered potentially high-risk patients as well, and so there are a number of definitions. The group at Arkansas has identified a 17-gene signature from gene arrays that they use to identify a high-risk subset of patients. So, there are lots of differing opinions about what those definitions are, but I think what that tells us and what that tells me as a practitioner, is that all myelomas are not the same, and just as we've learned that about lymphomas and we've learned that about lung cancers and breast cancers that not all breast cancers are the same, it is probably the same for myeloma, and how many different subsets of myeloma there are probably depend in many ways on which categories you use to create those subdivisions, but I think one of the things that many of us think about at least is that we shouldn't be treating them all the same way.

We really should approach how we treat individual subsets in different ways, and the best example I can give you for that is patients with what's called hyperdiploid myeloma, good risk myeloma. Those patients actually have very good responses to

melphalan-based therapy, and so those are patients who we wouldn't want to necessarily give up standard conventional chemotherapy even if you added new agents like bortezomib or lenalidomide to is, whereas other patients with very high-risk disease, abnormalities of their chromosomes, they don't have good responses at all to melphalan, and many could argue that they shouldn't even be considered for transplant independent of their age, and these are all risk stratification criteria that is an ongoing, moving process as we speak now, and in four or five years we'll probably be closer to saying you have type-A myeloma, you have type-B, you have type-C, and we know that patients with type-A get treated this way, and patients with type-B get treated a different way. Right now we just don't have that capability.

Andrew Schorr:
I will make one point though as a patient advocate, as you listen folks, though, you hear that these gentlemen who really focus almost totally, if not totally, on myeloma, they are slicing and dicing it in many different ways and trying to look for clues as to what to do for you, so if that is not the level of physician you have, somebody maybe more general, I would urge you to at least get a second opinion with a myeloma subspecialist in a time when so much is happening. It's really important, and it could make a critical difference for you and connect you with new regimens much sooner, and also I've always been told, I know my friends at MD Anderson like to say this and many of the major cancer centers, your first shot is your best shot. So, you really want to have a treatment plan for you that makes sense.

Here's a question, and I'll address this to Dr. Durie. This is from California, Tom from Murrieta, California. I'm not quite sure where that is. He says, 'What are the key factors to consider when deciding if and when it's time to go back on a treatment regimen after a treatment-free interval?' So, for instance, I know with Velcade you get to a certain level you can stop all treatment for a while. How do you know when you need to start again, Dr. Durie?

Dr. Durie:
This is obviously a key question for all patients with myeloma because the longer that you can safely stay off treatment, then you have a treatment-free interval, which obviously improves quality of life and you're ability to do the things that you need and want to do. On the other side of the coin, you don't want to delay treatment if you are really developing a medical problem, and so that is the key to the answer to this question. So, we now use not just the amount of the protein and the increase in the protein level, but what are called the "CRAB" criteria. These are the indicators that the myeloma is starting to impact your body. So, "C" is for calcium. Has the blood calcium gone up? "R" is for renal or kidney function. Has the serum creatinine, kidney function test, gone up? "A" is for anemia, and "B" is for bone disease. So, as the disease is being tracked, it's really crucial to see what

is the impact on these parameters, and although in these trials that we've been talking about, these large trials and some smaller trials, relapse is defined as just the increase in the protein level, but actually need for therapy is a little bit different even though the protein level may be creeping up, if one of those other CRAB features has not emerged, it may be possible to monitor closely and delay the time that new treatment needs to be considered.

Obviously, when the protein level is going up, testing needs to be done to make sure that one of these things I mentioned is not happening.

The Role of Transplant in Older Age Groups

Andrew Schorr:
Okay. Thank you for that. So, Jim Berenson, and I want Dr. Lonial to answer this too because I don't know if you guys are going to agree here, and that's fun for me. Derrick from San Diego writes, and he says, 'With the availability of many new drug combinations now, is there a role for transplant in the age group 55-70?' Dr. Berenson, you first.

Dr. Berenson:
Right now, no, I'm not transplanting actually anybody who has myeloma given all these new therapeutic options, and I think that in my experience, there probably is a very small minority of people that do benefit from transplant, and there is probably a small minority who actually make the disease worse not only in terms of toxicity but turn it into an angry gorilla, and I'd say the very vast majority we really have done nothing. So, I remain to be convinced, so I am not a transplant-heavy person at this point. I mean, we'll see what the results are. I, for example, wonder if the patient's on these Velcade combination trials, if they remain on those, would they do just as well as having going through a transplant? We really don't know that answer from the way these trials were designed. One of the questions is whether the newer therapies can replace that, and unfortunately I have to drift off now because I have another teleconference to run on, but I appreciate you're having me here.

Andrew Schorr:
We'll let you go. Thank you Dr. Jim Berenson.

Dr. Berenson:
Thank you very much.

Andrew Schorr:
Thank you. Dr. Lonial, I know you may have to go too. Can you just comment because you still do perform transplants, whether we'll still at an age where we

need to continue that as an option for some people? Dr. Berenson doesn't think so for most people. Where are you with this right now?

Dr. Lonial:
Yes, I think in many ways it depends on the response to the initial induction therapy. So our approach when we use the three-drug combination is that patients who achieve a complete remission with induction therapy, we will collect their stem cells but try and maintain them on therapy and see how long that first remission really lasts, whereas patients who are not in a complete remission early on, we'll collect their stem cells and use the transplant as a mechanism by which to get them into a complete remission. So, I think there is a role for transplant. I think that there is clearly a role for collecting stem cells, and the reason I say that is if we're talking about using multiple therapies as a chronic, long-term effect, then I think we need to make sure that if we run into problems with low blood counts three and four years from now, because of all the therapy we've given, that we have some way out, and that's that the stem cells provide. They give you an opportunity to sort of reset the bone marrow at a point when if you've delivered four or five different kinds of the treatment, and the white count is low, and the platelets are low, and you just can't get effective therapy in, you may be able to do that with a salvage transplant, where you give them normal counts once again. So, I think there are a number of reasons to think about collecting cells, about the role of transplant, and I think the timing of that really depends in many ways on the response patients have to their initial induction.

Andrew Schorr:
Dr. Sagar Lonial, thank you so much for being with us. We're going to let you go. I know the doctors are running around because there's so much conversation going on doctor to doctor now with the news from ASH. Thank you for being with us from the Winship Comprehensive Cancer Center.

We'll continue with Dr. Durie for a minute and warn Dr. Heffner we're going to have a lot of questions for him next week, okay?

Dr. Lonial:
Absolutely. Thank you for the chance to be here.

Andrew Schorr:
Thank you, sir.

In Summary the Outlook is Positive

So, Dr. Durie. Let's pull all this together. We'll try to summarize. You've been listening, and I've been listening, you've been talking, and I've been talking too, to

try to distill this down for people as we just take just a couple of more minutes, and then folks, send in your questions on the web site, and then we're going to pose them to another myeloma expert from Emory, Dr. Tom Heffner, next week.

So, we've talked about these five phase-III trials, like one of the ones from Europe, the Dr. San Miguel trial that he ran with a whole cooperative team from Europe, 1600 patients, and the other trials. It sounds like you have a lot to chew on, and it's important for people to maybe revisit some discussion with their doctor. If it's not broken, don't fix it as far as if they're on successful therapy now, but at least as far as a plan in managing this chronic condition or like Henry called up, and he's wondering how should he start. It's an important discussion now, isn't it?

Dr. Durie:
Absolutely. I think that these new data are exciting, and the outcomes are very good with some of these new combinations. So, if there is the opportunity, and if there's the time, it is particularly important to sit down with your doctor and get a second opinion if necessary to discuss well maybe one of those new combinations could be better for me than perhaps what was being considered up to now because the idea of having these really large trials is to have decisive information where we can say, okay well, this treatment definitely is better than this other one over here, and so this gives security and confidence both to the doctor and to the patient that they are getting the best option for them.

Andrew Schorr:
Also, I think people heard clearly today that you're looking at different types of myeloma among people, so it's really important to know what deck have you been dealt in this myeloma diagnosis, and is there evidence among these trials that in your situation this might be the way to go. Not all myeloma is alike. I think you all have said it several times, it's not one-size-fits-all.

Dr. Durie:
Right, and I think that, we didn't get into it earlier, but one other thing that was happening at ASH was that there were quite a number of mostly posters I would say, but quite important posters; there just was so much data; but these posters were looking at what we call subdata analysis where different investigators were looking at the subgroup who had abnormal kidney function, the subgroup that maybe had a delayed response, the subgroup that had different prognostic factors to try to break out how did the treatment work for those different situation. So, we are slowly but steadily getting more precise information to guide individual patients.

Andrew Schorr:
Yes, and I think there are happy stories to tell.

Dr. Durie:

Yes.

Andrew Schorr:
Whether Carol, your story sounded pretty good, smoldering in Cape May, New Jersey. That's okay. Let's hope that goes on forever. Or Henry, I think you have a lot to look forward to in new treatments. There was the gentleman who was on the NBC Nightly News in that same segment you were on the other day, Brian, the former football player who is doing well.

Dr. Durie:
Yes, absolutely.

Andrew Schorr:
Here in Seattle, where I live, Mel Stottlemeyer, former star and then pitching coach for the New York Yankees is going to be our pitching coach for the Seattle Mariners and doing well. So, as Jim Berenson said there in Los Angeles is, and you've said too, this is a marathon, and increasingly there are lines of therapies that are changing that have more and more effectiveness than every before, so exciting data.

So, Brian, when you go to bed at night, since ASH now, and your head is probably spinning with all the data, and you're part of it, you must feel as a myeloma specialist pretty good.

Dr. Durie:
It's a wonderful time to have these options available to think about and to discuss with patients because it's so positive. We can be planning to use this combination that we know can work well, but we're not closing the door to this other combination, which we have just heard about, which could be used later. So, an important concept right now is this notion of sequential therapy where one treatment can work for several years then some CRAB features develop, some relapse occurs, and then you can use another combination, and so it's very, very important for both the patient and the physician to be planning for the long term. You don't want to be closing doors. You don't want to be getting toxicity that could be troublesome to you in the longer term. Avoid neuropathy. Avoid other problems, and just do what's necessary to get the job done without putting yourself at risk.

So, yes, a lot of very, very positive ideas bouncing around in your brain right now.

Andrew Schorr:
That's good news. Also, remember that Brian's organization, if you don't personally have a relationship with is, is the International Myeloma Foundation. Here's their number again to begin to talk about what resources, what suggestions they would

make. If you're not connected with a myeloma subspecialist, they have of course the long list. Here's their phone number again, 1-800-452-CURE (1-800-452-2873).

Dr. Durie:
And perhaps I can also mention the web site, which is www.myeloma.org because our team was at ASH, and we were interviewing some of these key presenters of those trials that we've been talking about, and those interviews are now up on the web site, so Mike Katz and our staff are working hard to accomplish this, so this could be a helpful resource for you.

Andrew Schorr:
Right, I love your staff, and Mike is the most devoted guy I know. Good for you, Mike.

One last thing is, with all this happening, and that phone number 1-800-452-CURE, so are we closer to a cure doctor because that's really what people want.

Dr. Durie:
Absolutely, ever closer. I think that the step that we're at right now is chronic. Chronic is definitely here for a substantial number of patients with myeloma, where it used to be rare for patients to be treated for five years and then 10 years, but now there are patients 15 years and 20 years out. There was just recently a reunion in Little Rock where they had 10-year survivors, and this was an incredible experience where apparently somewhere around 10% of the 10-year survivors were able to go to this even, which was between 30 and 40 people, so there are several hundred patients who have undergone therapy there who are in this "over the 10-year" mark. So, it's just very, very good.

Andrew Schorr:
It sure is. We're going to go. We've gone longer. Thanks for sticking with us Dr. Durie.

Dr. Durie:
No problem.

Andrew Schorr:
Thank you all our listeners. That was Dr. Brian Durie who is of course Chairman of the International Myeloma Foundation and a multiple myeloma specialist at the Cedars-Sinai Comprehensive Cancer Center in Los Angeles. We had another Los Angeleno, Dr. James Berenson, who was with us, President and Chief Executive Officer of the Institute for Myeloma and Bone Cancer Research, and we had with us Dr. Sagar Lonial, who is a myeloma specialist at the Winship Comprehensive Cancer Center of Emory University in Atlanta.

We'll post another program a week from today with Dr. Tom Heffner from Winship at Emory, and send in those questions and take a look at all our replays. We'll post the replay of this. Listen to it, read it, and thank you for joining us. As always, knowledge can be the best medicine of all. I'm Andrew Schorr. Have a great day.