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State-of-the-Art Therapies for Multiple Myeloma

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Una Wilson

Hosted By Andrew Schorr

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Introduction

Andrew Schorr:

Hello and welcome once again to Patient Power, brought to you by the Seattle Cancer Care Alliance. I'm Andrew Schorr. I'm delighted you could be with us once again as we connect you with a leading cancer expert from the SCCA and also an inspiring patient. Today we're going to talk about the latest advances in the treatment of multiple myeloma, and there certainly have been some, and I'm really excited about it for you. First, what I'd like to do is connect you with someone who I think is really the example of a powerful patient, Una Wilson.

Una, I know you work for the City of Seattle as a software developer. What happened last February? What began to happen to you that then took you on a journey where you became a multiple myeloma patient?

Una:

I went on a backpacking trip early last year. I hurt my back along the way. It was minor, went away, but the back pain persisted, and I went to my doctor looking for advice. Went through some physical therapy and that didn't cure things. Doctor ended up with a kidney specialist. They thought maybe where the pain was it was something to do with that, and then blood and urine tests revealed that there was more to it than that and the suspicion of myeloma came into it. And finally it was confirmed by an oncologist in June of 2007 that I had multiple myeloma.

Andrew Schorr:

So there you are, you're diagnosed with something you really had never heard of before. It must have been terrifying.

Una's Story of Being Diagnosed with Multiple Myeloma

Una:

It was overwhelming. When I knew the tests were happening I did a little bit of research, but again didn't think that it would apply to me. From all the statistics it was something that older people were inclined to get. At that point I was 47 years old, and I thought if anything I had indolent myeloma, but I didn't expect to have full-blown, active myeloma.

Andrew Schorr:

So you are a computer person. You get on the internet, and what did that tell you and where did that lead you as far as a myeloma specialist?

Una:

Well, living here in Seattle as soon as I started doing some research it seemed obvious to me that the Seattle Cancer Care Alliance was the place for me to go because it had specialized and done some groundbreaking work with blood-related diseases in the past with cancers. So I focused my search then on the doctor who were there and who specialized on myeloma, and that led me to Dr. Bensinger. He's been very active in groups that are passing on information about myeloma, and I knew that this was the place for me. So I e-mailed Dr. Bensinger and gave him a brief overview and said that I thought I was probably a candidate for research or a clinical trial and hoped that he had something available that I could participate in.

Andrew Schorr:

And we're going to meet Dr. Bensinger in a minute, but you did meet him shortly thereafter and it was appropriate for you to be in a clinical trial combining various agents, all that could be even more effective maybe used together. How has it worked out for?

Una:

It worked out really well. I was on Velcade, dexamethasone and Cytosan for nine weeks, and after the first three weeks when my levels were tested I had decreased by 75 percent in the M-protein counts. So I knew I was on the right path and I was very confident that I was getting the best of treatment and the best of places. And it was working.

Andrew Schorr:

What is your live like today now, almost a year after this initial back pain?

Una:

I'm very fortunate to be asymptomatic. My back pain has healed, and I'm through the initial therapy. I harvested my stem cells just to have them there, and now I'm on a course where I'm just taking daily Revlimid three weeks out of four, and my quality of life is just fine. I've resumed most of my normal activities. I'm just a bit careful as far as bone fractures, so I'm inclined to be cautious maybe about lifting, those types of things. But other than that, life goes on just fine.

Andrew Schorr:

All right. And you continue to work and lead a normal life.

Una:

I certainly do.

Treatment Improvements for Patients with Multiple Myeloma

Andrew Schorr:

We will come back to you with maybe some advice to people about how to be a proactive patient. But let's meet your doctor. That's Dr. William Bensinger. He is a multiple myeloma specialist. He's a medical oncologist for the Seattle Cancer Care Alliance. He has a long history in the research and treatment of this illness, and he's also at the Fred Hutchinson Cancer Research Center.

Dr. Bensinger, I have a sense that things are changing in myeloma. How would you describe it, and are you encouraged?

Dr. Bensinger:

Yes. I would say that the treatment and outlook for patients with multiple myeloma has improved enormously in the past ten years. We have many new active agents that previously were unavailable for the treatment of this disease. These new drugs have been combined successfully with some of the more traditional drugs, and we're seeing levels of response that formerly were unobserved prior to the development of these drugs. And as a result of this, patients with myeloma are living longer and really doing much better than they were able to do formerly.

Andrew Schorr:

Okay. Give us a sense of what you've got that's new. And I know there was the recent meeting of the American Society of Hematology meeting in Atlanta and there were phase III trials presented that had studied thousands of patients. Particularly in Europe I know there was a big trial. What came out of that specifically that maybe is starting to change the face of treatment?

What are the Newest Available Drugs?

Dr. Bensinger:

Well, there are several new drugs. The oldest of course is thalidomide, which has been around approximately ten years, but additionally we have bortezomib, and that's been around for probably six or seven years ago. And then a second generation, IMiD, after thalidomide, which is lenalidomide. And these drugs all have been shown to be very active in myeloma, and they're now being combined with several new types of combinations. At ASH this year there were two I think important studies, actually multiple studies but two of the more important ones for patients who were potential transplant candidates, was a large French trial that compared the traditional regimen, V-A-D or VAD, which is vincristine, adriamycin, dexamethasone, with a combination of bortezomib and dexamethasone also referred to as Velcade dexamethasone.

This trial had more than 400 patients in it, and it clearly showed that major responses, which they defined in the study as a 90 percent reduction in monoclonal protein or greater, we also call this a very good PR, that the induction with the Velcade dexamethasone combination produced major responses in 47 percent of patients compared to only 19 percent with VAD. The other important finding was that after transplant, after undergoing autologous stem cell transplant, these responses were upgraded in both arms. The Velcade dexamethasone group increased their 90 percent response rate from 47 percent to 72 percent, and the VAD group increased from 19 percent to 51 percent.

Now, these are only responses, and the bottom line on all these studies is do these translate into improvements in survival and keeping the disease at bay, and we won't know that for probably a couple of more years.

The other study which was also I thought quite interesting was an Italian study that actually compared thalidomide dexamethasone, which is one of the most widely used regimens for induction, and that was compared with the same thalidomide dexamethasone but adding in bortezomib or Velcade. So it was a three-drug combination compared to the two-drug combination. And that combination showed again much higher very good partial response rate, 90 percent reduction or better, 60 percent compared to 27 percent. And then also after transplant both of those groups experienced an improvement in their very good PR rate to 77 and 54 percent. Again, we don't have survival data, but it looks very encouraging that we're getting most of the patients with this treatment into a major response with these therapies.

Role of Transplants and Drug Therapy Combinations

Andrew Schorr:

Now, there's a debate raging a little bit, at least in some quarters among myeloma specialists, about what is the role of transplant as you have more drug therapies and more drug combinations. Now, there at Fred Hutchinson, Seattle Cancer Care Alliance, you've been pioneers in transplant. What's your feeling about it?

Dr. Bensinger:

Well, I think that all these new therapies present a moving target. We're improving treatment, improving response rates. We believe all these things are going to translate into improvement in survival. It remains to be seen of course whether an autologous transplant can add additional value to that treatment. I would say that the preliminary results suggest that certainly if you measure just response rates there will be improvements with that. However, it is certainly something that remains to be proven.

One thing I try to underscore to all of my patients, even the patients who don't want to go on to transplant at this time, is to store their stem cells. If you do it early on you've got good quality stem cells. You've preserved a future transplant option even if you don't want

to do it up front. And there are data that suggests that a transplant later on in the course of the disease adds significant value. So even if you're not going to transplant you should seriously consider storing your stem cells.

Andrew Schorr:

And that's what Una did, as she mentioned a couple of minutes ago.

So Una was in trials. She was in nine weeks with one combination and then nine weeks with another and then now Revlimid maintenance. Help us understand in the trial setting what you're doing now with these combinations to try to get even better results.

Dr. Bensinger:

Well, as I mentioned, we've got several new classes of drugs, and now we're combining them with some of the more traditional agents such as cyclophosphamide and dexamethasone, which are the older standby drugs, which were active in myeloma but less active than one would hope. With these new combinations we're really evaluating what the role of these various combinations are in the outcomes for patient with myeloma. And fortunately Una was eligible for a new trial we were participating in with several other centers looking at four of the more active drugs that we have for the treatment of multiple myeloma.

Andrew Schorr:

Okay. So you combine drugs in new ways, and then also you're looking at what do you use when, right? Which comes first, which comes second, how long you do these different cycles, if you will.

Dr. Bensinger:

That's correct, yes. We're still learning about the best way to use these drugs, and I would say we don't know the best way at this time. It's still a learning curve, but I think the data already show that improvements have been made.

Andrew Schorr:

So is this a whole new ball game in myeloma now?

Dr. Bensinger:

I think it has opened up the treatment options dramatically for patients, so there is a lot of enthusiasm on all sides about the future for this disease.

Should Multiple Myeloma Patients get a Second Opinion?

Andrew Schorr:

So then that leads me to my next question. Many people see a community oncologist who deals with breast cancer and colon cancer and prostate cancer, and somewhere down the line is multiple myeloma. If things are changing and if a center like yours has trials which could be tomorrow's medicine, we don't know yet, should they have a consultation with someone like you? Una chose you as her doctor and she entered a trial, but other people might come for a second opinion, whether it's you or somebody who lives in another part of the country or the world. What would you recommend given the landscape is changing?

Dr. Bensinger:

I do think it's very important that patients with newly diagnosed myeloma consider a second opinion. And the reason is that this is not that common a disease. Despite the increased awareness of the disease in the community and among physicians, this is still a relatively rare disease. There's only about 17,000 new cases in the US. It's only one percent of all cancers and only ten percent of all blood cancers. And so it's a relatively uncommon disease, and I think there's so much new information out there that even practicing oncologists can't always keep up with the new information.

In addition, they should be made aware or least the patient should be made aware of possible trials that are available to them. That's how we've made all the progress in the treatment of this disease, is through clinical trials. So I strongly encourage patients if there is a trial that they are eligible for and that's available to them that they consider enrolling in such a trial.

Andrew Schorr:

Now, people living with multiple myeloma may be, either from the cancer itself or from some of the treatments over the years had affects on their bones, and so there have been various medications for that and other side effects. Where are we with the management of side effects for a myeloma patients now?

Dr. Bensinger:

Well, certainly the availability of a class of drugs known as bisphosphonates has been a major advance in myeloma. Prior to their advent, which was 12 to 15 years ago, bone disease was a major source of morbidity for patients with multiple myeloma, bone pain, bone fractures, high blood calcium levels really plagued the treatment of patients with myeloma. The drugs bisphosphonates, of which there are two main ones approved for myeloma, that is Aredia and Zometa, these drugs have remarkably reduced bone complications of the disease. They're not totally without side effects, but there is a small percentage of patients, very small percent, that develop problems with what's called ONJ or osteonecrosis of the jaw, and this is the type of bone resorption that can occur in the jaw. It isn't clear what the direct cause of it is, but it has been associated with bisphosphonate use.

Nevertheless, I would say this complications, which can range from three or four percent to perhaps eight or nine percent, should not prevent a patient from going on bisphosphonates because the benefits in terms of prevention of fractures and bone disease are much outweighed by this uncommon complication.

Side Effects of New Drug Therapies

Andrew Schorr:

Dr. Bensinger, one of the other side effects with some of these powerful drugs that you have, one side effect has traditionally been some neuropathy, some nerve issues. Where do we stand with that, controlling that? And what would you say about the importance of current myeloma patients who may be on some of these drugs having an active dialogue

with their doctor and nurse?

Dr. Bensinger:

Well, neuropathy certainly is one of the unfortunate side effects of some of these drugs. Bortezomib and thalidomide are both associated with neuropathy. And when they're combined it appears to be a higher risk of developing neuropathy. I think it's very important for a patient to be active, a proactive voice to their doctor or nurse what their symptoms, side effects are as they're on treatment, and if appropriate adjustments in the schedule are made you can avoid serious neuropathy.

Andrew Schorr:

Okay. I want to go back to Una and just ask some questions of her.

Una, so you really are the model of a proactive patient. What would you say to people so that they get the best care?

Una:

I think for me, you know, I was starting out six months ago knowing nothing. I've been able to tap into resources, and there are just an enormous amount of resources out there so that you can become informed, and by being informed the benefits are twofold. It helps you understand your treatment and be a part of the process. And it also, for me mentally, it also helped my mental well-being because I'm so encouraged by all of the research that's being done, by all of the progress that's being made, and I have great hope for the future from that.

Andrew Schorr:

Yes, we've been listening as we talked with Dr. Bensinger and it sounds good to me. Let's go back to him and fire some e-mail questions to him.

Dr. Bensinger we've gotten some e-mail questions in from people. Let's see. This was is from Simon in Raleigh, North Carolina, and he writes in, "My father, who is in his 70s, was diagnosed with multiple myeloma. A biopsy of his right thigh showed amyloids as well. What is the optimal treatment for curbing amyloidosis in the presence of myeloma? "

Dr. Bensinger:

Well, the very best way to control amyloidosis is to control the myeloma. Amyloidosis is a poorly understood deposition disease, but we believe it probably is a result of abnormal breakdown in processing of the abnormal proteins produced by myeloma cells. And these abnormal proteins then become deposited in various tissues of the body. They can deposit in some of the major organs and lead to organ dysfunction. And really the only way to stop this deposition process is to shut off production of the abnormal proteins, and the way to do that is to more effectively treat the myeloma.

Therapies and Transplant Options for Older Patients

Andrew Schorr:

Okay. Here's a question we got in from Brandon in Healdsburg, California. He writes, "My father has been diagnosed with multiple myeloma. He's 72 years old. Could he be a candidate for bone marrow transplant at his age? I feel that even though my dad is 72 he's still young, and before this he was very active and healthy."

Dr. Bensinger:

That's a very good question. Generally speaking, the trials that have looked at stem cell transplantation have looked at patients up to age 65 or in some trials up to age 70. Over age 70 there's far less data on the benefits of stem cell transplantation, and I would say as you get older the risks go up as well, the risks of infectious complications or bleeding complications, so I think it's less clear for older patients whether or not a stem cell transplant is of value.

Having said that, I can go back to the ASH data. There were several important studies that were reported at ASH looking at nontransplant options for older patients. There was a very good trial from a Spanish cooperative group, actually it was larger than that, it was an international trial but sponsored originally by a Spanish cooperative group called the VISTA Trial, which added the drug bortezomib to a standard regimen of melphalan and prednisone. And they compared that in a randomized trial to the standard melphalan–prednisone alone, so again three drugs versus two. That trial showed much better response rates, better disease–free survival and better overall survival compared melphalan–prednisone alone.

There was another trial that was actually an update of a trial previously reported at ASCO looking at thalidomide added to melphalan prednisone. Now, what was remarkable about this trial it was a 229 patient trial, and these were just in patients over the age of 75. And, for me, that is remarkable to have a trial where everyone is over 75. The median age of patients in this trial was 79 years. They again were randomized to a combination of melphalan–prednisone–thalidomide, but compared to melphalan–prednisone alone. And again that trial showed higher response rates, better disease–free survival and improved overall survival of the triple combination compared to melphalan–prednisone alone. So I think we have new standards now for nontransplant therapies for older patients.

Andrew Schorr:

Now Una is just 48 and she was in trial and had drug therapy. She hasn't had transplant at this time. And you're mentioning drug therapies also for older people. Are we at the place now though where with the older patients they can expect aggressive treatment, if you will, just as much as anyone, that all you have to offer can be brought to bear for them?

Dr. Bensinger:

Well, I think that we have, I wouldn't say more aggressive. We have new therapies for older patients that clearly improve outcomes for these patients. Where formerly they were relegated to our standard of care, which was melphalan–prednisone, which is a 30–year–old

therapy and nothing was shown to be any better, now with these new triplet combinations we can expect much better outcomes for these patients.

Can Patients Reduce Their Risk for Developing Multiple Myeloma?

Andrew Schorr:

Where are we headed now, Dr. Bensinger? You're at a research organization too as well as you see lots of patients. Where are we headed with this, and what are we learning about the disease? What's the Holy Grail of what you're trying to figure out that could be could make a huge difference?

Dr. Bensinger:

Ooh, that's a very tall question. I can say we're continuing to make progress with these new drug combinations. We're continuing to evaluate the role of transplants, both autologous stem cell transplants but also transplants from donors, allogeneic stem cell transplants, which also I believe have a place in the management of patients with myeloma.

Andrew Schorr:

Now, one last e-mail question. Jennifer from Atlanta, Georgia wrote in, "Is there anything a person can do to reduce the risk of developing myeloma?"

Dr. Bensinger:

Well, that's a very good question but unfortunately we don't really know the cause of myeloma, and so without knowing what the cause is we're really unable to define any way that a patient or a person could avoid developing this disease.

Andrew Schorr:

Now, I know that one signal to me that the face of myeloma is changing and I know it varies by patient for sure, but as you know here in Seattle the new pitching coach for the Seattle Mariners is going to be Mel Stottlemyre who's been living with myeloma for a while. He has great baseball expertise, and I think it's a tremendous vote of confidence that the Mariners say, you're our guy for a rigorous schedule and Mel Stottlemyre says, Yes, I'm living with myeloma, and I feel up to it.

Dr. Bensinger:

That's really quite remarkable.

Andrew Schorr:

Yeah, I really think it's neat. So you're encouraged. I want to go back to Una.

So Una, I want to hear what you feel about the future. What's your outlook? You're just 48, diagnosed with something you never heard of. Got connected with a guy like Dr. Bensinger, a wonderful specialist at the Seattle Cancer Care Alliance. How do you feel about your future?

Una:

I am encouraged. There is just so much development and research being done, and, as Dr. Bensinger has just outlined, so many success stories and improvements that have been



made. And we're not there yet, but I'm still confident that with all the work and all the research that's been done with the dedication and the qualified people who are working on this that great things will happen in my lifetime.

Andrew Schorr:

Well, Una, we wish you all the best with your life and good health and hopefully go on many healthy backpack trips with no complications.

Una:

Thank you.

Dr. Bensinger:

Such a great patient.

Andrew Schorr:

Yeah, isn't she?

Dr. William Bensinger, so what people should take away from this is you're encouraged, you have more to work with. It makes sense to consult with a myeloma specialist because there's more to look at, more to talk about and certainly consider whether a clinical trial might be appropriate for you because it could be where medicine is headed.

Dr. Bensinger:

Yes.

Andrew Schorr:

Okay. Yaay, I get an A from the professor. All right.

I'm delighted we can do these webcasts sponsored by the Seattle Cancer Care Alliance. And for those of you who are really interested in the latest connection with cancer specialists, this is what we do every two weeks on the SCCA website Patient Power programs. We welcome your suggestion any time.

On February 13th we're going to do a new program with Dr. Joachim Deeg, and it's going to be on state-of-the-art therapies for another serious condition, myelodysplastic syndrome. So that's February 13th.

And all of our replays are on the Seattle Cancer Care Alliance website.

Dr. William Bensinger from the Seattle Cancer Care Alliance, thank you so much for being with us today.

Dr. Bensinger:

It's a pleasure.

Andrew Schorr:

And, Una, thank you.



Una:

Thank you very much.

Andrew Schorr:

Okay. In Seattle, this is what we do. Andrew Schorr wishing you the best of the health. And remember knowledge can be some of the best medicine of all.

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